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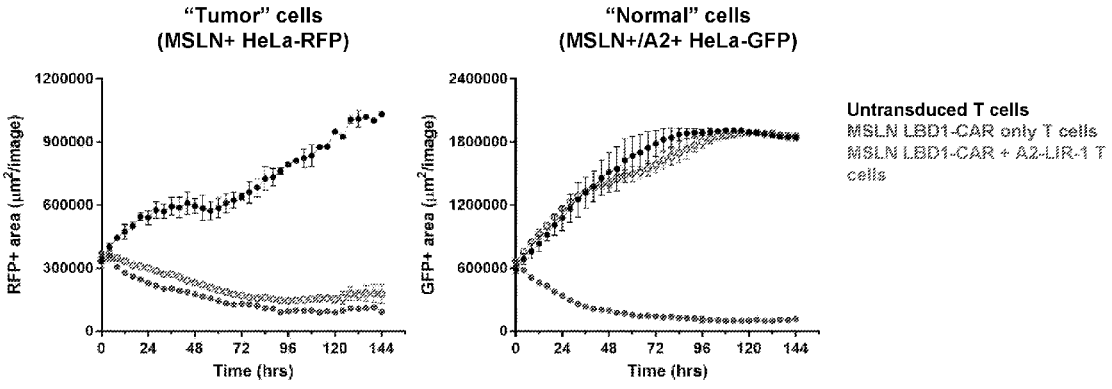
(54) Title: COMPOSITIONS AND METHODS FOR TREATING MESOTHELIN POSITIVE CANCERS

FIG. 15B



(57) Abstract: The disclosure provides immune cells comprising a first activator receptor specific to mesothelin and a second inhibitory receptor specific to a ligand that has been lost in a mesothelin-positive cancer cell, and methods of making and using same for the treatment of cancer.

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[Continued on next page]

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COMPOSITIONS AND METHODS FOR TREATING MESOTHELIN POSITIVE CANCERS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is claims benefit of priority to U.S. Provisional Application No. 63/085,971, filed on September 30, 2020, and U.S. Provisional Application No. 63/068,245, filed on August 20, 2020, each of which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] The disclosure relates to the fields of adoptive cell therapy and cancer therapeutics.

INCORPORATION BY REFERENCE OF SEQUENCE LISTING

[0003] The sequence listing paragraph application contains a Sequence Listing which has been submitted in ASCII format via EFS-WEB and is hereby incorporated by reference in its entirety. Said ASCII copy, created on August 17, 2021 is named A2BI_019_03WO_SeqList_ST25.txt and is 1.08 MB in size.

BACKGROUND

[0004] Cell therapy is a powerful tool for the treatment of various diseases, particularly cancers. In conventional adoptive cell therapies, immune cells are engineered to express specific receptors, for example chimeric antigen receptors (CARs) or T cell receptors (TCRs), which direct the activity of the immune cells to cellular targets via interaction of the receptor with a ligand expressed by the target cell. Identification of suitable target molecules remains challenging, as many targets are expressed in normal tissues. This expression can lead to toxicity when the transplanted cells target normal tissues expressing target molecules. There is thus a need in the art for compositions and methods useful in the treatment of disease, particularly cancers, by adoptive cell therapy.

[0005] Mesothelin (MSLN) was proposed as a cancer target in 1992 (Chang et al. *Cancer Res* 52:181-86), yet there is still no viable therapy that utilizes MSLN. Not only is it expressed on most mesotheliomas but also large subsets of ovarian, cervical, uterine, gastric, pancreatic and lung adenocarcinomas. (Hassan et al. *J Clin Oncol* 34:4171-79) In normal

adults, MSLN is present only in mesothelium, a tissue that itself may be nonessential. Several investigational therapeutics directed at MSLN have been tested; for example, immunotoxin-conjugates, antibody-drug conjugates, bispecific antibodies, CAR-Ts, and a hybrid TCR-scFv.

[0006] All active systemically administered therapeutics have been toxic. Accordingly, there exists a need in the art for compositions and methods related to treatment of MSLN(+) cancers.

SUMMARY

[0007] Provided herein are compositions and methods related to treatment of MSLN(+) cancers. Advantageously, the compositions and methods disclosed herein may exploits loss of heterozygosity (LOH) to address MSLN(+) cancer. The compositions and methods disclosed herein may, in some cases, avoid systemic toxicity to normal tissues by pairing a MSLN-targeted activator receptor with a blocker receptor. Without being bound by theory, the difference in blocker antigen expression in tumor versus. normal tissues caused by LOH at the locus encoding the blocker antigen may confer high selectivity for tumor killing.

[0008] The disclosure provides immune cells comprising: (a) a first receptor, comprising an extracellular ligand binding domain specific to Mesothelin (MSLN); and (b) a second receptor, comprising an extracellular ligand binding domain specific to a non-target antigen lost in a MSLN + cancer cell, wherein the first receptor is an activator receptor responsive to MSLN; and wherein the second receptor is an inhibitory receptor responsive to the non-target antigen.

[0009] In some embodiments of the immune cells of the disclosure, the non-target antigen is lost in the MSLN+ cancer cell through loss of heterozygosity.

[0010] In some embodiments of the immune cells of the disclosure, the extracellular ligand binding domain of the second receptor specifically binds an allelic variant of a major histocompatibility complex (MHC) protein. In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds an allelic variant of an HLA-A, HLA-B, or HLA-C protein. In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*01, HLA-A*02, HLA-A*03, HLA-A*11, HLA-B*07, or HLA-C*07. In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*02. In some embodiments, the extracellular ligand binding domain of the second receptor comprises complementarity determining

regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 6; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of Table 6 or Table 7. In some embodiments, the extracellular ligand binding domain of the second receptor comprises complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 of SEQ ID NOS: 42-47 or of SEQ ID NOS: 48-53; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of SEQ ID NOS: 42-47 or SEQ ID NOS: 48-53. In some embodiments, the extracellular ligand binding domain of the second receptor comprises a polypeptide sequence selected from the polypeptide sequence disclosed in Table 5; or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the extracellular ligand binding domain of the second receptor comprises any one of SEQ ID NOS: 30-41, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0011] In some embodiments of the immune cells of the disclosure, the first receptor is a chimeric antigen receptor (CAR). In some embodiments, the extracellular ligand binding domain of the first receptor comprises complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 2; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the CDRs of Table 2. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a variable heavy (VH) portion comprising a sequence set forth in Table 3 and a variable light (VL) portion comprising a sequence set forth in Table 4; or a sequence having at least 80%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a variable heavy (VH) portion comprising SEQ ID NO: 233 or a sequence having at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% identity thereto, and a variable light (VL) portion comprising SEQ ID NO: 279 or a sequence having 85%, at least 90%, at least 95%, at least 97%, or at least 99% identity thereto. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a sequence selected from the group consisting of SEQ ID NOS: 3-6, 80 and 154-215, or a sequence having at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% identity thereto. In some embodiments, the extracellular ligand binding domain of the first receptor comprises an scFv sequence of SEQ ID NO: 171; or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0012] In some embodiments of the immune cells of the disclosure, the first receptor comprises a hinge domain, a transmembrane domain and an intracellular domain. In some embodiments, the hinge domain comprises a CD8α hinge domain. In some embodiments, the CD8α hinge domain comprises a sequence of SEQ ID NO: 7, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the transmembrane domain comprises a CD28 transmembrane domain. In some embodiments, the CD28 transmembrane domain comprises a sequence of SEQ ID NO: 11, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the intracellular domain comprises a CD28 co-stimulatory domain, a 4-1BB co-stimulatory domain, and a CD3ζ activation domain. In some embodiments, the intracellular domain comprises a sequence of SEQ ID NO: 285, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first receptor comprises a sequence of SEQ ID NO: 303, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0013] In some embodiments of the immune cells of the disclosure, the second receptor comprises a LILRB1 intracellular domain or a functional variant thereof. In some embodiments, the LILRB1 intracellular domain comprises a sequence at least 90%, at least 95%, at least 97%, at least 99%, or is identical to SEQ ID NO: 70. In some embodiments, the second receptor comprises a LILRB1 transmembrane domain or a functional variant thereof. In some embodiments, the LILRB1 transmembrane domain or a functional variant thereof comprises a sequence at least 90%, at least 95%, at least 97%, at least 99% or is identical to SEQ ID NO: 74. In some embodiments, the second receptor comprises a LILRB1 hinge domain or functional variant thereof. In some embodiments, the LILRB1 hinge domain comprises a sequence at least 90%, at least 95%, at least 97%, at least 99% or is identical to SEQ ID NO: 73. In some embodiments, the second receptor comprises a LILRB1 intracellular domain, a LILRB1 transmembrane domain, a LILRB1 hinge domain, a functional variant of any of these, or combinations thereof. In some embodiments, the LILRB1 hinge domain, LILRB1 intracellular domain and LILRB1 transmembrane domain comprises SEQ ID NO: 71 or a sequence at least 90%, at least 95%, at least 97%, at least 99% or is identical to SEQ ID NO: 71. In some embodiments, the second receptor comprises a sequence of SEQ ID NO: 348, or a sequence having at least 90%, at least 95%, at least 97%, or at least 99% identity thereto.

[0014] In some embodiments of the immune cells of the disclosure, the MSLN+ cancer cell is a mesothelioma cancer cell, an ovarian cancer cell, a cervical cancer cell, a colorectal

cancer cell, an esophageal cancer cell, a head and neck cancer cell, a kidney cancer cell, an uterine cancer cell, a gastric cancer cell, a pancreatic cancer cell, a lung cancer cell, a colorectal cancer cell or a cholangiocarcinoma cell, or any cancer cell expressing MSLN. In some embodiments, the MSLN+ cancer cell is a mesothelioma cancer cell, an ovarian cancer cell, a cervical cell, a uterine cancer cell, a gastric cancer cell, a pancreatic cancer cell or a lung adenocarcinoma cell.

[0015] In some embodiments, the MSLN+ cancer cell is an epithelial cancer cell. Epithelial cancers are cancers that originate in the epithelial cells. In some embodiments, the MSLN+ epithelial cancer is a carcinoma.

[0016] In some embodiments of the immune cells of the disclosure, the MSLN+ cancer cell is a MSLN+/HLA-A*02– cancer cell that does not express HLA-A*02. In some embodiments, the MSLN+/HLA-A*02– cancer cell is derived from a MSLN+/HLA-A*02+ cell by loss of heterozygosity at HLA-A leading to loss of HLA-A*02. In some embodiments, the first receptor and the second receptor together specifically activate the immune cell in the presence of the MSLN+/HLA-A*02- cancer cell having loss of heterozygosity. In some embodiments, the first receptor and the second receptor together do not specifically activate the immune cell in the presence of an MSLN+ cell that has not lost HLA-A*02 by loss of heterozygosity.

[0017] In some embodiments of the immune cells of the disclosure, the immune cell is a T cell. In some embodiments, the T cell is a CD8+ CD4- T cell.

[0018] In some embodiments of the immune cells of the disclosure, expression and/or function of a MHC Class I gene has been reduced or eliminated. In some embodiments, the MHC Class I gene is beta-2-microglobulin (B2M). In some embodiments, the immune cells further comprise an interfering RNA, the interfering RNA comprising a sequence complementary to a sequence of a B2M mRNA. In some embodiments, the interfering RNA comprises a sequence selected from the group of sequences set forth in Table 13, or a sequence having at most 1, 2, 3, or 4 substitutions, insertions or deletions relative thereto. In some embodiments, the interfering RNA is capable of inducing RNAi-mediated degradation of the B2M mRNA. In some embodiments, the interfering RNA is a short hairpin RNA (shRNA). In some embodiments, the shRNA comprises: (a) a first sequence, having from 5' end to 3' end a sequence complementary to a sequence of the B2M mRNA; and (b) a second sequence, having from 5' end to 3' end a sequence complementary to the first sequence, wherein the first sequence and the second sequence form the shRNA. In some embodiments, the shRNA is encoded by a sequence comprising a sequence of

GCACTCAAAGCTTGTTAAGATCGAAATCTTAACAAGCTTTGAGTGC (SEQ ID NO: 349) or GTTAACTTCCAATTTACATACCGAAGTATGTAAATTGGAAGTTAAC (SEQ ID NO: 350), or a sequence having at least 80%, at least 90%, or at least 95% identity thereto.

[0019] In some embodiments of the immune cells of the disclosure, expression and/or function of a MHC Class I gene has been reduced or eliminated. In some embodiments, the MHC Class I gene is beta-2-microglobulin (B2M). In some embodiments, the immune cells comprise one or more modifications to a sequence encoding B2M, wherein the one or more modifications reduce the expression and/or eliminate the function of B2M. In some embodiments, the one or more modifications comprise one or more inactivating mutations of the endogenous gene encoding B2M. In some embodiments, the one or more inactivating mutations comprise a deletion, an insertion, a substitution, or a frameshift mutation. In some embodiments, the one or more inactivating mutations are introduced with a nucleic acid guided endonuclease in a complex with at least one guide In some embodiments e nucleic acid (gNA) that specifically targets a sequence of the endogenous gene encoding B2M. In some embodiments, the gNA comprises a sequence selected from the group of sequences set forth in Table 12, or a sequence having at most 1, 2, 3, or 4 substitutions, insertions or deletions relative thereto.

[0020] In some embodiments of the immune cells of the disclosure, expression and/or function of a MHC Class I gene has been reduced or eliminated. In some embodiments, the MHC Class I gene is HLA-A*02. In some embodiments, the immune cells comprise a polynucleotide comprising an interfering RNA, comprising a sequence complementary to a sequence of an HLA-A*02 mRNA. In some embodiments, the interfering RNA is capable of inducing RNA interference (RNAi)-mediated degradation of the HLA-A*02 mRNA. In some embodiments, the interfering RNA is a short hairpin RNA (shRNA) comprising: (a) a first sequence, having from 5' end to 3' end a sequence complementary to a sequence of the HLA-A*02 mRNA; and (b) a second sequence, having from 5' end to 3' end a sequence complementary to the first sequence, wherein the first sequence and the second sequence form the shRNA. In some embodiments, the shRNA comprises a sequence set forth in 14. In some embodiments, the immune cells comprise one or more modifications to a sequence of an endogenous gene encoding HLA-A*02, wherein the one or modifications reduce the expression and/or eliminate the function of HLA-A*02. In some embodiments, the one or more modifications comprise one or more inactivating mutations of the endogenous gene encoding HLA-A*02. In some embodiments, the one or more inactivating mutations are introduced with a nucleic acid guided endonuclease in a complex with at least one guide

nucleic acid (gNA) that specifically targets a sequence of the endogenous gene encoding HLA-A*02. In some embodiments, the gNA comprises a sequence set forth in Table 11.

[0021] In some embodiments of the immune cells of the disclosure, the first receptor comprises a sequence of SEQ ID NO: 164, and the second receptor comprises a sequence of SEQ ID NO: 52, or sequences having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the immune cells comprise an shRNA encoded by a sequence comprising GCACTCAAAGCTTGTTAAGATCGAAATCTTAACAAGCTTTGAGTGC (SEQ ID NO: 349) or GTTAACTTCCAATTTACATACCGAAGTATGTAAATTGGAAGTTAAC (SEQ ID NO: 350) or a sequence having at least 80%, at least 90%, or at least 95% identity thereto. In some embodiments, the first receptor and second receptor are encoded by a single polynucleotide, and wherein the sequences encoding the first and second receptors are separated by a sequence encoding a self-cleaving polypeptide. In some embodiments, the self-cleaving polypeptide comprises a T2A self-cleaving polypeptide comprising a sequence of GSGEGRGSLLTCGDVEENPGP (SEQ ID NO: 351).

[0022] In some embodiments of the immune cells of the disclosure, the immune cells are autologous.

[0023] In some embodiments of the immune cells of the disclosure, the immune cells are allogeneic.

[0024] The disclosure provides a pharmaceutical composition, comprising a therapeutically effective amount of the immune cells of the disclosure. In some embodiments, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier, diluent or excipient.

[0025] The disclosure provides a pharmaceutical composition, comprising a therapeutically effective amount of the immune cells of the disclosure for use as a medicament in the treatment of MSLN+ cancer.

[0026] The disclosure provides a polynucleotide or polynucleotide system, comprising one or more polynucleotides comprising polynucleotide sequences encoding: (a) a first receptor, comprising an extracellular ligand binding domain specific to Mesothelin (MSLN); and (b) a second receptor, comprising an extracellular ligand binding domain specific to a non-target antigen that has been lost in a MSLN+ cancer cell, wherein the first receptor is an activator receptor responsive to MSLN on the MSLN+ cancer cell; and wherein the second receptor is an inhibitory receptor responsive to the non-target antigen.

[0027] In some embodiments of the polynucleotide or polynucleotide system of the disclosure, the polynucleotide or polynucleotide system comprises one or more polynucleotides comprising polynucleotide sequences encoding the first receptor and the second receptor for use in generating the immune cells of the disclosure. In some embodiments, the polynucleotide or polynucleotide system comprises a sequence encoding an shRNA specific to B2M. In some embodiments, the sequences encoding the first receptor, the second receptor and the shRNA specific to B2M are encoded by the same polynucleotide. In some embodiments, (a) the sequence encoding the shRNA specific to B2M comprises GCACTCAAAGCTTGTTAAGATCGAAATCTTAACAAGCTTTGAGTGC (SEQ ID NO: 349) or GTTAACTTCCAATTTACATACCGAAGTATGTAAATTGGAAGTTAAC (SEQ ID NO: 350) or a sequence having at least 80%, at least 90%, or at least 95% identity thereto; (b) the sequence encoding the first receptor comprises a sequence encoding a polypeptide of SEQ ID NO: 303, or a sequence having at least 80%, at least 90%, or at least 95% identity thereto; and (c) the sequence encoding the second receptor comprises a sequence encoding a polypeptide of SEQ ID NO: 348, or a sequence having at least 80%, at least 90%, or at least 95% identity thereto.

[0028] The disclosure provides a vector, comprising the one or more polynucleotides of the disclosure.

[0029] The disclosure provides methods of killing a MSLN+ cancer cell having loss of heterozygosity at an MHC class I locus, comprising administering to the subject an effective amount of the immune cells or pharmaceutical composition of the disclosure.

[0030] The disclosure provides methods of treating MSLN+ cancer in a subject having a MSLN+ tumor having loss of heterozygosity at an MHC class I locus, comprising administering to the subject an effective amount of the immune cells or pharmaceutical composition of the disclosure.

[0031] The disclosure provides methods of treating a cancer in a subject comprising: (a) determining HLA-A genotype or expression of normal cells and a plurality of cancer cells of the subject; (b) optionally, determining the expression of MSLN in a plurality of cancer cells of the subject; and (c) administering to the subject an effective amount of the immune cells or pharmaceutical composition of the disclosure if the normal cells express HLA-A*02 and the plurality of cancer cells do not express HLA-A*02, and the plurality of cancer cells are MSLN-positive.

In some embodiments of the methods of the disclosure, the subject is a heterozygous HLA-A*02 patient with a malignancy that expresses MSLN (MSLN+) and has lost HLA-A*02

expression. In some embodiments, the subject is a heterozygous HLA-A*02 patient with recurrent unresectable or metastatic solid tumors that express MSLN and have lost HLA-A*02 expression. In some embodiments, the cancer comprises
mesothelioma cancer, ovarian cancer, cervical cancer, colorectal cancer, esophageal cancer, head and neck cancer, kidney cancer, uterine cancer, gastric cancer, pancreatic cancer, lung cancer, colorectal cancer, or cholangiocarcinoma. In some embodiments, the cancer comprises mesothelioma, ovarian cancer, cervical cancer, uterine cancer, gastric cancer, pancreatic cancer or lung adenocarcinoma. In some embodiments, the cancer has relapsed in a subject. In some embodiments, the cancer is refractory to one or more prior administered anticancer therapies. In some embodiments, the cancer is metastatic.

[0032] In some embodiments of the methods of the disclosure, the cancer cells comprise MSLN+/HLA-A*02– cancer cells that do not express HLA-A*02. In some embodiments, the MSLN+/HLA-A*02– cancer cells are derived from a MLSN+/HLA-A*02+ cell by loss of heterozygosity at HLA-A leading to loss of HLA-A*02. In some embodiments, the first receptor and the second receptor together specifically activate the immune cell in the presence of the MSLN+/HLA-A*02- cancer cells. In some embodiments, the first receptor and the second receptor together do not specifically activate the immune cell in the presence of a MSLN+ cell that has not lost HLA-A*02.

[0033] In some embodiments of the methods of the disclosure, administration of the immune cells or pharmaceutical composition reduces the size of a tumor in the subject. In some embodiments, the tumor is reduced by about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%. In some embodiments, the tumor is eliminated.

[0034] In some embodiments of the methods of the disclosure, administration of the immune cells or pharmaceutical composition arrests the growth of a tumor in the subject.

[0035] In some embodiments of the methods of the disclosure, administration of the immune cells or pharmaceutical composition reduces the number of tumors in the subject.

[0036] In some embodiments of the methods of the disclosure, administration of the immune cells or pharmaceutical composition results in selective killing of a cancer cell but not a normal cell in the subject. In some embodiments, at least about 60% of the cells killed are cancer cells, about 65% of the cells killed are cancer cells, about 70% of the cells killed are cancer cells, about 75% of the cells killed are cancer cells, about 80% of the cells killed are cancer cells, about 85% of the cells killed are cancer cells, about 90% of the cells killed are

cancer cells, about 95% of the cells killed are cancer cells, or about 100% of the cells killed are cancer cells. In some embodiments, administration of the immune cell or pharmaceutical composition results in the killing of at least about 40%, about 50%, about 60%, about 70%, about 80%, about 90% or all of the cancer cells of the subject.

[0037] In some embodiments of the methods of the disclosure, administration of the immune cell or the pharmaceutical composition results in fewer side effects for the subject than administration of an otherwise equivalent immune cell comprising the first activator receptor but no second inhibitory receptor.

[0038] The disclosure provides methods making a plurality of immune cells, comprising: (a) providing a plurality of immune cells, and (b) transforming the plurality of immune cells with the polynucleotide, polynucleotide system or vector of the disclosure.

[0039] The disclosure provides kits comprising the immune cells or pharmaceutical composition of the disclosure. In some embodiments, the kits further comprise instructions for use.

BRIEF DESCRIPTION OF THE DRAWINGS

[0040] FIG. 1 is a table showing expression of blocker candidate genes from the TCGA database. (*) indicates genes previously identified as being expressed in the mesothelium.

[0041] FIG. 2 is a plot showing Mesothelin (MSLN) expression in normal tissues.

[0042] FIG. 3 is a plot showing the expression of MSLN across TCGA cancers (with tumor and normal samples.) Abbreviations: BLCA (Bladder cancer), BRCA (Breast Cancer), CESC (Cervical squamous cell carcinoma and endocervical adenocarcinoma), CHOL Cholangiocarcinoma), COAD (Colon adenocarcinoma), ESCA (Esophageal carcinoma), GBM (Glioblastoma multiforme), HNSC (Head and Neck squamous cell carcinoma), KICH (Kidney Chromophobe), KIRP (Kidney renal papillary cell carcinoma), LIHC (Liver hepatocellular carcinoma), LUAD (Lung adenocarcinoma), LUSC (Lung squamous cell carcinoma), PAAD (Pancreatic adenocarcinoma), PRAD (Prostate adenocarcinoma), PCPG (Pheochromocytoma and Paraganglioma), READ (Rectum adenocarcinoma), SARC (Sarcoma), SKCM (Skin Cutaneous Melanoma), THCA (Thyroid carcinoma), THYM (Thymoma), STAD (Stomach adenocarcinoma), UCEC (Uterine Corpus Endometrial Carcinoma).

[0043] FIG. 4 is a plot showing MSLN expression in CCLE cell lines.

[0044] FIG. 5 is a plot showing LRRN4 expression in normal tissues.

[0045] FIG. 6 is a plot showing the expression of LRRN4 across TCGA cancers (with tumor and normal samples).

[0046] FIG. 7 is a plot showing the expression of LRRN4 across TCGA tumors.

[0047] FIG. 8 is a plot showing expression of LRRN4 in CCLE cell lines.

[0048] FIG. 9 is a plot showing the distribution of 10 leucine rich repeat (LRR) and Fibronectin Type III domains relative to the transmembrane domain of LRRN4. Most of these domains are likely located on the cell surface.

[0049] FIG. 10A shows that a pMHC HLA-A*02 scFv LIR-1 based inhibitory receptor can inhibit activation of Jurkat cells in *cis* in a cell-free bead based assay.

[0050] FIG. 10B that a pMHC HLA-A*02 scFv LIR-1 based inhibitory receptor can inhibit activation of Jurkat cells by a MSLN scFv CAR using the leukemia cell line K562 as target cells.

[0051] FIG. 11 is a diagram (left) and a chart (right) showing that a pMHC HLA-A*02 scFv LIR-1 based inhibitory receptor can inhibit activation of Jurkat cells, as measured by fold induction of IFNγ, by a MSLN scFv CAR using a pMHC HLA-A*02 scFv LIR-1 based inhibitory receptor and HLA-A*02+ HeLa and SiHa cells as target cells.

[0052] FIG. 12 shows that a pMHC HLA-A*02 scFv LIR-1 based inhibitory receptor inhibits killing by MSLN CAR activators using HLA-A*02+ SiHa cells but not HLA-A*02- SiHa cells.

[0053] FIG. 13 is a diagram of the bioinformatics pipeline used to identify potential inhibitory receptor targets that are lost in cancer cells due to loss of heterozygosity.

[0054] FIG. 14 is a of the bioinformatics pipeline used to identify potential inhibitory receptor targets that are not expressed in cancer cells.

[0055] FIG. 15A is a pair of plots showing that the HLA-A*02 blocker inhibits MSLN CAR activators directed at MSLN, a high-density antigen. Jurkat cells transfected with MSLN LBD1-CAR or MSLN LBD1-CAR & A2-LIR-1 co-cultured with K562 cells expressing either MSLN or MSLN & HLA-A*02 shows blocking of activation by a high-density antigen with A2-LIR-1 blocker only in the presence of HLA-A*02.

[0056] FIG. 15B is a pair of plots showing that the HLA-A*02 blocker inhibits MSLN CAR activators directed at MSLN, a high-density antigen. Killing of endogenous MSLN+ HeLa cells by MSLN LBD1-CAR T cells is blocked in the presence of HLA-A*02 with the A2-LIR-1 blocker.

[0057] FIG. 15C is a pair of plots showing that the HLA-A*02 blocker inhibits MSLN CAR activators directed at MSLN, a high-density antigen. Killing of endogenous MSLN+ HeLa

cells by MSLN LBD2-CAR T cells is shown. The effect of A2-LIR-1 blocker on T cell killing is in part controlled by the activator LBD, suggesting further optimization of the blocker module or pairs of activator/blockers may be required.

[0058] FIG. 16 is a series of plots showing that HLA-A*02 LIR1 inhibitory receptors (PA2.1, mouse and humanized) effectively block killing by T cells expressing MSLN Generation 3 CAR in the presence of HeLa cells that express MSLN and HLA-A*02. Top row: MSLN + HLA-A*02+ HeLa target cells; bottom row: MSLN+ HLA-A*02- HeLa cells (control). The murine SS1 generation 3 CAR (upper right, boxed) provides a better window than the humanized M5 and humanized SS1 CARs.

[0059] FIG. 17 is a series of plots showing that HLA-A*02 LIR1 inhibitory receptors (PA2.1, mouse and humanized) effectively block killing by T cells expressing MSLN Generation 3 CAR in the presence of MSLN+ HLA-A*02+ Capan-2 cells.

[0060] FIG. 18 is a pair of plots that shows that killing of MSLN + HLA-A*02+ HeLa cells (left) or HCT116 wild type (WT) cells that are natively MSLN + HLA-A*02+ by T cells expressing a 2nd generation CAR with a murine SS1 scFv is effectively blocked by an HLA-A*02 scFv LIR1 inhibitory receptor.

[0061] FIG. 19 is a series of fluorescence activated cell sorting (FACS) plots showing the expression of murine SS1 second generation CARs by T cells, with and without co-transduction of an HLA-A*02 scFv LIR-1 blocker.

[0062] FIG. 20A is a plot showing the effect of LIR-1 hinge on the ability of an HLA-A*02 inhibitory receptor to block activation of Jurkat cells by a KRAS TCR. H: hinge, T: transmembrane domain, ICD: intracellular domain, s: short. LIR-1 constructs are described in more detail in FIG. 20B. Humanized PA2.1 and humanized BB7.2 with shorter LIR-1 hinge block similarly to original, longer hinge

[0063] FIG. 20B is a plot and a table showing EC50 shift (+/- HLA-A*02 target cells) for Jurkat cells expressing a KRAS TCR activator and the HLA-A*02 scFv LIR-1 inhibitory receptors shown in the table at bottom (SEQ ID NOs: 352-356).

[0064] FIG. 21A is a plot showing the effect of LIR-1 hinge on the ability of an HLA-A*02 inhibitory receptor to block activation of Jurkat cells by a KRAS TCR. H: hinge, TM: transmembrane domain, ICD: intracellular domain, s: short; tr: truncated. LIR-1 constructs are described in more detail in FIG. 21B. Mouse PA2.1 with slightly longer hinges function similarly to original LIR-1 hinge in T2-Jurkat assay.

[0065] FIG. 21B is a plot and a pair of tables showing EC50 shift (+/- HLA-A*02 target cells) for Jurkat cells expressing a KRAS TCR activator and the HLA-A*02 scFv LIR-1

inhibitory receptors shown in the table at bottom (SEQ ID NOs: 357-361), with lengths shown in the table at left.

[0066] FIG. 22A and FIG. 22B show the Tmod approach to achieve selective cytotoxicity with two targets (Tmod refers to immune cells expressing the combination of activator and inhibitory receptor). FIG. 22A shows the lung (and other vital organs) are surrounded by the MSLN(+) mesothelial lining, creating high risk of on-target, off-tumor toxicity for MSLN-targeted medicines. By selecting patients heterozygous for HLA-A*02 whose tumors have lost this allele via LOH, there is an opportunity to target MSLN-activated CAR-T cells to kill tumor cells specifically and spare normal mesothelium. FIG. 22B shows the molecular composition of MSLN-targeted Tmod constructs (Tmod refers to the paired activator and inhibitory receptors). The two receptors are co-expressed in a single construct and the encoded fusion protein is cleaved in the cell to generate the activator and blocker.

[0067] FIG. 23A, FIG. 23B, FIG. 23C, and FIG. 23D show the isolation and characterization of selective MSLN binders. On-target probe was labeled soluble MSLN (Acro Bio); off-target probe used for counterselection was a mixture of soluble CEA and EGFR proteins. FIG. 23A shows enrichment of IgG library. FIG. 23B shows enrichment of scFv library. FIG. 23C shows surface expression of MSLN CARs (Gen3) in Jurkat cells. Cells were transfected with CAR constructs and stained with Protein L or monomeric soluble MSLN (see Methods). Benchmark and CAR1-6 expression histograms are labeled. PE, phycoerythrin; NA, neutravidin; SA, streptavidin. "On-target NGS" corresponds to the cell populations that are collected and subjected to DNA sequencing to determine enrichment of individual idiotypes. FIG. 23D shows the characterization of MSLN binders in solid-state Jurkat cell assays with MSLN protein attached to the surface (see Hamburger et al., 2020). 62 CAR constructs (Gen3) bearing different scFvs were transiently transfected in Jurkat cells to express CARs and a functional response to surface-bound recombinant human sMSLN (Acro Bio) was assessed after 6 hours. Most resulted in some degree of response.

[0068] FIG. 24A shows the sensitivity of MSLN CARs vs. benchmark CARs M5, SS1 and m912. All constructs were Gen3 except SS1 (Gen2). Jurkat cell dose-response (RLU) was measured to assess the sensitivity in a 6 hour co-culture assay: (1) Titrated MSLN-encoding mRNA was used to transfect HEK293 cells; (2) QIFIKIT (quantitative analysis kit, Agilent) was used to convert flow-cytometry based surface expression to MSLN molecules/cell; and, (3) The molecule/cell sensitivities (EC50) of 6 novel and three benchmark CARs were calculated from fitting the dose-response curves. For those CARs with sensitivities below the limit of detection of the assay, EC50 was reported as <3000 MSLN molecules/cell.

Maximum signal (Emax) for each construct was also noted. Experiments were repeated 1-4 times.

[0069] FIG. 24B shows CAR3 selectivity. An example of MSLN CAR3 selectivity benchmarked against the M5 CAR. Activation of CARs in a Jurkat cell functional assay by MSLN(+) or MSLN(-) cell lines was measured. For MSLN(+) cell lines, variant MSLN(-) versions were generated by MSLN knockout for comparison For more detailed off-target characterization, see FIG. 32B.

[0070] FIG. 25A shows expression of MSLN in human cell lines assessed by staining with MSLN mAb and flow cytometry. K562 displayed some cross-reactivity to the anti-MSLN antibody, although no functional reactivity to CAR3 or M5 benchmark CAR was observed.

[0071] FIG. 25B shows plotted levels of MSLN and A*02 mRNA (CCLE) and protein (QIFIKIT) show correlation. Conversions between protein and mRNA levels were calculated using the standard curves (see Methods for Example 8, *infra*).

[0072] FIG. 26A shows a summary of cell lines used in this study. Quantification of surface densities of MSLN and A*02 in various cancer cell lines, and corresponding reported mRNA levels in normal lung tissue (GTEx). Surface MSLN and A*02 of engineered and wildtype tumor cell lines was quantified using a QIFIKIT (quantitative analysis kit, Agilent). Where cell line HLA-A haplotypes are heterozygous for A*02, the TPM values were divided by 2. Note that in certain cases the HLA-A allele copy number is not known. The TPM value of MS751 + transduced A*02 (438 TPM) was estimated from measurement of its surface A*02 protein level using the standard curve. Cell lines transduced with HLA-A*02 better mimic the A*02:MSLN ratio of normal lung tissue than cell lines expressing endogenous levels of the proteins (bold black boxes). TPM, transcripts per million; na, not applicable; A*02: HLA-A*02.

[0073] FIG. 26B shows quantification of MSLN molecules/cell using QIFIKIT. Anti-human MSLN mouse antibody clone 618923 (R&D Systems) was used to stain ~100,000 cells. After washing the cells, anti-mouse IgG F(ab')2 secondary antibody (Invitrogen A21237) was used to stain both the cells and QIFI beads. The number of MSLN molecules on the surface was quantified using the QIFI antigen standard curve.

[0074] FIG. 27A shows the characterization of MSLN CAR Tmod constructs in Jurkat cell functional assays. Six HuTARG-derived MSLN activators (CAR1-6) and benchmark CARs M5 and SS1 activators were paired with A*02 blocker (closed circles) or empty vector control (open circles). Jurkat NFAT luciferase cells expressing the CAR +/- blocker were co-cultured with wild-type, endogenous MSLN(+) HeLa cells transfected with a titration of

A*02:01 mRNA. The functional response (RLU) was assessed after a 6 hour co-culture. Titrated antigen molecules on the surface were quantified using the QIFIKIT. IC50 (molecules/cell) values are indicated in the figure. CAR1-6 are Gen3; CAR M5 and SS1 are Gen2.

[0075] FIG. 27B shows a 2-dimensional titration of MSLN and A*02 mRNA in MSLN(-) HeLa target cells to establish EC50 for the MSLN CAR3 Tmod construct in Jurkat cells. MSLN(-) HeLa target cells were transfected with serially diluted MSLN mRNA and constant A*02 mRNA and Jurkat cells were transiently transfected to express MSLN CAR3 and A*02 blocker. The functional response (RLU) was assessed after a 6 hour co-culture.

[0076] FIG. 27C shows a transfection of MSLN(-) HeLa target cells with serially diluted A*02 mRNA and constant MSLN mRNA to establish IC50 for the MSLN CAR3 Tmod construct in Jurkat cells.

[0077] FIG. 28A shows plotted levels of MSLN and A*02 mRNA and protein. EC50 and IC50 of construct in relation to MSLN and HLA-A expression levels in normal (GTEx database) and tumor tissues and cell lines (TCGA, CCLE databases). Conversions between protein and mRNA levels were calculated using the standard curves shown in FIG. 25B; Methods). HeLa and MS751 A*02 transgenic cell line variants shown on the graph better mimic activator and blocker target ratios in normal tissues.

[0078] FIG. 28B shows MSLN CARs and CAR3 Tmod cytotoxicity in primary T cells. Primary T cells transduced with CARs or Tmod were co-cultured at an effector:target (E:T) = 1:1 for 48 hours with either tumor or normal target cells as shown. A*02:MSLN (B:A) target antigen ratios ranged from 2-27:1. M5 was a Gen2 CAR; all others Gen3. Tumor = MSLN(+)A*02(-) target cells; Normal = MSLN(+)A*02(+) target cells.

[0079] FIG. 29A shows a comparison of lead CAR3 receptor paired with A*02 blocker to benchmark CARs in cytotoxicity assays. SS1 CAR is a Gen2 construct; others are Gen3. Primary T cells transduced with various CARs +/- A*02 blocker using 2 separate lentiviral vectors were cultured with endogenous MSLN(+) A*02(-) tumor or MSLN(+)A*02(+) normal HeLa cells to assess cytotoxicity. Transduced primary T cells were normalized to a constant activator or activator-blocker double-positive population percentage [15% A(+) or A(+)B(+)] cells by dilution with untransduced T cells for a final effective effector:target (E:T) ratios of 0.6:1 or 0.3:1. Both E:T ratios resulted in selective killing in the presence of A*02 antigen when T cells also expressed A*02 blocker.

[0080] FIG. 29B shows secreted IFN-g after 48-hours of co-culture with tumor or normal target cells.

[0081] FIG. 30A shows MSLN CAR3 Tmod cells selectively kill RFP(+) tumor cells and spare GFP(+) normal cells in mixed tumor and normal cell co-cultures. Due to the adherent nature of the HeLa cell line, killed targets tend to remain as clusters on the surface. White arrows point to some examples of killed RFP(+) tumor cells. Example of E:T 0.6:1 and normal:tumor = 1:1.

[0082] FIG. 30B shows cytotoxicity in mixed normal and tumor co-cultures with E:T = 1:1 and normal:tumor = 9:1 (see FIG. 31B for other ratios). Primary T cells transduced with CAR3 or CAR3 Tmod construct were co-cultured with HeLa target cells for 48 hours and imaged using GFP and RFP expressed in MSLN(+)A*02(+) normal and MSLN(+)A*02(-) tumor cell lines, respectively.

[0083] FIG. 31A shows MSLN CAR3 Tmod cells selectively kill RFP(+) tumor cells in mixed tumor and normal cell co-cultures. Primary T cells transduced with CAR3 Tmod construct were co-cultured with HeLa cells for 48 hours and imaged using GFP and RFP expressed in MSLN(+)A*02(+) normal and MSLN(+)A*02(-) tumor cell lines, respectively.

[0084] FIG. 31B shows cytotoxicity of CAR3 and CAR3 Tmod in mixed normal and tumor co-cultures with normal:tumor ranging from 9:1 to 1:9; E:T = 0.6:1.

[0085] FIG. 32A shows the MSLN CAR3 Tmod construct mediates selective, persistent and reversible cytotoxicity. CAR3 or CAR3 Tmod transduced primary T cells were co-cultured with E:T = 1.2:1 for 48 hours with either tumor or normal target cells. T cells were then collected, depleted of dead or nonadherent target cells, and re-seeded onto fresh tumor or normal target cells for an additional 48 hours. RACA, repeat-antigen challenge assay. R1, round 1; R2, round 2.

[0086] FIG. 32B shows MSLN CAR3 Tmod construct selectivity in a Jurkat cell functional assay on a subset of MSLN(+) and MSLN(-) control target cells showed no off-target activity (see Methods for Example 8, *infra*). Bar height corresponds to the average from technical replicates.

[0087] FIG. 33A shows a schematic of RACA (repeat-antigen challenge assay) and reversibility assay. CAR3 or CAR3 Tmod transduced primary T cells were co-cultured with E:T = 1.2:1 for 48 hours with either tumor or normal targets. T cells were then collected, depleted of any dead or lifted target cells, and re-seeded onto fresh tumor or normal targets for an additional 48 hours.

[0088] FIG. 33B shows soluble circulating MSLN (sMSLN) does not affect CAR-T activity. Acute cytotoxicity of tumor or normal target cells by M5 benchmark CAR or CAR3 were not affected by the presence of 500ng/mL sMSLN (Acro Bio).

[0089] FIG. 33C shows the staining of transiently-transfected CAR(+) Jurkat cells with labeled sMSLN monomer or tetramer analyzed by flow cytometry shows that the sMSLN is structurally intact and able to bind the receptors.

[0090] FIG. 34A, FIG. 34B, and FIG. 34C show the Tmod construct mediates selective killing of tumor cells in a xenograft model. FIG. 34A shows a schematic diagram of the dual-flank tumor and normal MS751 xenograft model. FIG. 34B shows bioluminescence values are to the right of the color scale in flux units of photons/sec/cm2/sr. Day 0 = pre T cell injection; days 8 and 15 = post T cell injection. FIG. 34C shows graft sizes assessed by caliper measurement (see Results for Example 8, *infra*).

[0091] FIG. 35A, FIG. 35B, and FIG. 35C show MSLN CAR Tmod selectively kill tumors in xenograft model FIG. 35A shows primary T cells transduced with MSLN CARs or CAR3 Tmod were co-cultured with either HLA-A KO tumor or A*02-transgenic normal MS751 target cells in vitro at an E:T = 1.4:1 for 48 hours. M5 was a Gen2 CAR; all others Gen3. Tumor = MSLN(+)A*02(-) target cells; Normal = MSLN(+)A*02(+) target cells. FIG. 35B shows individual mouse xenograft growth curves for data shown in FIG 34C. FIG. 35C shows BLI quantification of normal and tumor cells post T cell injection.

[0092] FIG. 36 shows cis binding of A*02 blocker in A*02(+) or (-) T cells abrogates function. Binding of the blocker in A*02(+) Jurkat cells and primary T cells by A*02 tetramer was significantly reduced due to cis-binding of autologous A*02. Reduced binding (due to reduced availability of the blocker) correlated with reduced blocker activity. Cytotoxicity assay shown at an E:T = 0.5:1.

[0093] FIG. 37A, FIG. 37B, and FIG. 37C show the MSLN Tmod system can be extended to autologous T cells. FIG. 37A shows cis-binding of autologous A*02 in an A*02(+) donor eliminates binding to A*02 tetramer B2M knockout (KO) by CRISPR restores blocker availability as demonstrated by binding to A*02 tetramer, similar to observed levels in an A*02(-) donor. FIG. 37B shows a cytotoxicity assay showing activator-only and MSLN SS1 CAR Tmod primary T cells cultured with tumor (solid) or normal (open) target cells. MSLN SS1 CAR Tmod construct kills MSLN(+) A*02(-) tumor HeLa target cells but no longer blocks in the presence of autologous A*02 as a result of cis-binding. For the A*02(+) donor, blocking is only achieved through B2M CRISPR KO. E:T = 1.2:1. FIG. 37C shows representative images at 48h.

[0094] FIG. 38A shows enrichment of anti-HLA-A*11 binders through multiple rounds of cell sorting from scFv library. On-target probe was labeled HLA-A*11 tetramer; off-target proteins were a mixture of unrelated MHC tetramers.

[0095] FIG. 38B shows Jurkat cell activation in an mRNA titration assay: HeLa target cells were transfected with serially diluted HLA-A*11 mRNA and Jurkat cells were transiently transfected to express HLA-A*11 CAR4. The functional response (RLU) was assessed after a 6 hour co-culture. PE, phycoerythrin.

[0096] FIG. 39A shows Jurkat cells expressing MSLN CAR3 and A*03, A*11 or B*07 blocker constructs were blocked in the presence of increasing blocker antigen on endogenous MSLN(+) HeLa target cells.

[0097] FIG. 39B and FIG. 39C show primary T cell cytotoxicity assay of MSLN CAR3 + A*11 blocker. Primary T cells transduced with CAR3 and A*11:01-directed blocker efficiently blocks HeLa target cells with A*11:01 and kills wildtype HeLa cells as effectively as CAR-only cells. Transduced primary T cells were co-cultured with HeLa cells with or without HLA-A*11:01 at an E:T = 0.8:1. Note that both tumor and normal target cells used here expressed GFP. FIG. 39C shows representative co-culture images at 48 hours for FIG. 39B.

DETAILED DESCRIPTION

[0098] Provided herein are compositions and methods for treating cancers using immune cells comprising a two receptor system responsive to differences in gene expression of a ligand between cancer and normal (*i.e.* healthy or wild type) cells. These differences in expression can be due to loss of heterozygosity in the cancer cells. Alternatively, the differences in expression can be because the gene expression is not expressed in cancer cells, or is expressed in cancer cells at a lower level than normal cells. The two-receptor system is expressed in immune cells, for example immune cells used in adoptive cell therapy, and targets activity of these immune cells to cancer cells exhibiting loss of heterozygosity or expression differences. In this two receptor system, the first receptor (an activator receptor, sometimes referred to herein as an A module) activates, or promotes activation of the immune cells, while the second receptor (an inhibitory receptor, sometimes referred to herein as a blocker, inhibitor receptor, or B module) acts to inhibit activation of the immune cells by the first receptor. Each receptor contains a ligand-binding domain (LBD) that binds a specific ligand. Signals from the two receptors upon ligand binding are integrated by the immune cell. Differential expression of ligands for the first and second receptors in cancer and normal cells, for example through loss of heterozygosity of the locus encoding the inhibitory ligand

in cancer cells, or differences in transcription levels, mediates activation of immune cells by target cancer cells that express the first activator ligand but not the second inhibitory ligand.

[0099] Loss of heterozygosity (LOH) from large-scale chromosomal deletions is a source of genetic difference in tumors. LOH is a common event in tumorigenesis which affects nearly every locus in the genome, with approximately 20% of genes displaying LOH in an average tumor. LOH provides the means to discriminate tumor from normal tissue in a definitive way because tumors can be found in which all malignant cells lack certain germline alleles. One locus that undergoes LOH is the human leukocyte antigen (HLA) locus, which encodes polymorphic, abundant, ubiquitous surface antigens. The two-receptor system described herein employs one receptor to activate T cells exposed to tumor-antigen-positive tumor cells (sometimes referred to as an "activator module"), and a second receptor to prevent activation of the immune cells in the presence of a surface blocker antigen such as HLA-A*02 protein. The dual-receptor system described herein (sometimes referred to herein as "Tmod") possesses other advantageous properties as a cell therapy, including but not limited to reversible activation/blockade of immune cells, and selectivity in mixtures of tumor and "normal" cells.

[0100] In particular embodiments of the compositions and methods provided herein, immune cells comprising the two receptor system described herein are used to treat Mesothelin (MSLN) positive cancers. This includes mesothelioma cancer, ovarian cancer, cervical cancer, colorectal cancer, esophageal cancer, head and neck cancer, kidney cancer, uterine cancer, gastric cancer, pancreatic cancer, lung cancer, colorectal cancer, or cholangiocarcinoma. In some embodiments, the cancer has relapsed in a subject. In some embodiments, the cancer is refractory to one or more prior administered anticancer therapies. In some embodiments, the cancer is metastatic. In the case of MSLN-positive cancers, the target antigen of the activator receptor is MSLN, or a peptide antigen thereof, in a complex with a major histocompatibility complex class I (MHC-I). MSLN is expressed in normal adipose, fallopian tube, lung and salivary gland tissues, among others (FIG. 2). Because of its expression in certain tumors, MSLN is an attractive tumor-specific antigen that could mediate selective killing of MSLN+ tumors if these cancer cells could be specifically targeted with an appropriate therapeutic. However, normal MSLN expression in non-cancer (non-target) cells has prevented the effective use of MSLN for targeted therapies such as adoptive cell therapies. By pairing an MSLN activator receptor with an inhibitory receptor, the methods provided herein increase the specificity of adoptive cell therapies and decrease harmful effects associated with these therapies, such as dose-limited toxicity.

[0101] In some embodiments, the ligand for the activator is a MSLN peptide complexed with MHC class I. In the methods described herein, this MSLN targeted activator receptor is paired with an inhibitory receptor, which increases the safety window of the activator by blocking its cytolytic effect on normal MSLN-positive tissues. However, the activator receptor still directs the targeted killing of tumor cells by immune cells comprising the two-receptor system, as the tumor cells do not express the ligand for the inhibitor, or blocker, receptor. The target for the second, inhibitory receptor is expressed by MSLN positive tissues such as lung, mesothelium and adipose tissues, but not in cancer cells, and the inhibitory receptor recognizes this "non-target antigen" as an inhibitory stimulus. An exemplary target for the second inhibitory receptor is expressed by lung tissue, and is lost from MSLN positive cancer cells due to loss of heterozygosity (LOH) or other mechanisms, leaving a single allelic form in cancer cells that can be distinguished from other alleles via an allele-specific ligand binding domain on the inhibitory receptor. Exemplary targets of the inhibitory receptor include, but are not limited to, Major Histocompatibility Complex (MHC) proteins such as human leukocyte antigen A (HLA-A). HLA-B, HLA-C, and other HLAs. HLAs are encoding by variant genes, such as HLA-A*01., HLA-A*02, HLA-A*03, HLA-C*07, and others, which can be lost from MSLN positive cancer cells through loss of heterozygosity. Alternatively, further exemplary targets of the inhibitory receptor include, but are not limited to, intercellular adhesion molecule 1 (ICAM1), catechol-O-methyltransferase (COMT) and C-X-C motif chemokine ligand 16 (CXCL16). Each of these has a common nonsynonymous variant form, with the amino-acid alteration in its extracellular domain accessible to antibodies, which can be used as a inhibitory receptor, or blocker receptor target for a cellular integrator designed to safely treat patients with MSLN positive cancers with engineered T cells activated by an activator receptor such as a MSLN or MSLN pMHC responsive activator receptor.

[0102] The compositions and methods of the disclosure can reduce or eliminate dose-limiting toxicity (DLT) caused by expression of MSLN on normal tissue. The disclosure provides methods of targeting MSLN in cancer cells to treat MSLN positive cancers using adoptive cell therapies by adding a second inhibitory receptor that blocks activation of the adoptive immune cells in the presence of a second ligand (a ligand other than MSLN, termed the non-target antigen or alternatively, blocker antigen). Using the compositions and methods described herein, tumor cells that express MSLN are attacked by the adoptive cells, such as immune cells, expressing the two receptors because these tumor cells express only the activator ligand, MSLN. In contrast, normal cells that express MSLN plus the non-target

antigen are protected from the adoptive immune cells. The inhibitory receptor response to the non-target antigen on normal cells prevents activation of immune cells by the MSLN-targeted activator receptor. This dual-targeting approach creates the therapeutic window that will allow a MSLN-directed cell therapy to be dosed safely and effectively in MSLN-positive cancer patients.

[0103] The disclosure provides methods and compositions that allow the use of potent MSLN CAR and TCRs that induce on-target toxicity, and renders these MSLN targeted receptors useful as a therapeutic by mitigating their toxicity.

[0104] In variations, the compositions and methods described herein may be used to kill target cells and/or treat subjects in which expression of the non-target antigen is partially or completely decreased by causes other than loss of heterozygosity, including but not limited to partial gene deletion, epigenetic silencing, and point mutations or truncating mutations in the sequence encoding the non-target antigen.

Definitions

[0105] Prior to setting forth this disclosure in more detail, it may be helpful to an understanding thereof to provide definitions of certain terms to be used herein.

[0106] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by those of ordinary skill in the art to which the disclosure belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of particular embodiments, preferred embodiments of compositions, methods and materials are described herein. For the purposes of the present disclosure, the following terms are defined below. Additional definitions are set forth throughout this disclosure.

[0107] As used herein, the term "about" or "approximately" refers to a quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length that varies by as much as 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2% or 1% to a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length. In one embodiment, the term "about" or "approximately" refers a range of quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length ± 15%, ± 10%, ± 9%, ± 8%, ± 7%, ± 6%, ± 5%, ± 4%, ± 3%, ± 2%, or ± 1% about a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length.

[0108] As used herein, the term "isolated" means material that is substantially or essentially free from components that normally accompany it in its native state. In particular embodiments, the term "obtained" or "derived" is used synonymously with isolated.

[0109] The terms "subject," "patient" and "individual" are used interchangeably herein to refer to a vertebrate, preferably a mammal, more preferably a human. Tissues, cells, and their progeny of a biological entity obtained in vivo or cultured in vitro are also encompassed. A "subject," "patient" or "individual" as used herein, includes any animal that exhibits pain that can be treated with the vectors, compositions, and methods contemplated herein. Suitable subjects (e.g., patients) include laboratory animals (such as mouse, rat, rabbit, or guinea pig), farm animals, and domestic animals or pets (such as a cat or dog). Non-human primates and, preferably, human patients, are included.

[0110] As used herein "treatment" or "treating," includes any beneficial or desirable effect, and may include even minimal improvement in symptoms. "Treatment" does not necessarily indicate complete eradication or cure of the disease or condition, or associated symptoms thereof.

[0111] As used herein, "prevent," and similar words such as "prevented," "preventing" etc., indicate an approach for preventing, inhibiting, or reducing the likelihood of a symptom of disease. It also refers to delaying the onset or recurrence of a disease or condition or delaying the occurrence or recurrence of the symptoms of a disease. As used herein, "prevention" and similar words also includes reducing the intensity, effect, symptoms and/or burden of disease prior to onset or recurrence.

[0112] As used herein, the term "amount" refers to "an amount effective" or "an effective amount" of a virus to achieve a beneficial or desired prophylactic or therapeutic result, including clinical results.

[0113] A "therapeutically effective amount" of a virus or cell may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the virus or cell to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effects of the virus or cell are outweighed by the therapeutically beneficial effects. The term "therapeutically effective amount" includes an amount that is effective to "treat" a subject (e.g., a patient).

[0114] An "increased" or "enhanced" amount of a physiological response, e.g., electrophysiological activity or cellular activity, is typically a "statistically significant" amount, and may include an increase that is 1.1, 1.2, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30 or more times (e.g., 500, 1000 times) (including all integers and decimal points in between and above 1, e.g., 1.5, 1.6, 1.7. 1.8, etc.) the level of activity in an untreated cell.

[0115] A "decreased" or "reduced" amount of a physiological response, e.g., electrophysiological activity or cellular activity, is typically a "statistically significant"

amount, and may include an decrease that is 1.1, 1.2, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30 or more times (e.g., 500, 1000 times) (including all integers and decimal points in between and above 1, e.g., 1.5, 1.6, 1.7. 1.8, etc.) the level of activity in an untreated cell.

[0116] By "maintain," or "preserve," or "maintenance," or "no change," or "no substantial change," or "no substantial decrease" refers generally to a physiological response that is comparable to a response caused by either vehicle, or a control molecule/composition. A comparable response is one that is not significantly different or measurable different from the reference response.

[0117] In general, "sequence identity" or "sequence homology" refers to an exact nucleotide-to-nucleotide or amino acid-to-amino acid correspondence of two polynucleotides or polypeptide sequences, respectively. Typically, techniques for determining sequence identity include determining the nucleotide sequence of a polynucleotide and/or determining the amino acid sequence encoded thereby, and comparing these sequences to a second nucleotide or amino acid sequence. Two or more sequences (polynucleotide or amino acid) can be compared by determining their "percent identity." The percent identity of two sequences, whether nucleic acid or amino acid sequences, is the number of exact matches between two aligned sequences divided by the length of the shorter sequences and multiplied by 100. Percent identity may also be determined, for example, by comparing sequence information using the advanced BLAST computer program, including version 2.2.9, available from the National Institutes of Health. The BLAST program is based on the alignment method of Karlin and Altschul, Proc. Natl. Acad. Sci. USA 87:2264-2268 (1990) and as discussed in Altschul, et al., J. Mol. Biol. 215:403-410 (1990); Karlin And Altschul, Proc. Natl. Acad. Sci. USA 90:5873-5877 (1993); and Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997). Briefly, the BLAST program defines identity as the number of identical aligned symbols (generally nucleotides or amino acids), divided by the total number of symbols in the shorter of the two sequences. The program may be used to determine percent identity over the entire length of the proteins being compared. Default parameters are provided to optimize searches with short query sequences in, for example, with the blastp program. The program also allows use of an SEG filter to mask-off segments of the query sequences as determined by the SEG program of Wootton and Federhen, Computers and Chemistry 17:149-163 (1993). Ranges of desired degrees of sequence identity are approximately 80% to 100% and integer values therebetween. Typically, the percent identities between a disclosed sequence and a claimed sequence are at least 80%, at least 85%, at least 90%, at least 95%, or at least 98%.

[0118] As used herein, a "polynucleotide system" refers to one or more polynucleotides. The one or more polynucleotides may be designed to work in concert for a particular application, or to produce a desired transformed cell.

[0119] The term "exogenous" is used herein to refer to any molecule, including nucleic acids, protein or peptides, small molecular compounds, and the like that originate from outside the organism. In contrast, the term "endogenous" refers to any molecule that originates from inside the organism (i.e., naturally produced by the organism).

[0120] The term "MOI" is used herein to refer to multiplicity of infection, which is the ratio of agents (e.g. viral particles) to infection targets (e.g. cells).

[0121] In the present description, any concentration range, percentage range, ratio range, or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated. The term "about", when immediately preceding a number or numeral, means that the number or numeral ranges plus or minus 10%.

[0122] As used herein, a "target cell" refers to cell that is targeted by an adoptive cell therapy. For example, a target cell can be cancer cell, which can be killed by the transplanted T cells of the adoptive cell therapy. Target cells of the disclosure express a target antigen, as described herein, and do not express a non-target antigen.

[0123] As used herein, a "non-target cell" refers to cell that is not targeted by an adoptive cell therapy. For example, in an adoptive cell targeting cancer cells, normal, healthy, non-cancerous cells are non-target cells. Some, or all, non-target cells in a subject may express both the target antigen and the non-target antigen. Non-target cells in a subject may express the non-target antigen irrespective of whether or not these cells also express the target antigen.

[0124] As used herein, a "non-target allelic variant" refers to an allele of a gene whose product is expressed by non-target cells, but is not expressed by target cells. For example, a non-target allelic variant is an allele of a gene that is expressed by normal, non-cancer cells of subject, but not expressed by cancer cells of the subject. The expression of the non-target allelic variant can be lost in the cancer cells by any mechanism, including, but not limited to, loss of heterozygosity, mutation, or epigenetic modification of the gene encoding the non-target allelic variant.

[0125] As used herein, "specific to" or "specifically binds to" when used with respect to a ligand binding domain, such as an antigen binding domain, refers to a ligand binding domain that has a high specificity for a named target. Antibody specificity can viewed as a measure

of the goodness of fit between the ligand binding domain and the corresponding ligand, or the ability of the ligand binding domain to discriminate between similar or even dissimilar ligands. In comparison with specificity, affinity is a measure of the strength of the binding between the ligand binding domain and ligand, such that a low-affinity ligand binding domain binds weakly and high-affinity ligand binding domain binds firmly. A ligand binding domain that is specific to a target allele is one that can discriminate between different alleles of a gene. For example, a ligand binding domain that is specific to HLA-A*02 will not bind, or bind only weakly to, other HLA-A alleles such as HLA-A*01 or HLA-A*03. The person of skill in the art will appreciate that a ligand binding domain can be said to be specific to a particular target, and yet still have low levels of binding to one or more additional targets that do not affect its function in the receptor systems described herein.

[0126] As used herein, a "target antigen," whether referred to using the term antigen or the name of a specific antigen, refers to an antigen expressed by a target cell, such as a cancer cell. Expression of target antigen is not limited to target cells. Target antigens may be expressed by both cancer cells and normal, non-cancer cells in a subject.

[0127] As used herein, a "non-target antigen" (or "blocker antigen") whether referred to using the term antigen or the name of a specific antigen, refers to an antigen that is expressed by normal, non-cancer cells and is not expressed in cancer cells. This difference in expression allows the inhibitory receptor to inhibit immune cell activation in the presence of non-target cells, but not in the presence of target cells.

[0128] Polymorphism refers to the presence of two or more variants of a nucleotide sequence in a population. A polymorphism may comprise one or more base changes, an insertion, a repeat, or a deletion. A polymorphism includes e.g. a simple sequence repeat (SSR) and a single nucleotide polymorphism (SNP), which is a variation, occurring when a single nucleotide of adenine (A), thymine (T), cytosine (C) or guanine (G) is altered.

[0129] As used herein, "affinity" refers to strength of binding of a ligand to a single ligand binding site on a receptor, for example an antigen for the antigen binding domain of any of the receptors described herein. Ligand binding domains can have a weaker interaction (low affinity) with their ligand, or a stronger interaction (high affinity).

[0130] Kd, or dissociation constant, is a type of equilibrium constant that measures the propensity of a larger object to separate reversibly into smaller components, such as, for example, when a macromolecular complex comprising receptor and its cognate ligand separates into the ligand and the receptor. When the Kd is high, it means that a high

concentration of ligand is need to occupy the receptor, and the affinity of the receptor for the ligand is low. Conversely, a low Kd means that the ligand has a high affinity for the receptor.

[0131] As used herein, a receptor that is "responsive" or "responsive to" refers to a receptor comprising an intracellular domain, that when bound by a ligand (*i.e.* antigen) generates a signal corresponding to the known function of the intracellular domain. An activator receptor bound to a target antigen can generate a signal that causes activation of an immune cell expressing the activator receptor. An inhibitory receptor bound to a non-target antigen can generate an inhibitory signal that prevents or reduces an activation of an immune cell expressing the activator receptor. Responsiveness of receptors, and their ability to activate or inhibit immune cells expressing the receptors, can be assayed by any means known in the art and described herein, including, but not limited to, reporter assays and cytotoxicity assays.

[0132] As used herein, "activation" of an immune cell or an immune cell that is "activated" refers to an immune cell that can carry out one or more functions characteristic of an immune response. These functions include proliferation, release of cytokines, and cytotoxicity, i.e. killing of a target cell. Activated immune cells express markers that will be apparent to persons of skill in the art. For example, activated T cells can express one or more of CD69, CD71, CD25 and HLA-DR. An immune cell expressing an activator receptor (*e.g.* a MSLN CAR) can be activated by the activator receptor when it becomes responsive to the binding of the receptor to a target antigen (*e.g.* MSLN) expressed by the target cell. A "target antigen" can also be referred to an "activator antigen" and may be isolated or expressed by a target cell. Activation of an immune cell expressing an inhibitory receptor can be prevented when the inhibitory receptor becomes responsive to a non-target antigen (*e.g.* HLA-A*02), even when the activator receptor is bound to the target activator ligand. A "non-target antigen" can also be referred to as an "inhibitory ligand" or a "blocker", and may be isolated or expressed by a target cell.

[0133] Receptor expression on an immune cell can be verified by assays that report the presence of the activator receptors and inhibitory receptors described herein. For example, a population of immune cells can be stained with a labeled molecule (*e.g.* a fluorophore labeled receptor-specific antibody or a fluorophore-labeled receptor-specific ligand), and quantified using fluorescence activated cell sorting (FACS) flow cytometry. This method allows a percentage of immune cells in a population of immune cells to be characterized as expressing an activator receptor, an inhibitory receptor, or both receptors. The ratio of activator receptor and inhibitory receptors expressed by the immune cells described herein can be determined by, for example, digital droplet PCR. These approaches can be used to characterize the

population of cells for the production and manufacturing of the immune cells, pharmaceutical compositions, and kits described herein. For the immune cells, pharmaceutical compositions, and kits described herein, it is understood that a suitable percentage of immune cells expressing both an activator receptor and an inhibitory receptor is determined specifically for the methods described herein. For example, a suitable percentage of immune cells expressing both an activator receptor and in inhibitory receptor can be at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95%. As a further example, between 50% and 99%, between 60% and 95%, between 65% and 95%, between 65% and 90%, between 70% and 90% , between 75% and 90%, between 75% and 85%, between 80% and 99%, between 85% and 99%, between 90% and 99% or between 95% and 99% of immune cells can express both the activator receptor and the inhibitory receptor. For example, a suitable ratio of activator receptor and inhibitory receptor in an immune cell can be about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 1:2, about 1:3, about 1:4, or about 1:5. It is understood that purification, enrichment, and/or depletion steps can be used on populations of immune cells to meet suitable values for the immune cells, pharmaceutical compositions, and kits described herein.

[0134] A responsive receptor expressed by the immune cells described herein can be verified by assays that measure the generation of a signal expected to be generated by the intracellular domain of the receptor. Reporter cell lines, such as Jurkat-Luciferase NFAT cells (Jurkat cells), can be used to characterize a responsive receptor. Jurkat cells are derived from T cells and comprise a stably integrated nuclear factor of activated T-cells (NFAT)-inducible luciferase reporter system. NFAT is a family of transcription factors required for immune cell activation, whose activation can be used as a signaling marker for T cell activation. Jurkat cells can be transduced or transfected with the activator receptors and/or inhibitory receptors described herein. The activator receptor is responsive to the binding of a ligand if the Jurkat cell expresses a luciferase reporter gene, and the level of responsiveness can be determined by the level of reporter gene expression. The presence of luciferase can be determined using any known luciferase detection reagent, such as luciferin. An inhibitory receptor is responsive to the binding of a ligand if, when co-expressed with an activator receptor in Jurkat cells, it prevents a normally responsive immune cell from expressing luciferase in response to the activator receptor. For example, the responsiveness of an inhibitory receptor can be determined and quantified in a Jurkat cell expressing both an activator and an inhibitor by observing the following: 1) the Jurkat cell expresses luciferase in the presence of activator receptor ligand and absence of inhibitory receptor ligand; and 2) luciferase expression in the

Jurkat cell is reduced or eliminated in the presence of both an activator receptor ligand and an inhibitory receptor ligand. This approach can be used to determine the sensitivity, potency, and selectivity of activator receptors and specific pairs of activator receptors and inhibitory receptors. The sensitivity, potency, and selectivity can be quantified by EC50 or IC50 values using dose-response experiments, where an activator receptor ligand and/or inhibitory receptor ligand is titrated into a culture of Jurkat cells expressing an activator receptor or a specific pair of activator and inhibitory receptors. Alternatively, the EC50 and IC50 values can be determined in a co-culture of immune cells (*e.g.* Jurkat cells or primary immune cells) expressing an activator receptor or a specific pair of activator and inhibitory receptors and target cells expressing an increasing amount of an activator ligand or inhibitor ligand. An increasing amount of activator ligand or inhibitor ligand can be accomplished in the target cell by, for example, titration of activator ligand or inhibitor ligand encoding mRNA into target cells, or use of target cells that naturally express different levels of the target ligands. Exemplary suitable EC50 and IC50 values for the activator and inhibitory receptors as determined used target cells expressing varying amounts of the target and non-target ligands include an EC50 of 10 transcripts per million (TPM) or less for the activator receptor, for example an EC50 of between 2-10 TPM, and an IC50 of 25 TPM or less for the inhibitory receptor, for example an IC50 of 5-21 TPM.

[0135] Activation of the immune cells described herein that express an activator receptor or specific pairs of activator and inhibitory receptors can be further determined by assays that measure the viability of a target cell following co-incubation with said immune cells. The immune cells, sometimes referred to as effector cells, are co-incubated with target cells that express an activator receptor ligand, an inhibitory receptor ligand, or both an activator and inhibitory receptor ligand. Following co-incubation, viability of the target cell is measured using any method to measure viability in a cell culture. For example, viability can be determined using a mitochondrial function assay that uses a tetrazolium salt substrate to measure active mitochondrial enzymes. Viability can also be determined using imaging based methods. Target cells can express a fluorescent protein, such as green fluorescent protein or red fluorescent protein. Reduction in total cell fluorescence indicates a reduction in viability of the target cell. A reduction in viability of the target cell following incubation with immune cells expressing an activator receptor or a specific pair of activator and inhibitory receptors is interpreted as target cell-mediated activation of the immune cell. A measure of the selectivity of the immune cells can also be determined using this approach. The immune cell expressing a pair of activator and inhibitory receptors is selective if the following is observed: 1)

viability is reduced in target cells expressing the activator receptor ligand but not the inhibitory receptor ligand; 2) viability is not reduced in target cells expressing both an activator receptor ligand and an inhibitory receptor ligand. From these measurements, a "specific killing" value can be derived that quantifies the percentage of immune cell activation based on the reduction in viability of target cell as a percentage of a negative control (immune cells that do not express an activator receptor). Further, from these measurements a "selectivity ratio" value can be derived that represents the ratio of the specific killing observed in target cells expressing an activator receptor ligand in the absence of inhibitory receptor ligand to the specific killing observed in target cells expressing both an activator receptor ligand and an inhibitory receptor ligand. This approach can be used to characterize the population of cells for the production and manufacturing of the immune cells, pharmaceutical compositions, and kits described herein. A suitable specific killing value for the immune cells, pharmaceutical compositions, and kits can be, for example, the following criteria: 1) at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 97% or at least 99% specific killing following a 48 hour co-incubation of immune cells and target cells expressing activator receptor ligand in the absence of inhibitory receptor ligand; and 2) less than or equal to 40%, less than or equal to 35%, less than or equal to 30%, less than or equal to 25%, less than or equal to 20%, less than or equal to 15%, less than or equal to 10%, less than or equal to 5%, less than or equal to 3% or less than or equal to 1% specific killing of target cell expressing both an activator receptor ligand and an inhibitory receptor ligand.

[0136] As a further example, a suitable specific killing value for the immune cells, pharmaceutical compositions and kits can be the following criteria: 1) between 30% and 99%, between 40% and 99%, between 50% and 99%, between 55% and 95%, between 60% and 95%, between 60% and 90%, between 50% and 80%, between 50% and 70% or between 50% and 60% of target cells expressing the activator ligand but not the inhibitor ligand are killed; and 2), between 1% and 40%, between 3% and 40%, between 5% and 40%, between 5% and 30%, between 10% and 30%, between 15% and 30% or between 5% and 20% of target cells expressing the activator ligand and the inhibitor ligand are killed. As a still further example, a suitable specific killing value for the immune cells, pharmaceutical compositions, and kits can be, for example, the following criteria: 1) at least 50% specific killing following a 48 hour co-incubation of immune cells and target cells expressing activator receptor ligand in the absence of inhibitory receptor ligand; and 2) less than or equal to 20% specific killing of target cell expressing both an activator receptor ligand and an

inhibitory receptor ligand. As a further example, the immune cells are capable of killing at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 97% or at least 99% of target cells expressing the activator ligand and not the inhibitor ligand over a period of 6 hours, 12 hours, 18 hours, 24 hours, 30 hours, 36 hours, 42 hours, 48 hours, 54 hours, or 60 hours, while killing less than 40%, less than 30%, less than 20%, less than 10%, less than 5%, less than 3% or less than 1% of target cells expressing the activator and inhibitor ligands over the same time period.

[0137] A suitable specific killing value of the target cell expressing an activator ligand in the absence of an inhibitory ligand value for the immune cells, pharmaceutical compositions, and kits can be, for example, at least about 50% to at least about 95%. A suitable specific killing value of the target cell expressing an activator ligand in the absence of an inhibitory ligand value for the immune cells, pharmaceutical compositions, and kits can be, for example, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95%. A suitable specific killing value of the target cell expressing an activator ligand in the absence of an inhibitory ligand value for the immune cells, pharmaceutical compositions, and kits can be, for example, at most about 50%, at most about 55%, at most about 60%, at most about 65%, at most about 70%, at most about 75%, at most about 80%, at most about 85%, at most about 90%, or at most about 95%. A suitable specific killing value of target cells expressing both an activator receptor ligand and an inhibitory receptor ligand for the immune cells, pharmaceutical compositions, and kits can be can be less than about 50%, less than about 45%, less than about 40%, less than about 35%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, or less than about 5%. The suitable specific killing value for the immune cells, pharmaceutical compositions, and kits can be can be determined following about 6 hours, about 12 hours, about 18 hours, about 24, about 30 hours, about 36 hours, about 42 hours, about 48 hours, about 54 hours, about 60 hours, about 66 hours, or about 72 hours of co-incubation of immune cells with target cells.

[0138] A suitable specific killing value of the target cell expressing an activator ligand in the absence of an inhibitory ligand value for the immune cells, pharmaceutical compositions, and kits can be, for example, at least about 50% to at least about 95%. A suitable specific killing value of the target cell expressing an activator ligand in the absence of an inhibitory ligand value for the immune cells, pharmaceutical compositions, and kits can be, for example, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about

70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95%. A suitable specific killing value of the target cell expressing an activator ligand in the absence of an inhibitory ligand value for the immune cells, pharmaceutical compositions, and kits can be, for example, at most about 50%, at most about 55%, at most about 60%, at most about 65%, at most about 70%, at most about 75%, at most about 80%, at most about 85%, at most about 90%, or at most about 95%. A suitable specific killing value of target cells expressing both an activator receptor ligand and an inhibitory receptor ligand for the immune cells, pharmaceutical compositions, and kits can be can be less than about 50%, less than about 45%, less than about 40%, less than about 35%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, or less than about 5%. The suitable specific killing value for the immune cells, pharmaceutical compositions, and kits can be can be determined following about 6 hours, about 12 hours, about 18 hours, about 24, about 30 hours, about 36 hours, about 42 hours, about 48 hours, about 54 hours, about 60 hours, about 66 hours, or about 72 hours of co-incubation of immune cells with target cells.

[0139] As used herein, the term "functional variant" refers to a protein that has one or more amino-acid substitutions, insertions, or deletions as compared to a parental protein, and which retains one or more desired activities of the parental protein. A functional variant may be a fragment of the protein (*i.e.* a variant having N- and/or C-terminal deletions) that retain the one or more desired activities of the parental protein.

[0140] All publications and patents mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference. In case of conflict, the present application, including any definitions herein, will control. However, mention of any reference, article, publication, patent, patent publication, and patent application cited herein is not, and should not be taken as an acknowledgment, or any form of suggestion, that they constitute valid prior art or form part of the common general knowledge in any country in the world.

Activator Receptors

[0141] The disclosure provides a first receptor, comprising a first extracellular ligand binding domain specific to a target antigen comprising a cancer cell-specific antigen, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I). The first receptor is an activator receptor, and mediates activation of an immune cell expressing the first receptor upon binding of the target antigen by the extracellular ligand binding

domain of the first receptor. The first receptor is responsive to a target antigen (*i.e.* activator ligand). For example, when a target antigen binds to or contacts the first receptor, the first receptor is responsive and activates an immune cell expressing the first receptor upon binding of the target antigen by the extracellular ligand binding domain of the first receptor. In some embodiments, the first receptor is a chimeric antigen receptor (CAR). In some embodiments, the first receptor is a T cell receptor (TCR).

[0142] In some embodiments, the first receptor is humanized. As used herein, "humanized" refers to the replacement of a sequence or a subsequence in a transgene that has been isolated or derived from a non-human species with a homologous, or functionally equivalent, human sequence. For example, a humanized antibody can be created by grafting mouse CDRs into human framework sequences, followed by back substitution of certain human framework residues for the corresponding mouse residues from the source antibody.

Activator Targets

[0143] In some embodiments, the target antigen for the first receptor is a cancer cell specific antigen. Any cell surface molecule expressed by the target cancer cells may be a suitable target antigen for the first receptor ligand binding domain. For example, a cell adhesion molecule, a cell-cell signaling molecule, an extracellular domain, a molecule involved in chemotaxis, a glycoprotein, a G protein-coupled receptor, a transmembrane, a receptor for a neurotransmitter or a voltage gated ion channel can be used as a target antigen.

[0144] In some embodiments, the target antigen is a peptide antigen of a cancer cell-specific antigen in a complex with a major histocompatibility complex class I (MHC-I). Any molecule expressed by the target cancer cells and presented by the major histocompatibility complex class I (MHC-I) on the cancer cell surface as a peptide antigen (pMHC) may be a suitable target antigen for the first receptor extracellular ligand binding domain.

[0145] In some embodiments, the cancer cell-specific antigen is Mesothelin (MSLN), or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I).

[0146] The major histocompatibility complex class I (MHC-I) is a protein complex that displays antigens to cells of the immune system, triggering an immune response. The Human Leukocyte Antigens (HLAs) corresponding to MHC-I are HLA-A, HLA-B and HLA-C.

[0147] Cancer cell-specific pMHC antigens comprising any of HLA-A, HLA-B, HLA-C, HLA-E, HLA-F or HLA-G are envisaged as within the scope of the disclosure. In some embodiments, the cancer cell-specific antigen comprises HLA-A. HLA-A receptors are heterodimers comprising a heavy α chain and smaller β chain. The α chain is encoded by a

variant of HLA-A, while the β chain (β2-microglobulin) is an invariant. There are several thousand variant HLA-A genes, all of which fall within the scope of the instant disclosure. In some embodiments, the MHC-I comprises a human leukocyte antigen A*02 allele (HLA-A*02).

[0148] In some embodiments, the cancer cell-specific antigen comprises HLA-B. Hundreds of versions (alleles) of the HLA-B gene are known, each of which is given a particular number (such as HLA-B*27).

[0149] In some embodiments, the cancer cell-specific antigen comprises HLA-C. HLA-C belongs to the HLA class I heavy chain paralogues. This class I molecule is a heterodimer consisting of a heavy chain and a light chain (beta-2 microglobulin). Over one hundred HLA-C alleles are known in the art.

[0150] In some embodiments, the cancer cell-specific antigen is an ovarian cancer antigen, a pancreatic cancer antigen, a lung cancer antigen, a colorectal cancer antigen or a mesothelioma antigen. In some embodiments, the cancer cell-specific antigen is a colorectal cancer antigen. In some embodiments, the cancer cell-specific antigen is MSLN or a peptide antigen thereof.

[0151] In some embodiments, the cancer cell-specific antigen is MSLN, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I). MSLN is a 40 KDa protein that is normally expressed in mesothelial cells, as well as lung, fallopian tube, salivary gland and adipose tissues (FIG. 2). MSLN is expressed in multiple human tumor types, including mesothelioma cancer, ovarian cancer, cervical cancer, colorectal cancer, esophageal cancer, head and neck cancer, kidney cancer, uterine cancer, gastric cancer, pancreatic cancer, lung cancer, colorectal cancer, or cholangiocarcinoma. In some embodiments, the cancer has relapsed in a subject. In some embodiments, the cancer is refractory to one or more prior administered anticancer therapies. In some embodiments, the cancer is metastatic.

[0152] All isoforms of MSLN are envisaged as cancer cell-specific antigens of the disclosure. MSLN isoform 1 preprotein is described in NCBI record number NP_005814.2, the contents of which are incorporated by reference herein. In some embodiments, MSLN comprises an amino acid sequence of:

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  1 MALPTARPLL GSCGTPALGS LLFLLFSLGW VQPSRTLAGE TGQEAAPLDG VLANPPNISS
 61 LSPRQLLGFP CAEVSGLSTE RVRELAVALA QKNVKLSTEQ LRCLAHRLSE PPEDLDALPL
121 DLLLFLNPDA FSGPQACTRF FSRITKANVD LLPRGAPERQ RLLPAALACW GVRGSLLSEA
181 DVRALGGLAC DLPGRFVAES AEVLLPRLVS CPGPLDQDQQ EAARAALQGG GPPYGPPSTW
241 SVSTMDALRG LLPVLGQPII RSIPQGIVAA WRQRSSRDPS WRQPERTILR PRFRREVEKT
301 ACPSGKKARE IDESLIFYKK WELEACVDAA LLATQMDRVN AIPFTYEQLD VLKHKLDELY
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361 PQGYPESVIQ HLGYLFLKMS PEDIRKWNVT SLETLKALLE VNKGHEMSPQ VATLIDRFVK
421 GRGQLDKDTL DTLTAFYPGY LCSLSPEELS SVPPSSIWAV RPQDLDTCDP RQLDVLYPKA
481 RLAFQNMNGS EYFVKIQSFL GGAPTEDLKA LSQQNVSMDL ATFMKLRTDA VLPLTVAEVQ
541 KLLGPHVEGL KAEERHRPVR DWILRQRQDD LDTLGLGLQG GIPNGYLVLD LSMQEALSGT
601 PCLLGPGPVL TVLALLLAST LA
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(SEQ ID NO: 1).

[0153] In some embodiments, MSLN comprises a sequence that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 1.

[0154] MSLN isoform 2 preprotein is described in NCBI record number NP_037536.2, the contents of which are incorporated by reference herein. In some embodiments, MSLN comprises an amino acid sequence of:

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  1 MALPTARPLL GSCGTPALGS LLFLLFSLGW VQPSRTLAGE TGQEAAPLDG VLANPPNISS
 61 LSPRQLLGFP CAEVSGLSTE RVRELAVALA QKNVKLSTEQ LRCLAHRLSE PPEDLDALPL
121 DLLLFLNPDA FSGPQACTRF FSRITKANVD LLPRGAPERQ RLLPAALACW GVRGSLLSEA
181 DVRALGGLAC DLPGRFVAES AEVLLPRLVS CPGPLDQDQQ EAARAALQGG GPPYGPPSTW
241 SVSTMDALRG LLPVLGQPII RSIPQGIVAA WRQRSSRDPS WRQPERTILR PRFRREVEKT
301 ACPSGKKARE IDESLIFYKK WELEACVDAA LLATQMDRVN AIPFTYEQLD VLKHKLDELY
361 PQGYPESVIQ HLGYLFLKMS PEDIRKWNVT SLETLKALLE VNKGHEMSPQ APRRPLPQVA
421 TLIDRFVKGR GQLDKDTLDT LTAFYPGYLC SLSPEELSSV PPSSIWAVRP QDLDTCDPRQ
481 LDVLYPKARL AFQNMNGSEY FVKIQSFLGG APTEDLKALS QQNVSMDLAT FMKLRTDAVL
541 PLTVAEVQKL LGPHVEGLKA EERHRPVRDW ILRQRQDDLD TLGLGLQGGI PNGYLVLDLS
601 MQEALSGTPC LLGPGPVLTV LALLLASTLA
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(SEQ ID NO: 2).

[0155] In some embodiments, MSLN comprises a sequence that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 2.

In some embodiments, the cancer cell-specific antigen is a peptide antigen derived from MSLN. In some embodiments, the peptide antigen is comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to a subsequence of SEQ ID NO: 1 and/or SEQ ID NO: 2. In some embodiments, the peptide antigen comprises a sequence identical to a subsequence of SEQ ID NO: 1 and/or SEQ ID NO: 2.

Extracellular Ligand Binding Domain

[0156] The disclosure provides a first receptor, comprising a first extracellular ligand binding domain specific to a target antigen. In some embodiments, the target antigen comprises a cancer cell-specific antigen.

[0157] In some embodiments, the cancer cell-specific antigen is MSLN or a MSLN-derived peptide antigen complexed with MHC-I, and the ligand binding domain of the first receptor recognizes and binds to the MSLN antigen.

[0158] Any type of ligand binding domain that can regulate the activity of a receptor in a ligand dependent manner is envisaged as within the scope of the instant disclosure. In some

embodiments, the ligand binding domain is an antigen binding domain. Exemplary antigen binding domains include, *inter alia*, scFv, SdAb, Vβ-only domains, and TCR antigen binding domains derived from the TCR α and β chain variable domains.

[0159] Any type of antigen binding domain is envisaged as within the scope of the instant disclosure.

[0160] For example, the first extracellular ligand binding domain may be part of a contiguous polypeptide chain including, for example, a Vβ-only domain, a single domain antibody fragment (sdAb) or heavy chain antibodies HCAb, a single chain antibody (scFv) derived from a murine, humanized or human antibodies (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, N.Y.; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, N.Y.; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426). In some aspects, the first extracellular ligand binding domain comprises an antigen binding domain that comprises an antibody fragment. In further aspects, the first extracellular ligand binding domain comprises an antibody fragment that comprises a scFv or an sdAb.

[0161] The term "antibody," as used herein, refers to a protein, or polypeptide sequences derived from an immunoglobulin molecule, which specifically binds to an antigen. Antibodies can be intact immunoglobulins of polyclonal or monoclonal origin, or fragments thereof and can be derived from natural or from recombinant sources.

[0162] The terms "antibody fragment" or "antibody binding domain" refer to at least one portion of an antibody, or recombinant variants thereof, that contains the antigen binding domain, *i.e.*, an antigenic determining variable region of an intact antibody, that is sufficient to confer recognition and specific binding of the antibody fragment to a target, such as an antigen and its defined epitope. Examples of antibody fragments include, but are not limited to, Fab, Fab′, F(ab′)2, and Fv fragments, single-chain (sc)Fv ("scFv") antibody fragments, linear antibodies, single domain antibodies (abbreviated "sdAb") (either VL or VH), camelid VHH domains, and multi-specific antibodies formed from antibody fragments.

[0163] The term "scFv" refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein the light and heavy chain variable regions are contiguously linked via a short flexible polypeptide linker, and capable of being expressed as a single polypeptide chain, and wherein the scFv retains the specificity of the intact antibody from which it is derived.

[0164] "Heavy chain variable region" or "VH" (or, in the case of single domain antibodies, *e.g.*, nanobodies, "VHH") with regard to an antibody refers to the fragment of the heavy chain that contains three CDRs interposed between flanking stretches known as framework regions, these framework regions are generally more highly conserved than the CDRs and form a scaffold to support the CDRs.

[0165] Unless specified, as used herein a scFv may have the VL and VH variable regions in either order, *e.g.*, with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

[0166] In some embodiments, the antigen binding domain of the activator and/or inhibitory receptor comprises an scFv. In some embodiments, the scFv comprises a VL and VH region joined by a linker. In some embodiments, the linker comprises a glycine serine linker, for example GGGGSGGGGSGGGGSGG (SEQ ID NO: 152). In some embodiments, the scFv further comprises a signal sequence at the N terminus of the scFv. Exemplary signal sequences include MDMRVPAQLLGLLLLWLRGARC (SEQ ID NO: 362), which is encoded by ATGGACATGAGGGTCCCCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCGAG GTGCCAGATGT (SEQ ID NO: 153).

[0167] The term "antibody light chain," refers to the smaller of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations. Kappa ("K") and lambda ("λ") light chains refer to the two major antibody light chain isotypes.

[0168] The term "recombinant antibody" refers to an antibody that is generated using recombinant DNA technology, such as, for example, an antibody expressed by a bacteriophage or yeast expression system. The term should also be construed to mean an antibody which has been generated by the synthesis of a DNA molecule encoding the antibody and which DNA molecule expresses an antibody protein, or an amino acid sequence specifying the antibody, wherein the DNA or amino acid sequence has been obtained using recombinant DNA or amino acid sequence technology which is available and well known in the art.

[0169] The term "Vβ domain", "Vβ-only domain", "β chain variable domain" or "single variable domain TCR (svd-TCR)" refers to an antigen binding domain that consists essentially of a single T Cell Receptor (TCR) beta variable domain that specifically binds to an antigen in the absence of a second TCR variable domain. The Vβ-only domain engages antigen using complementarity-determining regions (CDRs). Each Vβ-only domain contains three complement determining regions (CDR1, CDR2, and CDR3). Additional elements may

be combined provided that the Vβ domain is configured to bind the epitope in the absence of a second TCR variable domain.

[0170] In some embodiments, the extracellular ligand binding domain of the first receptor comprises an antibody fragment, a single chain Fv antibody fragment (scFv), or a β chain variable domain (Vβ).

[0171] In some embodiments, the extracellular ligand binding domain of the first receptor comprises a TCR α chain variable domain and a TCR β chain variable domain.

[0172] In some embodiments, the extracellular ligand binding domain of the first receptor comprises an scFv antigen binding domain. Exemplary MSLN scFv are shown in Table 1 below.

Table 1: Exemplary MSLN scFv domains

	Protein Sequence	DNA Sequence
M5	QVQLVQSGAEV EKPGASVKVSCK ASGYTFTDYYM HWVRQAPGQGL EWMGWINPNSG GTNYAQKFQGR VTMTRDTSISTA YMELSRLRSDDT AVYYCASGWDF DYWGQGTLVTV SSGGGGSGGGGS GGGGSGGDIVM TQSSSLSASVGD RVTITCRASQSIR YYLSWYQQKPG KAPKLLIYTASIL QNGVPSRFSGSG SGTDFTLTISSLQ PEDFATYYCLQT YTTPDFGPGTKV EIK (SEQ ID NO: 3)	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGGA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATACACCTTCACCGACTACTATATGCACT GGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGG ATGGGATGGATCAACCCTAACAGTGGTGGCACAAA CTATGCACAGAAGTTTCAGGGCAGGGTCACCATGA CCAGGGACACGTCCATCAGCACAGCCTACATGGAG CTGAGCAGGCTGAGATCTGACGACACGGCCGTGTA TTACTGTGCGTCTGGCTGGGACTTTGACTACTGGGG CCAGGGAACCCTGGTCACCGTGTCCTCAGGCGGAG GTGGAAGCGGAGGGGGAGGATCTGGCGGCGGAGG AAGCGGAGGCGACATCGTGATGACCCAGTCTTCCT CCCTGTCTGCATCTGTCGGAGACAGAGTCACCATCA CTTGCCGGGCCAGTCAGAGCATTAGGTACTATTTAA GTTGGTATCAGCAGAAACCAGGAAAAGCCCCTAAG CTCCTGATCTATACTGCATCCATTTTACAAAATGGG GTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGAC AGATTTCACTCTCACCATCAGCAGCCTGCAACCTGA GGATTTTGCAACTTATTACTGCCTCCAGACTTACAC TACTCCGGACTTTGGCCCAGGGACCAAGGTGGAAA TCAAA (SEQ ID NO: 363)
M14	QVQLVQSGAEV RAPGASVKISCK ASGFTFRGYYIH WVRQAPGQGLE WMGIINPSGGSR AYAQKFQGRVT MTRDTSTSTVY MELSSLRSDDTA MYYCARTASCG GDCYYLDYWGQ	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAG GGCACCTGGGGCCTCAGTGAAGATTTCCTGCAAGG CTTCTGGATTCACCTTCAGAGGCTACTATATCCACT GGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGG ATGGGAATCATCAACCCTAGTGGTGGTAGCAGAGC CTACGCACAGAAGTTCCAGGGCAGGGTCACCATGA CCAGGGACACTTCCACGAGCACAGTCTACATGGAG CTGAGCAGCCTGAGATCTGACGACACGGCCATGTA TTACTGTGCGAGAACCGCAAGTTGTGGTGGTGACTG CTACTACCTTGACTACTGGGGCCAGGGAACCCTGGT

	GTLVTVSSGGGG SGGGGSGGGGS GGDIQMTQSPPT LSASVGDRVTIT CRASENVNIWLA WYQQKPGKAPK LLIYKSSSLASGV PSRFSGSGSGAEF TLTISSLQPDDFA TYYCQQYQSYPL TFGGGTKVEIK (SEQ ID NO 4)	CACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGG GAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATC CAGATGACCCAGTCTCCTCCCACCCTGTCTGCATCT GTAGGAGACAGAGTCACCATCACTTGCCGGGCCAG TGAGAATGTTAATATCTGGTTGGCCTGGTATCAGCA GAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATA AGTCATCCAGTTTAGCAAGTGGGGTCCCATCAAGGT TCAGTGGCAGTGGATCTGGGGCAGAATTCACTCTCA CCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTT ATTACTGCCAACAGTATCAAAGTTACCCCCTCACTT TCGGCGGAGGGACCAAGGTGGAAATCAAA (SEQ ID NO: 364)
S5H	QVQLVQSGAEV KKPGASVKVSC KASGYSFTGYT MNWVRQAPGQR LEWMGLITPYNG ASSYNQKFRGRV TITRDTSASTAY MELSSLRSEDTA VYYCARGGYDG RGFDYWGQGTT VTVSSGGGGSGG GGSGGGGSGGDI QMTQSPSSLSAS VGDRVTITCSAS SSVSYMHWYQQ KPGKAPKRLIYD TSKLASGVPSRF SGSGSGTEFTLTI SSLQPEDFATYY CQQWSGYPLTF GQGTKLEIK (SEQ ID NO: 5)	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTTTCCTGCAAGG CTTCTGGATACTCATTCACCGGCTACACCATGAACT GGGTGAGGCAGGCCCCTGGACAAAGACTTGAGTGG ATGGGACTTATCACCCCTTACAATGGTGCTTCTAGC TACAACCAGAAGTTCAGGGGCAGGGTCACAATCAC TAGAGACACGTCAGCCAGCACAGCCTACATGGAGC TCTCCAGCCTGAGATCTGAAGACACTGCAGTCTATT ACTGTGCAAGGGGGGGTTACGACGGGAGGGGTTTT GACTACTGGGGCCAGGGAACCACGGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGACATCCAGATGACC CAGTCTCCTTCAAGCTTGTCTGCATCTGTAGGAGAC AGGGTCACCATCACTTGCAGTGCCAGCTCAAGTGTA AGTTACATGCACTGGTATCAGCAGAAACCAGGCAA GGCCCCTAAGAGATTGATCTATGACACATCCAAATT AGCAAGTGGGGTCCCAAGTCGCTTCAGTGGCAGTG GATCTGGGACCGAATTCACTCTCACCATCAGCAGCT TGCAGCCTGAGGATTTTGCAACTTATTACTGCCAGC AGTGGAGTGGTTACCCTCTCACGTTCGGTCAGGGGA CAAAGTTGGAAATCAAA (SEQ ID NO: 365)
S5M	QVQLQQSGPELE KPGASVKISCKA SGYSFTGYTMN WVKQSHGKSLE WIGLITPYNGAS SYNQKFRGKATL TVDKSSSTAYM DLLSLTSEDSAV YFCARGGYDGR GFDYWGQGTTV TVSSGGGGSGGG GSGGGGSGGDIE	CAGGTGCAGCTGCAGCAGTCTGGGCCTGAGCTGGA GAAGCCTGGGGCCTCAGTGAAGATTTCCTGCAAGG CTTCTGGATACTCATTCACCGGCTACACCATGAACT GGGTGAAGCAGAGCCATGGAAAAAGCCTTGAGTGG ATTGGACTTATCACCCCTTACAATGGTGCTTCTAGC TACAACCAGAAGTTCAGGGGCAAGGCCACATTAAC TGTAGACAAGTCATCCAGCACAGCCTACATGGACC TCCTCAGCCTGACATCTGAAGACTCTGCAGTCTATT TCTGTGCAAGGGGGGGTTACGACGGGAGGGGTTTT GACTACTGGGGCCAGGGAACCACGGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGACATCGAGCTCACC CAGTCTCCTGCAATCATGTCTGCATCTCCAGGAGAG

	LTQSPAIMSASP GEKVTMTCSASS SVSYMHWYQQK SGTSPKRWIYDT SKLASGVPGRFS GSGSGNSYSLTIS SVEAEDDATYY CQQWSGYPLTF GAGTKLEIK (SEQ ID NO: 6)	AAGGTCACCATGACTTGCAGTGCCAGCTCAAGTGT AAGTTACATGCACTGGTATCAGCAGAAATCAGGCA CCTCCCCTAAGAGATGGATCTATGACACATCCAAAT TGGCAAGTGGGGTCCCAGGTCGCTTCAGTGGCAGT GGATCTGGGAACTCTTACTCTCTCACCATCAGCAGC GTGGAGGCTGAGGATGATGCAACTTATTACTGCCA GCAGTGGAGTGGTTACCCTCTCACGTTCGGTGCTGG GACAAAGTTGGAAATCAAA (SEQ ID NO: 366)
SS1	QVQLQQSGPELE KPGASVKISCKA SGYSFTGYTMN WVKQSHGKSLE WIGLITPYNGAS SYNQKFRGKATL TVDKSSSTAYM DLLSLTSEDSAV YFCARGGYDGR GFDYWGQGTTV TVSSGGGGSGGG GSGGGGSDIELT QSPAIMSASPGE KVTMTCSASSSV SYMHWYQQKSG TSPKRWIYDTSK LASGVPGRFSGS GSGNSYSLTISSV EAEDDATYYCQ QWSGYPLTFGA GTKLEI (SEQ ID NO: 80	ND
1	EVQLVESGGGLVKP GGSLRLSCAASGFTF SNAWMSWVRQAP GKGLEWVGRIKSKT DGGTTDYAAPVKGR FTISRDDSKNTLYLQ MNSLKTEDTAVYYC TTDLPKLRNFHIWG QGTLVTVSSGGGGS GGGGSGGGGSGGDI QMTQSPSSLSASVG DRVTITCRASQSISSY LNWYQQKPGKAPKL LIYAASSLQSGVPSRF SGSGSGTDFTLTISSL	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCTCGAACGCCTGGATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTCGGACGGATCAAGAGCAAGACCGACGG CGGCACCACCGACTACGCTGCCCCCGTGAAGGGCCGGTTCACC ATCAGCCGGGACGACAGCAAGAACACCCTGTACCTGCAGATGA ACAGCCTGAAAACCGAGGACACCGCCGTGTATTACTGTACCAC AGATCTTCCTAAGCTTAGGAATTTTCATATTTGGGGCCAGGGAA CCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGG GAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGA CCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAA TTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAG TGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTC

	QPEDFATYYCQQSYS TPLTFGGGTKVEIK (SEQ ID NO: 154)	TGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTAC AGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCA AG (SEQ ID NO: 367)
2	EVQLVESGGGLVQP GGSLRLSCAASGFTF SSYAMHWVRQAPG KGLEYVSAISSNGGS TYYANSVKGRFTISR DNSKNTLYLQMGSL RAEDMAVYYCASLE YHGFRQYGLRYWH WGQGTLVTVSSGG GGSGGGGSGGGGS GGDIQMTQSPSSLS ASVGDRVTITCRASQ SISSYLNWYQQKPGK APKLLIYAASSLQSGV PSRFSGSGSGTDFTL TISSLQPEDFATYYCQ QSYSTPLTFGGGTKV EIK (SEQ ID NO: 155)	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGCACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATACGTGTCCGCCATCAGCTCGAACGGCGGCAGC ACCTACTACGCCAACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACAGCAAGAACACCCTGTACCTGCAGATGGGCAGCCT GCGGGCCGAGGATATGGCCGTGTATTACTGTGCGAGCCTAGAA TACCATGGCTTTCGACAATATGGGCTTCGTTATTGGCATTGGGG CCAGGGAACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGC GGAGGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACAT CCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAG ACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAG CTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAG CTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATC AAGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACC ATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCA ACAGAGTTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAG GTGGAGATCAAG (SEQ ID NO: 368)
3	QLQLQESGSGLVKPS QTLSLTCAVSGGSISS GGYSWSWIRQPPGK GLEWIGYIYHSGSTY YNPSLKSRVTISVDRS KNQFSLKLSSVTAAD TAVYYCASIKFWFAG INYFFPWGQGTLVT VSSGGGGSGGGGSG GGGSGGDIQMTQS PSSLSASVGDRVTITC RASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 156)	CAGCTGCAGCTCCAGGAAAGCGGCAGCGGCCTGGTGAAACCC AGCCAGACCCTGAGCCTGACCTGTGCCGTGTCCGGCGGCAGCA TCAGCAGCGGCGGCTACAGCTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCTACCACAGCGGC TCGACCTACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCAG CGTGGACAGAAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAG CGTGACAGCCGCCGACACCGCTGTGTATTACTGTGCCAGCATAA AATTCTGGTTTGCGGGGATTAATTATTTTTTTCCGTGGGGCCAG GGAACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGA GGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCA GATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACA GAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTA TTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTC CTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAG GTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCA GCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAG AGTTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGG AGATCAAG (SEQ ID NO: 369)
4	EVQLVESGGGLVQP GGSLRLSCAASGFTF SSYWMHWVRQAP GKGLVWVSRINSDG SSTSYADSVKGRFTIS RDNAKNTLYLQMNS LRAEDTAVYYCASGF	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACTGGATGCACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGTCTGGGTGTCTCGAATCAACAGCGACGGCAGCAGC ACCAGCTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACACCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCAAGCGGATTT

	LGMGSNFIWGQGTL VTVSSGGGGSGGGG SGGGGSGGDIQMT QSPSSLSASVGDRVT ITCRASQSISSYLNWY QQKPGKAPKLLIYAA SSLQSGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQSYSTPLT FGGGTKVEIK (SEQ ID NO: 157)	TTGGGAATGGGCTCGAATTTTATTTGGGGCCAGGGAACCCTGG TCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGT CTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATC ACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTA TCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCT GCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCA GTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAA CCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTAC CCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 370)
5	QVQLQESGPGLVKP SQTLSLTCTVSGGSIS SGGYYWSWIRQHP GKGLEWIGYIYYSGS TYYNPSLKSLVTISVD TSKNQFSLKLSSVTA ADTAVYYCASGDRA RYFDLWGRGTLVTV SSGGGGSGGGGSG GGGSGGDIQMTQS PSSLSASVGDRVTITC RASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 158)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCCAGACCCTGAGCCTGACCTGCACAGTGTCCGGCGGCAGCA TCAGCAGCGGCGGCTACTACTGGTCCTGGATCAGACAGCACCC CGGCAAGGGCCTGGAATGGATCGGCTACATCTACTACAGCGGC AGCACCTACTACAACCCCAGCCTGAAGTCCCTGGTGACAATCTC CGTCGATACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGC GTGACAGCCGCCGACACCGCTGTGTATTACTGTGCAAGCGGGG ACAGGGCACGGTACTTCGATCTCTGGGGCCGTGGCACCCTGGT CACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTC TCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCA CTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTAT CAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTG CATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAG TGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAAC CTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACC CCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 371)
6	EVQLVESGGGLVQP GGSLRLSCAASGFTF SSYWMHWVRQAP GKGLVWVSRINSDG SSTSYADSVKGRFTIS RDNAKNTLYLQMNS LRAEDTAVYYCARYP RGYHQMVDAFDIW GQGTMVTVSSGGG GSGGGGSGGGGSG GDIQMTQSPSSLSAS VGDRVTITCRASQSI SSYLNWYQQKPGKA PKLLIYAASSLQSGVP SRFSGSGSGTDFTLTI SSLQPEDFATYYCQQ SYSTPLTFGGGTKVEI K (SEQ ID NO: 159)	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACTGGATGCACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGTCTGGGTGTCTCGAATCAACAGCGACGGCAGCAGC ACCAGCTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACACCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCAAGATATCCA CGTGGATATCATCAGATGGTTGATGCTTTTGATATCTGGGGCCA AGGGACAATGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGG AGGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCC AGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGAC AGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCT ATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCT CCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAA GGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC AGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACA GAGTTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTG GAGATCAAG (SEQ ID NO: 372)

7	QLQLQESGPGLVKPS ETLSLTCTVSGGSISS SSYYWGWIRQPPGK GLEWIGSIYYSGSTYY NPSLKSRVTISVDTSK NQFSLKLSSVTAADT AVYYCARVRFLAART TIPEANFLWGQGTL VTVSSGGGGSGGGG SGGGGSGGDIQMT QSPSSLSASVGDRVT ITCRASQSISSYLNWY QQKPGKAPKLLIYAA SSLQSGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQSYSTPLT FGGGTKVEIK (SEQ ID NO: 160)	CAGCTGCAGCTCCAGGAAAGCGGCCCTGGCCTGGTGAAACCCA GCGAGACACTGAGCCTGACCTGCACCGTGTCCGGCGGCAGCAT CAGCAGCAGCAGCTACTACTGGGGCTGGATCAGACAGCCCCCT GGCAAGGGCCTGGAATGGATCGGCTCGATCTACTACAGCGGCT CCACCTACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCAGC GTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCG TGACAGCCGCCGACACCGCTGTGTATTACTGTGCGAGAGTACG ATTTTTGGCTGCTCGCACTACTATTCCGGAGGCGAATTTTCTTTG GGGCCAGGGAACCCTGGTCACCGTGTCCTCAGGCGGAGGTGG AAGCGGAGGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCG ACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAG GAGACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAG CAGCTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCT AAGCTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCC ATCAAGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCA CCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGT CAACAGAGTTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAA GGTGGAGATCAAG (SEQ ID NO: 373)
8	EVQLVESGGGLVQP GGSLRLSCAASGFTF SSYSMNWVRQAPG KGLEWVSYISSSSSTI YYADSVKGRFTISRD NAKNSLYLQMNSLR AEDTAVYYCARVLSR ARFDYWGQGTLVTV SSGGGGSGGGGSG GGGSGGDIQMTQS PSSLSASVGDRVTITC RASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 161)	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACAGCATGAACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCAGCTCCACC ATCTACTACGCCGACAGCGTGAAGGGTCGATTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGTACTC TCCAGGGCTAGGTTTGACTACTGGGGCCAGGGAACCCTGGTCA CCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTCTC CATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACT TGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCA GCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCA TCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTG GATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCT GAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCC TCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 374)
9	EVQLVESGGGLVKP GGSLRLSCAASGFTF SSYSMNWVRQAPG KGLEWVSSISSSSSYI YYADSVKGRFTISRD NAKNSLYLQMNSLR AEDTAVYYCARLRGR VFDPWGQGTLVTVS SGGGGSGGGGSGG GGSGGDIQMTQSPS SLSASVGDRVTITCR	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACAGCATGAACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTCGATCAGCAGCAGCAGCTCCTAC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGATTACGA GGGAGGGTGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACC GTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGGC GGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTCTCCA TCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTG

	ASQSISSYLNWYQQ KPGKAPKLLIYAASSL QSGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 162)	CCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAG CAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCATC CAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGA TCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGA AGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCCTCT CACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 375)
10	QLQLQESGPGLVKPS ETLSLTCTVSGGSISS SSYYWGWIRQPPGK GLEWIGSIYYSGSTYY NPSLKSRVTISVDTSK NQFSLKLSSVTAADT AVYYCARIKFTSFLYV HGFLWGQGTLVTVS SGGGGSGGGGSGG GGSGGDIQMTQSPS SLSASVGDRVTITCR ASQSISSYLNWYQQ KPGKAPKLLIYAASSL QSGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 163)	CAGCTGCAGCTCCAGGAAAGCGGCCCTGGCCTGGTGAAACCCA GCGAGACACTGAGCCTGACCTGCACCGTGTCCGGCGGCAGCAT CAGCAGCAGCAGCTACTACTGGGGCTGGATCAGACAGCCCCCT GGCAAGGGCCTGGAATGGATCGGCTCGATCTACTACAGCGGCT CCACCTACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCAGC GTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCG TGACAGCCGCCGACACCGCTGTGTATTACTGTGCGAGAATAAA ATTTACCAGCTTTTTATATGTTCATGGTTTTCTGTGGGGCCAGG GAACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAG GGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAG ATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAG AGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATT TAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT GATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGT TCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC AGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAG TTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAG ATCAAG (SEQ ID NO: 376)
11	QVQLVQSGAEVKKP GASVKVSCKASGYTF TSYAMHWVRQAPG QRLEWMGWINAG NGNTKYSQKFQGRV TITRDTSASTAYMEL SSLRSEDTAVYYCAR GQRWLYLGGIRRH WGQGTLVTVSSGG GGSGGGGSGGGGS GGDIQMTQSPSSLS ASVGDRVTITCRASQ SISSYLNWYQQKPGK APKLLIYAASSLQSGV PSRFSGSGSGTDFTL TISSLQPEDFATYYCQ QSYSTPLTFGGGTKV EIK (SEQ ID NO: 164)	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCT GGCGCCTCCGTGAAGGTGTCCTGCAAGGCCAGCGGCTACACCT TCACCAGCTACGCCATGCACTGGGTTCGACAGGCCCCTGGCCA GAGACTGGAATGGATGGGCTGGATCAACGCCGGCAACGGCAA CACCAAGTACAGCCAGAAATTCCAGGGCAGAGTGACCATCACC CGGGACACCAGCGCCAGCACCGCCTACATGGAACTGAGCAGCC TGCGGAGCGAGGACACCGCTGTGTATTACTGTGCGAGAGGCCA GAGATGGCTGTACCTCGGGGGGATTCGTCGGCATTGGGGCCA GGGAACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGG AGGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCC AGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGAC AGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCT ATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCT CCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAA GGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC AGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACA GAGTTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTG GAGATCAAG (SEQ ID NO: 377)
12	QVQLQESGPGLVKP SETLSLTCTVSGGSIS SYYWSWIRQPPGKG	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCGAGACACTGAGCCTGACCTGCACCGTGTCCGGCGGCAGCA TCAGCAGCTACTACTGGTCCTGGATCAGACAGCCCCCTGGCAA

	LEWIGYIYYSGSTNY NPSLKSRVTISVDTSK NQFSLKLSSVTAADT AVYYCAREWIPSRPY YFDYWGQGTLVTVS SGGGGSGGGGSGG GGSGGDIQMTQSPS SLSASVGDRVTITCR ASQSISSYLNWYQQ KPGKAPKLLIYAASSL QSGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 165)	GGGCCTGGAATGGATCGGCTACATCTACTACAGCGGCAGCACC AACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCTCCGTCGA TACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACA GCCGCCGACACCGCTGTGTATTACTGTGCGAGAGAATGGATTC CCAGCCGTCCGTACTACTTTGACTACTGGGGCCAGGGAACCCTG GTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGA TCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAG TCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGT ATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGC TGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA ACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTA CCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 378)
13	QVQLQESGPGLVKP SQTLSLTCTVSGGSIS SGGYYWSWIRQPPG KGLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCARESTGTGA FDIWGQGTMVTVSS GGGGSGGGGSGGG GSGGDIQMTQSPSS LSASVGDRVTITCRA SQSISSYLNWYQQKP GKAPKLLIYAASSLQS GVPSRFSGSGSGTDF TLTISSLQPEDFATYY CQQSYSTPLTFGGGT KVEIK (SEQ ID NO: 166)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCCAGACCCTGAGCCTGACCTGCACAGTGTCCGGCGGCTCGA TCAGCAGCGGCGGCTACTACTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCTACTACAGCGGC AGCACCTACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCA GCGTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAG CGTGACAGCCGCCGACACCGCTGTGTATTACTGTGCGAGAGAA AGTACCGGTACAGGAGCTTTTGATATCTGGGGCCAAGGGACAA TGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCC AGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACC ATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTG GTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTAT GCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTG GCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTG CAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAG TACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 379)
14	EVQLVESGGGVVRP GGSLRLSCAASGFTF DDYGMSWVRQAPG KGLEWVSGINWNG GSTGYADSVKGRFTI SRDNAKNSLYLQMN SLRAEDTALYHCARE RYRRVLHWYFDLW GRGTLVTVSSGGGG SGGGGSGGGGSGG DIQMTQSPSSLSASV GDRVTITCRASQSISS YLNWYQQKPGKAPK LLIYAASSLQSGVPSR	GAAGTGCAGCTGGTGGAAAGCGGAGGCGGAGTGGTTCGACCT GGCGGAAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TTGACGACTACGGCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCGGCATCAACTGGAACGGCGGCAG CACCGGCTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCTTGTATCACTGTGCGAGAGAGAG GTACAGGCGGGTACTCCACTGGTACTTCGATCTCTGGGGCCGT GGCACCCTGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGA GGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCA GATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACA GAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTA TTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTC CTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAG

	FSGSGSGTDFTLTISS LQPEDFATYYCQQSY STPLTFGGGTKVEIK (SEQ ID NO: 167)	GTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCA GCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAG AGTTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGG AGATCAAG (SEQ ID NO: 380)
15	QVQLVQSGAEVKKP GASVKVSCKASGYTF TSYDINWVRQATGQ GLEWMGWMNPNS GNTGYAQKFQGRVT MTRNTSISTAYMELS SLRSEDTAVYYCARE PDAFDIWGQGTMV TVSSGGGGSGGGGS GGGGSGGDIQMTQ SPSSLSASVGDRVTIT CRASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 168)	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCT GGCGCCTCCGTGAAGGTGTCCTGCAAGGCCAGCGGCTACACCT TCACCAGCTACGACATCAACTGGGTCCGCCAGGCCACCGGACA GGGCCTGGAATGGATGGGCTGGATGAACCCCAACAGCGGCAA CACCGGCTACGCCCAGAAATTCCAGGGCAGAGTGACCATGACC CGGAACACCTCGATCAGCACCGCCTACATGGAACTGAGCAGCC TGCGGAGCGAGGACACCGCTGTGTATTACTGTGCGAGAGAACC GGATGCTTTTGATATCTGGGGCCAAGGGACAATGGTCACCGTG TCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGGCGG CGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTCTCCATCC TCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCG GGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAG AAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCATCCAG TTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCT GGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGA TTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCCTCTCAC TTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 381)
16	QVQLQESGPGLVKP SQTLSLTCTVSGGSIS SGGYYWSWIRQPPG KGLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCAREHMGTI PYYFDYWGQGTLVT VSSGGGGSGGGGSG GGGSGGDIQMTQS PSSLSASVGDRVTITC RASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 169)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCCAGACCCTGAGCCTGACCTGCACAGTGTCCGGCGGCTCGA TCAGCAGCGGCGGCTACTACTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCTACTACAGCGGC AGCACCTACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCA GCGTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAG CGTGACAGCCGCCGACACCGCTGTGTATTACTGTGCGAGAGAA CATATGGGGACGATTCCGTACTACTTTGACTACTGGGGCCAGG GAACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAG GGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAG ATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAG AGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATT TAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT GATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGT TCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC AGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAG TTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAG ATCAAG (SEQ ID NO: 382)
17	QVQLQESGPGLVKP SQTLSLTCTVSGGSIS SGGYYWSWIRQPPG KGLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCAREEFGYGD	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCCAGACCCTGAGCCTGACCTGCACAGTGTCCGGCGGCTCGA TCAGCAGCGGCGGCTACTACTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCTACTACAGCGGC AGCACCTACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCA GCGTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAG CGTGACAGCCGCCGACACCGCTGTGTATTACTGTGCGAGAGAA

	VLYWGQGTLVTVSS GGGGSGGGGSGGG GSGGDIQMTQSPSS LSASVGDRVTITCRA SQSISSYLNWYQQKP GKAPKLLIYAASSLQS GVPSRFSGSGSGTDF TLTISSLQPEDFATYY CQQSYSTPLTFGGGT KVEIK (SEQ ID NO: 170)	GAGTTTGGTTATGGGGACGTCCTCTACTGGGGCCAGGGAACCC TGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCC AGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACC ATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTG GTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTAT GCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTG GCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTG CAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAG TACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 383)
18	QVQLQESGPGLVKP SQTLSLTCTVSGGSIS SGDYYWSWIRQPPG KGLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCAREDVVKG AFDIWGQGTMVTV SSGGGGSGGGGSG GGGSGGDIQMTQS PSSLSASVGDRVTITC RASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 171)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCCAGACCCTGAGCCTGACCTGCACAGTGTCCGGCGGCAGCA TCAGCAGCGGCGACTACTACTGGTCCTGGATCAGACAGCCCCCT GGCAAGGGCCTGGAATGGATCGGCTACATCTACTACAGCGGCA GCACCTACTACAACCCCAGCCTGAAGTCTCGAGTGACCATCAGC GTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCG TGACAGCCGCCGACACCGCTGTGTATTACTGTGCCAGAGAGGA CGTAGTCAAAGGCGCTTTTGATATCTGGGGCCAAGGGACAATG GTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGA TCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAG TCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGT ATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGC TGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA ACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTA CCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 384)
19	EVQLVESGGGLVQP GGSLRLSCAASGFTF SSYSMNWVRQAPG KGLEWVSYISSSSSTI YYADSVKGRFTISRD NAKNSLYLQMNSLR AEDTAVYYCAREDFS HKLGYFQHWGQGT LVTVSSGGGGSGGG GSGGGGSGGDIQM TQSPSSLSASVGDRV TITCRASQSISSYLNW YQQKPGKAPKLLIYA ASSLQSGVPSRFSGS GSGTDFTLTISSLQPE DFATYYCQQSYSTPL TFGGGTKVEIK (SEQ ID NO: 172)	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACAGCATGAACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCAGCTCCACC ATCTACTACGCCGACAGCGTGAAGGGTCGATTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGAAGA CTTCTCGCATAAGCTAGGGTACTTCCAGCACTGGGGCCAGGGC ACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGG GGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGAT GACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAG TCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTA AATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA TCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCA GTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGT TACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGA TCAAG (SEQ ID NO: 385)

20	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARDYDY VWGQGTLVTVSSG GGGSGGGGSGGGG SGGDIQMTQSPSSLS ASVGDRVTITCRASQ SISSYLNWYQQKPGK APKLLIYAASSLQSGV PSRFSGSGSGTDFTL TISSLQPEDFATYYCQ QSYSTPLTFGGGTKV EIK (SEQ ID NO: 173)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGATTAC GATTACGTGTGGGGCCAGGGAACCCTGGTCACCGTGTCCTCAG GCGGAGGTGGAAGCGGAGGGGGAGGATCTGGCGGCGGAGGA AGCGGAGGCGACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCAAGT CAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAG GGAAAGCCCCTAAGCTCCTGATCTATGCTGCATCCAGTTTGCAA AGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAG ATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAA CTTACTACTGTCAACAGAGTTACAGTACCCCTCTCACTTTCGGCG GCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 386)
21	QVQLQESGPGLVKP SQTLSLTCTVSGGSIS SGDYYWSWIRQPPG KGLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCARDRRDWD WFDPWGQGTLVTV SSGGGGSGGGGSG GGGSGGDIQMTQS PSSLSASVGDRVTITC RASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 174)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCCAGACCCTGAGCCTGACCTGCACAGTGTCCGGCGGCAGCA TCAGCAGCGGCGACTACTACTGGTCCTGGATCAGACAGCCCCCT GGCAAGGGCCTGGAATGGATCGGCTACATCTACTACAGCGGCA GCACCTACTACAACCCCAGCCTGAAGTCTCGAGTGACCATCAGC GTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCG TGACAGCCGCCGACACCGCTGTGTATTACTGTGCCAGAGATCG CCGTGATTGGGACTGGTTCGACCCCTGGGGCCAGGGAACCCTG GTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGA TCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAG TCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGT ATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGC TGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA ACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTA CCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 387)
22	QVQLQESGPGLVKP SGTLSLTCAVSGGSIS SSNWWSWVRQPP GKGLEWIGEIYHSGS TNYNPSLKSRVTISV DKSKNQFSLKLSSVT AADTAVYYCARDQQ ALKYRVDWGQGTLV TVSSGGGGSGGGGS GGGGSGGDIQMTQ SPSSLSASVGDRVTIT	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCGGCACCCTGAGCCTGACCTGTGCCGTGTCTGGCGGCAGCA TCAGCAGCAGCAACTGGTGGTCCTGGGTCCGCCAGCCTCCCGG CAAGGGCCTCGAATGGATCGGCGAGATCTACCACAGCGGCAGC ACCAACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCAGCG TGGACAAGAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGT GACAGCCGCCGACACCGCTGTGTATTACTGTGCGAGAGATCAG CAGGCGTTGAAATACCGTGTGGATTGGGGCCAGGGAACCCTG GTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGA TCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAG TCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT

	CRASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 175)	CACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGT ATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGC TGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA ACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTA CCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 388)
23	QVQLVQSGAEVKKP GASVKVSCKASGYTF TSYGISWVRQAPGQ GLEWMGWISAYNG NTNYAQKLQGRVT MTTDTSTSTAYMEL RSLRSDDTAVYYCAR DLTLGCFDYWGQGT LVTVSSGGGGSGGG GSGGGGSGGDIQM TQSPSSLSASVGDRV TITCRASQSISSYLNW YQQKPGKAPKLLIYA ASSLQSGVPSRFSGS GSGTDFTLTISSLQPE DFATYYCQQSYSTPL TFGGGTKVEIK (SEQ ID NO: 176)	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCT GGCGCCTCCGTGAAGGTGTCCTGCAAGGCCAGCGGCTACACCT TCACCAGCTACGGCATCAGCTGGGTCCGCCAGGCTCCTGGACA GGGACTGGAATGGATGGGCTGGATCAGCGCCTACAACGGCAA CACCAACTACGCCCAGAAACTGCAGGGCAGAGTGACCATGACC ACCGACACCAGCACCAGCACCGCCTACATGGAACTTCGAAGCC TGAGAAGCGACGACACCGCCGTGTATTACTGTGCGAGAGATCT TACGCTAGGATGCTTTGACTACTGGGGCCAGGGAACCCTGGTC ACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCT GGCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTCT CCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCAC TTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATC AGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGC ATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGT GGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACC TGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCC CTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 389)
24	EVQLVESGGGLVQP GGSLRLSCAASGFTV SSNYMSWVRQAPG KGLEWVSVIYSGGST YYADSVKGRFTISRD NSKNTLYLQMNSLR AEDTAVYYCARDGS NSWYFDLWGRGTL VTVSSGGGGSGGGG SGGGGSGGDIQMT QSPSSLSASVGDRVT ITCRASQSISSYLNWY QQKPGKAPKLLIYAA SSLQSGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQSYSTPLT FGGGTKVEIK (SEQ ID NO: 177)	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCG TGTCCAGCAACTACATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCGTGATCTACAGCGGCGGCAGCAC CTACTACGCCGACAGCGTGAAGGGTCGATTCACCATCAGCCGG GACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCCTGC GGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGATGGGTC AAACTCTTGGTACTTCGATCTCTGGGGCCGTGGCACCCTGGTCA CTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTCTC CATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACT TGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCA GCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCA TCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTG GATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCT GAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCC TCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 390)
25	QVQLVESGGGVVQP GRSLRLSCAASGFTF SSYGMHWVRQAPG KGLEWVAVIWYDGS	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCGTGGTGCAGCCC GGCAGAAGCCTTCGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGGCATGCACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGGCCGTGATTTGGTACGACGGCAGCAA

	NKYYADSVKGRFTIS RDNSKNTLYLQMNS LRAEDTAVYYCARAF LFLSFSVWGQGTLVT VSSGGGGSGGGGSG GGGSGGDIQMTQS PSSLSASVGDRVTITC RASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 178)	CAAGTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGGGCATT TTTATTCCTGTCTTTTTCGGTTTGGGGCCAGGGAACCCTGGTCA CCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTCTC CATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACT TGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCA GCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCA TCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTG GATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCT GAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCC TCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 391)
26	EVQLVESGGVVVQP GGSLRLSCAASGFTF DDYTMHWVRQAPG KGLEWVSLISWDGG STYYADSVKGRFTISR DNSKNSLYLQMNSL RTEDTALYYCAKGIFY SSKEDFDYWGQGTL VTVSSGGGGSGGGG SGGGGSGGDIQMT QSPSSLSASVGDRVT ITCRASQSISSYLNWY QQKPGKAPKLLIYAA SSLQSGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQSYSTPLT FGGGTKVEIK (SEQ ID NO: 179)	GAAGTGCAGCTGGTGGAATCTGGCGGCGTGGTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCGACGACTACACCATGCACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCCTGATCAGCTGGGACGGCGGCTCT ACCTACTACGCCGACTCCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACAGCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGACCGAGGACACCGCCTTGTATTACTGTGCAAAAGGGATA TTCTACTCGAGTAAAGAGGATTTTGACTACTGGGGCCAGGGAA CCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGG GAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGATGA CCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAA TTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAG TGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTC TGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTAC AGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCA AG (SEQ ID NO: 392)
27	EVQLVESGGVVVQP GGSLRLSCAASGFTF DDYTMHWVRQAPG KGLEWVSLISWDGG STYYADSVKGRFTISR DNSKNSLYLQMNSL RTEDTALYYCAKDIW IFYSSNPKPTVYWGQ GTLVTVSSGGGGSG GGGSGGGGSGGDI QMTQSPSSLSASVG DRVTITCRASQSISSY LNWYQQKPGKAPKL LIYAASSLQSGVPSRF SGSGSGTDFTLTISSL	GAAGTGCAGCTGGTGGAATCTGGCGGCGTGGTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCGACGACTACACCATGCACTGGGTCCGCCAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCCTGATCAGCTGGGACGGCGGCTCT ACCTACTACGCCGACTCCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACAGCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGACCGAGGACACCGCCTTGTATTACTGTGCAAAAGATATA TGGATATTCTACTCGAGTAATCCAAAGCCGACGGTCTACTGGG GCCAGGGAACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAA GCGGAGGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGAC ATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGG AGACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGC AGCTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTA AGCTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCA TCAAGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCAC

	QPEDFATYYCQQSYS TPLTFGGGTKVEIK (SEQ ID NO: 180)	CATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTC AACAGAGTTACAGTACCCCTCTCACTTTCGGCGGCGGAACAAA GGTGGAGATCAAG (SEQ ID NO: 393)
28	QVQLVQSGSELKKP GASVKVSCKASGYTF TSYAMNWVRQAPG QGLEWMGWINTNT GNPTYAQGFTGRFV FSFDTSVSTAYLQICS LKAEDTAVYYCARKD QTLTYGNWFDPWG QGTLVTVSSGGGGS GGGGSGGGGSGGDI QMTQSPSSLSASVG DRVTITCRASQSISSY LNWYQQKPGKAPKL LIYAASSLQSGVPSRF SGSGSGTDFTLTISSL QPEDFATYYCQQSYS TPLTFGGGTKVEIK (SEQ ID NO: 181)	CAGGTGCAGCTGGTGCAGAGCGGCAGCGAGCTGAAGAAACCT GGCGCCTCCGTGAAGGTGTCCTGCAAGGCCAGCGGCTACACCT TCACCAGCTACGCCATGAACTGGGTCCGCCAGGCCCCAGGCCA GGGACTGGAATGGATGGGCTGGATCAACACCAACACCGGCAA CCCCACCTACGCCCAGGGCTTCACCGGCAGATTCGTGTTCAGCT TCGACACCAGCGTGTCCACCGCCTACCTGCAGATCTGTAGCCTG AAGGCCGAGGACACCGCCGTGTATTACTGTGCGAGGAAGGATC AGACGCTGACCTACGGAAACTGGTTCGACCCCTGGGGCCAGGG AACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGG GGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGA TGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGA GTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTT AAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTG ATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTT CAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCA GTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGT TACAGTACCCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGA TCAAG (SEQ ID NO: 394)
29	QVQLQESGPGLVKP SETLSLTCTVSGGSVS SGSYYWSWIRQPPG KGLEWIGYIYYSGST NYNPSLKSRVTISVD TSKNQFSLKLSSVTA ADTAVYYCARDHYE RGLYWGQGTLVTVS SGGGGSGGGGSGG GGSGGDIQMTQSPS SLSASVGDRVTITCR ASQSISSYLNWYQQ KPGKAPKLLIYAASSL QSGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 182)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGTGAAACCC AGCGAGACACTGAGCCTGACCTGCACCGTGTCCGGCGGCTCTG TGTCCAGCGGCTCCTACTACTGGTCCTGGATCAGACAGCCCCCT GGCAAGGGCCTCGAATGGATCGGCTACATCTACTACAGCGGCA GCACCAACTACAACCCCAGCCTGAAGTCCAGAGTGACCATCAG CGTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGC GTGACAGCCGCCGACACCGCTGTGTATTACTGTGCGAGAGATC ATTACGAGCGGGGGCTCTACTGGGGCCAGGGAACCCTGGTCAC CGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGG CGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGTCTCC ATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTT GCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCA GCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCA TCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTG GATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCT GAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCC TCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 395)
30	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARYMYN WYFDLWGRGTLVTV	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGATATATG TATAACTGGTACTTCGATCTCTGGGGCCGTGGCACCCTGGTCAC

	SSGGGGSGGGGSG GGGSGGDIQMTQS PSSVSASVGDRVTIT CRASQGISSWLAWY QQKPGKAPKLLIYAA SSLQSGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQANSFPLT FGGGTKVEIK (SEQ ID NO: 183)	TGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGG CGGCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGAGCCC CAGCAGCGTGTCCGCCAGCGTGGGCGATCGAGTGACCATCACC TGTCGGGCCTCCCAGGGCATCAGCAGCTGGCTGGCCTGGTATC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGC CAGCAGCCTGCAGAGCGGCGTGCCAAGCAGATTCAGCGGCAG CGGCTCCGGCACCGACTTCACCCTGACCATCAGCTCCCTGCAGC CCGAGGACTTCGCCACCTACTACTGCCAGCAGGCTAACAGTTTC CCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 396)
31	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARDRRP AFDIWGQGTMVTV SSGGGGSGGGGSG GGGSGGDIQMTQS PSSVSASVGDRVTIT CRASQGISSWLAWY QQKPGKAPKLLIYAA SSLQSGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQANSFPLT FGGGTKVEIK (SEQ ID NO: 184)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGATCGA AGGCCTGCTTTTGATATCTGGGGCCAAGGGACAATGGTCACCG TGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGGCG GCGGAGGAAGCGGAGGCGACATCCAGATGACCCAGAGCCCCA GCAGCGTGTCCGCCAGCGTGGGCGATCGAGTGACCATCACCTG TCGGGCCTCCCAGGGCATCAGCAGCTGGCTGGCCTGGTATCAG CAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGCCA GCAGCCTGCAGAGCGGCGTGCCAAGCAGATTCAGCGGCAGCG GCTCCGGCACCGACTTCACCCTGACCATCAGCTCCCTGCAGCCC GAGGACTTCGCCACCTACTACTGCCAGCAGGCTAACAGTTTCCC TCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 397)
32	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCAVHLKRR PYFDYWGQGTLVTV SSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 185)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGGTACATTTG AAACGACGTCCCTACTTTGACTACTGGGGCCAGGGAACCCTGG TCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCAT CACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGG TATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACG ACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGG CAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGC AGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGT TACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 398)

33	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASVHKKP IFDYWGQGTLVTVSS GGGGSGGGGSGGG GSGGAIQLTQSPSSL SASVGDRVTITCRAS QGISSALAWYQQKP GKAPKLLIYDASSLES GVPSRFSGSGSGTDF TLTISSLQPEDFATYY CQQFNSYPLTFGGG TKVEIK (SEQ ID NO: 186)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGCGTACAT AAGAAACCCATCTTTGACTACTGGGGCCAGGGAACCCTGGTCA CCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAGCC CCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATCAC CTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGTAT CAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGACG CCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGCAG CGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGC CCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTTAC CCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 399)
34	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASTSRRC TFQHWGQGTLVTVS SGGGGSGGGGSGG GGSGGAIQLTQSPSS LSASVGDRVTITCRA SQGISSALAWYQQK PGKAPKLLIYDASSLE SGVPSRFSGSGSGTD FTLTISSLQPEDFATY YCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 187)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGTACCAGT CGGCGCTGTACCTTCCAGCACTGGGGCCAGGGCACCCTGGTCA CCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAGCC CCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATCAC CTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGTAT CAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGACG CCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGCAG CGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGC CCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTTAC CCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 400)
35	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASTSPRP LFQHWGQGTLVTVS SGGGGSGGGGSGG GGSGGAIQLTQSPSS LSASVGDRVTITCRA	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGTACCAGC CCGCGTCCTCTCTTCCAGCACTGGGGCCAGGGCACCCTGGTCAC CGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGG CGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAGCCC CAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATCACC

	SQGISSALAWYQQK PGKAPKLLIYDASSLE SGVPSRFSGSGSGTD FTLTISSLQPEDFATY YCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 188)	TGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGTATC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGACGC CAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGCAGC GGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCC CGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTTACC CTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 401)
36	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASPYQVR GVYFDYWGQGTLVT VSSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 189)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGCCCTTAC CAAGTCCGAGGAGTCTACTTTGACTACTGGGGCCAGGGAACCC TGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCC AGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGA CCATCACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGC CTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATC TACGACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCA GCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAG CCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTA ATAGTTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGAT CAAG (SEQ ID NO: 402)
37	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASPYKKR RTVFDYWGQGTLVT VSSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 190)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGCCCCTAT AAGAAACGACGAACGGTCTTTGACTACTGGGGCCAGGGAACCC TGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCC AGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGA CCATCACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGC CTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATC TACGACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCA GCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAG CCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTA ATAGTTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGAT CAAG (SEQ ID NO: 403)
38	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC

	YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASLQRGL ALFQHWGQGTLVT VSSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 191)	ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGTCTTTACAG CGCGGGCTGGCCCTCTTCCAGCACTGGGGCCAGGGCACCCTGG TCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCAT CACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGG TATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACG ACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGG CAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGC AGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGT TACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 404)
39	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASILSVPY FDLWGRGTLVTVSS GGGGSGGGGSGGG GSGGAIQLTQSPSSL SASVGDRVTITCRAS QGISSALAWYQQKP GKAPKLLIYDASSLES GVPSRFSGSGSGTDF TLTISSLQPEDFATYY CQQFNSYPLTFGGG TKVEIK (SEQ ID NO: 192)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCTAGCATATTG TCAGTTCCGTACTTCGATCTCTGGGGCCGTGGCACCCTGGTCAC TGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGG CGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAGCCC CAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATCACC TGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGTATC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGACGC CAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGCAGC GGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCC CGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTTACC CTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 405)
40	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCASGWIR VPLRLPLFQHWGQG TLVTVSSGGGGSGG GGSGGGGSGGAIQL TQSPSSLSASVGDRV TITCRASQGISSALA WYQQKPGKAPKLLI YDASSLESGVPSRFS GSGSGTDFTLTISSLQ	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGTGGGTG GATTCGTGTACCTTTACGATTGCCCCTCTTCCAGCACTGGGGCC AGGGCACCCTGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCG GAGGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATC CAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGC GATAGAGTGACCATCACCTGTCGCGCCAGCCAGGGCATCAGCA GCGCTCTGGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAA GCTGCTGATCTACGACGCCAGCTCCCTGGAAAGCGGCGTGCCC AGCAGATTCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGA

	PEDFATYYCQQFNSY PLTFGGGTKVEIK (SEQ ID NO: 193)	CCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGC CAGCAGTTTAATAGTTACCCTCTCACTTTCGGCGGCGGAACAAA GGTGGAGATCAAG (SEQ ID NO: 406)
41	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARVTIFAI FDIWGQGTMVTVSS GGGGSGGGGSGGG GSGGAIQLTQSPSSL SASVGDRVTITCRAS QGISSALAWYQQKP GKAPKLLIYDASSLES GVPSRFSGSGSGTDF TLTISSLQPEDFATYY CQQFNSYPLTFGGG TKVEIK (SEQ ID NO: 194)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGTAACC ATATTTGCGATATTTGATATCTGGGGCCAAGGGACAATGGTCAC CGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTGG CGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAGCCC CAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATCACC TGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGTATC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGACGC CAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGCAGC GGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCC CGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTTACC CTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 407)
42	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARVGRG FVHFDLWGRGTLVT VSSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 195)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGTGGG ACGTGGATTCGTTCATTTTGATCTCTGGGGCCGTGGCACCCTGG TCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCAT CACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGG TATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACG ACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGG CAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGC AGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGT TACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 408)
43	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARTSRGL CVLFDYWGQGTLVT	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGGACGTCA AGAGGTTTGTGTGTTTTATTTGACTACTGGGGCCAGGGAACCCT

	VSSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 196)	GGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCC AGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGA CCATCACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGC CTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATC TACGACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCA GCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAG CCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTA ATAGTTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGAT CAAG (SEQ ID NO: 409)
44	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARSGPSS YWYFDLWGRGTLVT VSSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 197)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAAGTGG GCCCAGTAGCTACTGGTACTTCGATCTCTGGGGCCGTGGCACCC TGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCC AGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGA CCATCACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGC CTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATC TACGACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCA GCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAG CCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTA ATAGTTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGAT CAAG (SEQ ID NO: 410)
45	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARNIYM GGIWFDPWGQGTL VTVSSGGGGSGGGG SGGGGSGGAIQLTQ SPSSLSASVGDRVTIT CRASQGISSALAWY QQKPGKAPKLLIYDA SSLESGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQFNSYPLT FGGGTKVEIK (SEQ ID NO: 198)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAAACATT TACATGGGCGGGATCTGGTTCGACCCCTGGGGCCAGGGAACCC TGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCC AGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGA CCATCACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGC CTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATC TACGACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCA GCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAG CCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTA ATAGTTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGAT CAAG (SEQ ID NO: 411)

46	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARLTVRT GAFDIWGQGTMVT VSSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 199)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGACTTACA GTCCGCACTGGAGCTTTTGATATCTGGGGCCAAGGGACAATGG TCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCAT CACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGG TATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACG ACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGG CAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGC AGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGT TACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 412)
47	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARLRTAH LDFDLWGRGTLVTV SSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 200)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGACTAAGA ACTGCCCACCTGGACTTCGATCTCTGGGGCCGTGGCACCCTGGT CACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAG CCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATC ACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGT ATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGA CGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGC AGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCA GCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTT ACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 413)
48	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARDLIFP VVFDYWGQGTLVTV SSGGGGSGGGGSG GGGSGGAIQLTQSP SSLSASVGDRVTITCR	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGATCTC ATATTTCCAGTAGTCTTTGACTACTGGGGCCAGGGAACCCTGGT CACCGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAG CCCCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATC

	ASQGISSALAWYQQ KPGKAPKLLIYDASSL ESGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 201)	ACCTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGT ATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGA CGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGC AGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCA GCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTT ACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 414)
49	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARDGYR KYGYVFFDIWGQGT MVTVSSGGGGSGG GGSGGGGSGGAIQL TQSPSSLSASVGDRV TITCRASQGISSALA WYQQKPGKAPKLLI YDASSLESGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQFNSY PLTFGGGTKVEIK (SEQ ID NO: 202)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGATGG ATATCGCAAATATGGTTACGTATTTTTTGATATCTGGGGCCAAG GGACAATGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGAG GGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAG CTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGATA GAGTGACCATCACCTGTCGCGCCAGCCAGGGCATCAGCAGCGC TCTGGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTG CTGATCTACGACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGCA GATTCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATC AGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGC AGTTTAATAGTTACCCTCTCACTTTCGGCGGCGGAACAAAGGTG GAGATCAAG (SEQ ID NO: 415)
50	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARDGRY RRFWHAFDIWGQG TMVTVSSGGGGSG GGGSGGGGSGGAI QLTQSPSSLSASVGD RVTITCRASQGISSAL AWYQQKPGKAPKLL IYDASSLESGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQFNSY PLTFGGGTKVEIK (SEQ ID NO: 203)	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGATGG GAGGTACAGGCGGTTCTGGCATGCTTTTGATATCTGGGGCCAA GGGACAATGGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGA GGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCA GCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGAT AGAGTGACCATCACCTGTCGCGCCAGCCAGGGCATCAGCAGCG CTCTGGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCT GCTGATCTACGACGCCAGCTCCCTGGAAAGCGGCGTGCCCAGC AGATTCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCA TCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAG CAGTTTAATAGTTACCCTCTCACTTTCGGCGGCGGAACAAAGGT GGAGATCAAG (SEQ ID NO: 416)
51	QVQLVESGGGLVKP GGSLRLSCAASGFTF SDYYMSWIRQAPGK GLEWVSYISSSGSTIY	CAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTGAAACCT GGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCT TCAGCGACTACTACATGAGCTGGATCAGACAGGCCCCTGGCAA GGGACTGGAATGGGTGTCCTACATCAGCAGCAGCGGCTCGACC

	YADSVKGRFTISRDN AKNSLYLQMNSLRA EDTAVYYCARAHIRG YFDLWGRGTLVTVS SGGGGSGGGGSGG GGSGGAIQLTQSPSS LSASVGDRVTITCRA SQGISSALAWYQQK PGKAPKLLIYDASSLE SGVPSRFSGSGSGTD FTLTISSLQPEDFATY YCQQFNSYPLTFGG GTKVEIK (SEQ ID NO: 204)	ATCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGCC GGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCT GCGGGCCGAGGACACCGCCGTGTATTACTGTGCGAGAGCCCAT ATACGGGGGTACTTCGATCTCTGGGGCCGTGGCACCCTGGTCA CTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCTG GCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGAGCC CCAGCAGCCTGAGCGCCAGCGTGGGCGATAGAGTGACCATCAC CTGTCGCGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTGGTAT CAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGACG CCAGCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCGGCAG CGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGC CCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATAGTTAC CCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 417)
52	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCATW MGGGGRWYFDLW GRGTLVTVSSGGGG SGGGGSGGGGSGG AIQLTQSPSSLSASVG DRVTITCRASQGISS ALAWYQQKPGKAP KLLIYDASSLESGVPS RFSGSGSGTDFTLTIS SLQPEDFATYYCQQF NNYPLTFGGGTKVEI K (SEQ ID NO: 205)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGACGTGGAT GGGGGGCGGGGGACGATGGTACTTCGATCTCTGGGGCCGTGG CACCCTGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGG GGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCT GACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAG AGTGACCATCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCT CTGGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGC TGATCTACGACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAG ATTCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCA GCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCA GTTTAATAATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGG AGATCAAG (SEQ ID NO: 418)
53	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCARTSR TTWYFDLWGRGTLV TVSSGGGGSGGGGS GGGGSGGAIQLTQS PSSLSASVGDRVTITC RASQGISSALAWYQ QKPGKAPKLLIYDAS SLESGVPSRFSGSGS GTDFTLTISSLQPEDF	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAGAACTAG TCGTACAACCTGGTACTTCGATCTCTGGGGCCGTGGCACCCTGG TCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAGTGACCA TCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTG GTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC GACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCG GCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCT

	ATYYCQQFNNYPLTF GGGTKVEIK (SEQ ID NO: 206)	GCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATA ATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAA G (SEQ ID NO: 419)
54	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKW MGGGGRLYFDLWG RGTLVTVSSGGGGS GGGGSGGGGSGGAI QLTQSPSSLSASVGD RVTITCRASQGISSAL AWYQQKPGKAPKLL IYDASSLESGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQFNN YPLTFGGGTKVEIK (SEQ ID NO: 207)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAATGGAT GGGGGGCGGGGGACGATTATACTTCGATCTCTGGGGCCGTGG CACCCTGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGG GGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCT GACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAG AGTGACCATCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCT CTGGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGC TGATCTACGACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAG ATTCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCA GCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCA GTTTAATAATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGG AGATCAAG (SEQ ID NO: 420)
55	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKWG GRLYWYFDLWGRG TLVTVSSGGGGSGG GGSGGGGSGGAIQL TQSPSSLSASVGDRV TITCRASQGISSALA WYQQKPGKAPKLLI YDASSLESGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQFNN YPLTFGGGTKVEIK (SEQ ID NO: 208)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAATGGGG GGGGCGGTTGTACTGGTACTTCGATCTCTGGGGCCGTGGCACC CTGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGA GGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACC CAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAGTG ACCATCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCTCTGG CCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGAT CTACGACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAGATTC AGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCA GCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTT AATAATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGA TCAAG (SEQ ID NO: 421)
56	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKVIR QLWYFDLWGRGTL	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAAGTTAT TCGGCAACTCTGGTACTTCGATCTCTGGGGCCGTGGCACCCTGG

	VTVSSGGGGSGGGG SGGGGSGGAIQLTQ SPSSLSASVGDRVTIT CRASQGISSALAWY QQKPGKAPKLLIYDA SSLESGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQFNNYPLT FGGGTKVEIK (SEQ ID NO: 209)	TCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAGTGACCA TCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTG GTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC GACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCG GCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCT GCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATA ATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAA G (SEQ ID NO: 422)
57	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKVFA NSWYFDLWGRGTL VTVSSGGGGSGGGG SGGGGSGGAIQLTQ SPSSLSASVGDRVTIT CRASQGISSALAWY QQKPGKAPKLLIYDA SSLESGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQFNNYPLT FGGGTKVEIK (SEQ ID NO: 210)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAAGTTTT CGCCAACTCCTGGTACTTCGATCTCTGGGGCCGTGGCACCCTGG TCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAGTGACCA TCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTG GTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC GACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCG GCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCT GCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATA ATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAA G (SEQ ID NO: 423)
58	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKVD RTTWYFDLWGRGTL VTVSSGGGGSGGGG SGGGGSGGAIQLTQ SPSSLSASVGDRVTIT CRASQGISSALAWY QQKPGKAPKLLIYDA SSLESGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQFNNYPLT FGGGTKVEIK (SEQ ID NO: 211)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAAGTAGA TAGGACTACCTGGTACTTCGATCTCTGGGGCCGTGGCACCCTGG TCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGAT CTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAGA GCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAGTGACCA TCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCTCTGGCCTG GTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC GACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGCG GCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCCT GCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAATA ATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCAA G (SEQ ID NO: 424)

59	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKRW GKDGPYWYFDLWG RGTLVTVSSGGGGS GGGGSGGGGSGGAI QLTQSPSSLSASVGD RVTITCRASQGISSAL AWYQQKPGKAPKLL IYDASSLESGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQFNN YPLTFGGGTKVEIK (SEQ ID NO: 212)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAACGATG GGGTAAGGATGGTCCTTACTGGTACTTCGATCTCTGGGGCCGT GGCACCCTGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGA GGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCA GCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGA CAGAGTGACCATCACCTGTCGGGCCAGCCAGGGCATCAGCAGC GCTCTGGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGC TGCTGATCTACGACGCGTCCTCCCTGGAAAGCGGCGTGCCCAG CAGATTCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACC ATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGTTTAATAATTACCCTCTCACTTTCGGCGGCGGAACAAAGG TGGAGATCAAG (SEQ ID NO: 425)
60	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKRR DSYGPYWYFDLWG RGTLVTVSSGGGGS GGGGSGGGGSGGAI QLTQSPSSLSASVGD RVTITCRASQGISSAL AWYQQKPGKAPKLL IYDASSLESGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQFNN YPLTFGGGTKVEIK (SEQ ID NO: 213)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAAAGAAG AGACAGTTATGGTCCTTACTGGTACTTCGATCTCTGGGGCCGTG GCACCCTGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAG GGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAG CTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACA GAGTGACCATCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGC TCTGGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTG CTGATCTACGACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCA GATTCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATC AGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGC AGTTTAATAATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTG GAGATCAAG (SEQ ID NO: 426)
61	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKNR PPPGYWYFDLWGR GTLVTVSSGGGGSG GGGSGGGGSGGAI QLTQSPSSLSASVGD	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAGAATCG TCCCCCGCCCGGGTACTGGTACTTCGATCTCTGGGGCCGTGGCA CCCTGGTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGG GAGGATCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGA CCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAG

	RVTITCRASQGISSAL AWYQQKPGKAPKLL IYDASSLESGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQFNN YPLTFGGGTKVEIK (SEQ ID NO: 214)	TGACCATCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCTCT GGCCTGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTG ATCTACGACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAGAT TCAGCGGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAG CAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGT TTAATAATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAG ATCAAG (SEQ ID NO: 427)
62	EVQLLESGGGLVQP GGSLRLSCAASGFTF SSYAMSWVRQAPG KGLEWVSAISGSGGS TYYADSVKGRFTISR DNSKNTLYLQMNSL RAEDTAVYYCAKGR RFSWYFDLWGRGTL VTVSSGGGGSGGGG SGGGGSGGAIQLTQ SPSSLSASVGDRVTIT CRASQGISSALAWY QQKPGKAPKLLIYDA SSLESGVPSRFSGSG SGTDFTLTISSLQPED FATYYCQQFNNYPLT FGGGTKVEIK (SEQ ID NO: 215)	GAAGTGCAGCTGCTGGAAAGCGGCGGAGGCCTGGTGCAGCCT GGCGGCAGCCTGAGACTGTCTTGCGCCGCCAGCGGCTTCACCT TCAGCAGCTACGCCATGAGCTGGGTCCGCCAGGCCCCTGGCAA GGGACTCGAATGGGTGTCCGCCATCAGCGGCAGCGGCGGCAG CACCTACTACGCCGACAGCGTGAAGGGCCGGTTCACCATCAGC CGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCC TGCGGGCCGAGGACACCGCCGTATATTACTGTGCGAAGGGAA GACGATTTAGCTGGTACTTCGATCTCTGGGGCCGTGGCACCCTG GTCACTGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGA TCTGGCGGCGGAGGAAGCGGAGGCGCCATCCAGCTGACCCAG AGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAGTGACC ATCACCTGTCGGGCCAGCCAGGGCATCAGCAGCGCTCTGGCCT GGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTA CGACGCGTCCTCCCTGGAAAGCGGCGTGCCCAGCAGATTCAGC GGCAGCGGCTCCGGCACCGACTTCACCCTGACCATCAGCAGCC TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGTTTAAT AATTACCCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGATCA AG (SEQ ID NO: 428)

[0173] In some embodiments, the extracellular ligand binding domain of the first receptor is an scFv. In some embodiments, the scFv domain binds to MSLN. In some embodiments, the scFv is the ligand binding domain of a CAR. Exemplary scFv domains specific to MSLN are shown in Table 1, *supra*. In Table 1, underlining indicates CDR sequences.

[0174] In some embodiments, the extracellular ligand binding domain of the first receptor comprises an antigen binding domain having at least 80% identity, at least 85% identity, at least 90% identity, at least 95% identity, at least 97% identity or at least 99% identity to a sequence of SEQ ID NOS: 3-6, 80 or 154-215, or a sequence as set forth in Table 1. In some embodiments, the extracellular ligand binding domain of the first receptor comprises an antigen binding domain comprising a sequence of SEQ ID NOS: 3-6, 80 or 154-215, as set forth in Table 1.

[0175] In some embodiments, the extracellular ligand binding domain of the first receptor comprises an binding domain having at least 80% identity, at least 85% identity, at least 90% identity, at least 95% identity, at least 97% identity or at least 99% identity to a sequence of SEQ ID NO: 171. In some embodiments, the extracellular ligand binding domain of the first receptor comprises an binding domain comprising a sequence of SEQ ID NO: 171.

[0176] In some embodiments, the extracellular ligand binding domain of the first receptor comprises an scFv antigen binding domain having at least 80% identity, at least 85% identity, at least 90% identity, at least 95% identity, at least 97% identity or at least 99% identity to any one of SEQ ID NOs: 3-6. In some embodiments, the extracellular ligand binding domain of the first receptor comprises an scFv antigen binding domain comprising a sequence of any one of SEQ ID NOs: 3-6 or 80. In some embodiments, the extracellular ligand binding domain of the first receptor consists essentially of a sequence selected from the group consisting of SEQ ID NOs: 3-6 or 80.

Table 2: Sequences of MSLN complementary determining regions (CDRs)

#	**HC CDR1**	**HC CDR2**	**HC CDR3**	**LC**
1	NAWMS (SEQ ID NO: 429)	RIKSKTDGGTTDYAAP VKG (SEQ ID NO: 450)	DLPKLRNFHI (SEQ ID NO: 471)	A
2	SYAMH (SEQ ID NO: 430)	AISSNGGSTYYANSVK G (SEQ ID NO: 451)	LEYHGFRQYGLRYWH (SEQ ID NO: 472)	A
3	SGGYSWS (SEQ ID NO: 431)	YIYHSGSTYYNPSLKS (SEQ ID NO: 452)	IKFWFAGINYFFP (SEQ ID NO: 473)	A
4	SYWMH (SEQ ID NO: 449)	RINSDGSSTSYADSVKG (SEQ ID NO: 453)	GFLGMGSNFI (SEQ ID NO: 474)	A
5	SGGYYWS (SEQ ID NO: 432)	YIYYSGSTYYNPSLKS (SEQ ID NO: 454)	GDRARYFDL (SEQ ID NO: 475)	A
6	SYWMH (SEQ ID NO: 449)	RINSDGSSTSYADSVKG (SEQ ID NO: 453)	YPRGYHQMVDAFDI (SEQ ID NO: 476)	A
7	SSSYYWG (SEQ ID NO: 433)	SIYYSGSTYYNPSLKS (SEQ ID NO: 455)	VRFLAARTTIPEANFL (SEQ ID NO: 477)	A
8	SYSMN (SEQ ID NO: 434)	YISSSSSTIYYADSVKG (SEQ ID NO: 456)	VLSRARFDY (SEQ ID NO: 478)	A
9	SYSMN (SEQ ID NO: 434)	SISSSSSYIYYADSVKG (SEQ ID NO: 457)	LRGRVFDP (SEQ ID NO: 479)	A
10	SSSYYWG (SEQ ID NO: 433)	SIYYSGSTYYNPSLKS (SEQ ID NO: 455)	IKFTSFLYVHGFL (SEQ ID NO: 480)	A
11	SYAMH (SEQ ID NO: 430)	WINAGNGNTKYSQKFQ G (SEQ ID NO: 458)	GQRWLYLGGIRRH (SEQ ID NO: 481)	A

12	SYYWS (SEQ ID NO: 435)	YIYYSGSTNYNPSLKS (SEQ ID NO: 459)	EWIPSRPYYFDY (SEQ ID NO: 482)	A
13	SGGYYWS (SEQ ID NO: 432)	YIYYSGSTYYNPSLKS (SEQ ID NO: 454)	ESTGTGAFDI (SEQ ID NO: 483)	A
14	DYGMS (SEQ ID NO: 436)	GINWNGGSTGYADSVKG (SEQ ID NO: 460)	ERYRRVLHWYFDL (SEQ ID NO: 484)	A
15	SYDIN (SEQ ID NO: 437)	WMNPNSGNTGYAQKFQG (SEQ ID NO: 461)	EPDAFDI (SEQ ID NO: 485)	A
16	SGGYYWS (SEQ ID NO: 432)	YIYYSGSTYYNPSLKS (SEQ ID NO: 454)	EHMGTIPYYFDY (SEQ ID NO: 486)	A
17	SGGYYWS (SEQ ID NO: 432)	YIYYSGSTYYNPSLKS (SEQ ID NO: 454)	EEFGYGDVLY (SEQ ID NO: 487)	A
18	SGDYYWS (SEQ ID NO: 438)	YIYYSGSTYYNPSLKS (SEQ ID NO: 454)	EDVVKGAFDI (SEQ ID NO: 488)	A
19	SYSMN (SEQ ID NO: 434)	YISSSSSTIYYADSVKG (SEQ ID NO: 456)	EDFSHKLGYFQH (SEQ ID NO: 489)	A
20	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	DYDYV (SEQ ID NO: 490)	A
21	SGDYYWS (SEQ ID NO: 438)	YIYYSGSTYYNPSLKS (SEQ ID NO: 454)	DRRDWDWFDP (SEQ ID NO: 491)	A
22	SSNWWS (SEQ ID NO: 440)	EIYHSGSTNYNPSLKS (SEQ ID NO: 463)	DQQALKYRVD (SEQ ID NO: 492)	A
23	SYGIS (SEQ ID NO: 441)	WISAYNGNTNYAQKLQG (SEQ ID NO: 464)	DLTLGCFDY (SEQ ID NO: 493)	A
24	SNYMS (SEQ ID NO: 442)	VIYSGGSTYYADSVKG (SEQ ID NO: 465)	DGSNSWYFDL (SEQ ID NO: 494)	A
25	SYGMH (SEQ ID NO: 443)	VIWYDGSNKYYADSVKG (SEQ ID NO: 466)	AFLFLSFSV (SEQ ID NO: 495)	A
26	DYTMH (SEQ ID NO: 444)	LISWDGGSTYYADSVKG (SEQ ID NO: 467)	GIFYSSKEDFDY (SEQ ID NO: 496)	A
27	DYTMH (SEQ ID NO: 444)	LISWDGGSTYYADSVKG (SEQ ID NO: 467)	DIWIFYSSNPKPTVY (SEQ ID NO: 497)	A

28	SYAMN (SEQ ID NO: 445)	WINTNTGNPTYAQGFTG (SEQ ID NO: 468)	KDQTLTYGNWFDP (SEQ ID NO: 498)	A
29	SGSYYWS (SEQ ID NO: 446)	YIYYSGSTNYNPSLKS (SEQ ID NO: 459)	DHYERGLY (SEQ ID NO: 499)	A
30	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	YMYNWYFDL (SEQ ID NO: 500)	B
31	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	DRRPAFDI (SEQ ID NO: 501)	B
32	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	HLKRRPYFDY (SEQ ID NO: 502)	C
33	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	VHKKPIFDY (SEQ ID NO: 503)	C
34	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	TSRRCTFQH (SEQ ID NO: 504)	C
35	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	TSPRPLFQH (SEQ ID NO: 505)	C
36	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	PYQVRGVYFDY (SEQ ID NO: 506)	C
37	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	PYKKRRTVFDY (SEQ ID NO: 507)	C
38	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	LQRGLALFQH (SEQ ID NO: 508)	C
39	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	ILSVPYFDL (SEQ ID NO: 509)	C
40	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	GWIRVPLRLPLFQH (SEQ ID NO: 510)	C
41	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	VTIFAIFDI (SEQ ID NO: 511)	C
42	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	VGRGFVHFDL (SEQ ID NO: 512)	C
43	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	TSRGLCVLFDY (SEQ ID NO: 513)	C

44	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	SGPSSYWYFDL (SEQ ID NO: 514)	C
45	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	NIYMGGIWFDP (SEQ ID NO: 515)	C
46	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	LTVRTGAFDI (SEQ ID NO: 516)	C
47	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	LRTAHLDFDL (SEQ ID NO: 517)	C
48	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	DLIFPVVFDY (SEQ ID NO: 518)	C
49	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	DGYRKYGYVFFDI (SEQ ID NO: 519)	C
50	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	DGRYRRFWHAFDI (SEQ ID NO: 520)	C
51	DYYMS (SEQ ID NO: 439)	YISSSGSTIYYADSVKG (SEQ ID NO: 462)	AHIRGYFDL (SEQ ID NO: 521)	C
52	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	WMGGGGRWYFDL (SEQ ID NO: 522)	C
53	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	TSRTTWYFDL (SEQ ID NO: 523)	C
54	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	WMGGGGRLYFDL (SEQ ID NO: 524)	C
55	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	WGGRLYWYFDL (SEQ ID NO: 525)	C
56	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	VIRQLWYFDL (SEQ ID NO: 526)	C
57	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	VFANSWYFDL (SEQ ID NO: 527)	C
58	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	VDRTTWYFDL (SEQ ID NO: 528)	C
59	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	RWGKDGPYWYFDL (SEQ ID NO: 529)	C

60	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	RRDSYGPYWYFDL (SEQ ID NO: 530)	C
61	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	NRPPPGYWYFDL (SEQ ID NO: 531)	C
62	SYAMS (SEQ ID NO: 447)	AISGSGGSTYYADSVKG (SEQ ID NO: 469)	GRRFSWYFDL (SEQ ID NO: 532)	C
	SGDYYWS (SEQ ID NO: 438)	YIYYSGSTYYNPSLKS (SEQ ID NO: 454)	CAREDVVKGAFDIW (SEQ ID NO: 533)	A
	GYTMN (SEQ ID NO: 448)	LITPYNGASSYNQKFRG (SEQ ID NO: 470)	GGYDGRGFDY (SEQ ID NO: 534)	D
Light chain CDRs				
	LC CDR1	**LC CDR2**	**LC CDR3**	
A	RASQSISSYLN (SEQ ID NO: 535)	AASSLQS (SEQ ID NO: 539)	QQSYSTPLT (SEQ ID NO: 542)	
B	RASQGISSWLA (SEQ ID NO: 536)	AASSLQS (SEQ ID NO: 539)	QQANSFPLT (SEQ ID NO: 543)	
C	RASQGISSALA (SEQ ID NO: 537)	DASSLES (SEQ ID NO: 540)	QQFNSYPLT (SEQ ID NO: 544)	
D	SASSSVSYMH (SEQ ID NO: 538)	DTSKLAS (SEQ ID NO: 541)	QQWSGYPLT (SEQ ID NO: 545)	

[0177] In Table 2, the light chain (LC) CDRs paired with the indicated heavy chain (HC) CDRs are indicated in the left column.

[0178] In some embodiments, the extracellular ligand binding domain of the first receptor comprises the HC CDR1, the HC CDR2, and the HC CDR3 set forth in Table 2 (e.g., the HC CDR 1, the HC CDR2, and the HC CDR 3 of line #1, line #2, line #3, etc. of Table 2) or sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of Table 2. In some embodiments, the extracellular ligand binding domain of the first receptor comprises the LC CDR1, the LC CDR2, and the LC CDR3 set forth in Table 2 (e.g., the LC CDR 1, the LC CDR2, and the LC CDR 3 of line A, line B, or line C of Table 2) or sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs

of Table 2. In some embodiments, the extracellular ligand binding domain of the first receptor comprises the HC CDR1, the HC CDR2, and the HC CDR3 set forth in Table 2 (e.g., the HC CDR 1, the HC CDR2, and the HC CDR 3 of line #1, line #2, line #3, etc. of Table 2). In some embodiments, the extracellular ligand binding domain of the first receptor comprises the LC CDR1, the LC CDR2, and the LC CDR3 set forth in Table 2 (e.g., the LC CDR 1, the LC CDR2, and the LC CDR 3 of line A, line B, or line C of Table 2).

[0179] In some embodiments, the extracellular ligand binding domain of the first receptor comprises the HC CDR1, HC CDR2, HC CDR3, LC CDR1, the LC CDR2, and the LC CDR3 set forth in Table 2 (e.g., the HC CDR1, HC CDR2 and HC CDR3 set forth in line 1, and the LC CDR 1, the LC CDR2, and the LC CDR 3 in line A) In some embodiments, the extracellular ligand binding domain of the first receptor comprises the HC CDR1, the HC CDR2, and the HC CDR3 set forth in Table 2 (e.g., the HC CDR 1, the HC CDR2, and the HC CDR 3 of line #1, line #2, line #3, etc. of Table 2) or sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of Table 2. In some embodiments, the extracellular ligand binding domain of the first receptor comprises the LC CDR1, the LC CDR2, and the LC CDR3 set forth in Table 2 (e.g., the LC CDR 1, the LC CDR2, and the LC CDR 3 of line A, line B, or line C of Table 2) or sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of Table 2. In some embodiments, an extracellular ligand binding domain of the first receptor comprises one or more HC CDRs set forth in Table 2 and one or more LC CDRs set forth in Table 2. In some embodiments, the extracellular ligand binding domain of the first receptor comprises (i) the HC CDR1, the HC CDR2, and the HC CDR3 set forth in one line of Table 2 (e.g., the HC CDR 1, the HC CDR2, and the HC CDR 3 of line #1, line #2, line #3, etc. of Table 2) and (ii) the LC CDR1, the LC CDR2, and the LC CDR3 set forth in one line of Table 2 (e.g., the LC CDR 1, the LC CDR2, and the LC CDR 3 of line A, line B, or line C of Table 2). In each case, the HC CDRs may be paired with any of the LC CDRs, as the heavy chains and light chains share similarity, with routine testing to confirm desired expression and binding activity; however, preferred pairing between heavy and light chains of some embodiments are indicated in the right hand column of Table 2.

[0180] In some embodiments, the extracellular ligand binding domain of the first receptor comprises a HC CDR1 comprising a sequence of SGDYYWS (SEQ ID NO: 438), a HC CDR2 comprising a sequence of YIYYSGSTYYNPSLKS (SEQ ID NO: 454), and HC CDR3 comprising a sequence of CAREDVVKGAFDIW (SEQ ID NO: 533), or CDR sequences having at most 1, 2 or 3 amino acid substitutions, insertions or deletions relative thereto. In

some embodiments, the extracellular ligand binding domain of the first receptor comprises a HC CDR1 comprising a sequence of SGDYYWS (SEQ ID NO: 438), a HC CDR2 comprising a sequence of YIYYSGSTYYNPSLKS (SEQ ID NO: 454), and HC CDR3 comprising a sequence of CAREDVVKGAFDIW (SEQ ID NO: 533). In some embodiments, the extracellular ligand binding domain of the first receptor comprises a LC CDR1 comprising a sequence of RASQSISSYLN (SEQ ID NO: 535), a LC CDR2 comprising a sequence of AASSLQS (SEQ ID NO: 539), and a LC CDR3 comprising a sequence of QQSYSTPLT (SEQ ID NO: 542), or CDR sequences having at most 1, 2 or 3 amino acid substitutions, insertions or deletions relative thereto. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a LC CDR1 comprising a sequence of RASQSISSYLN (SEQ ID NO: 535), a LC CDR2 comprising a sequence of AASSLQS (SEQ ID NO: 539), and a LC CDR3 comprising a sequence of QQSYSTPLT (SEQ ID NO: 542). In some embodiments, the extracellular ligand binding domain of the first receptor comprises a HC CDR1 comprising a sequence of SGDYYWS (SEQ ID NO: 438), a HC CDR2 comprising a sequence of YIYYSGSTYYNPSLKS (SEQ ID NO: 454), HC CDR3 comprising a sequence of CAREDVVKGAFDIW (SEQ ID NO: 533), a LC CDR1 comprising a sequence of RASQSISSYLN (SEQ ID NO: 535), a LC CDR2 comprising a sequence of AASSLQS (SEQ ID NO: 539), and a LC CDR3 comprising a sequence of QQSYSTPLT (SEQ ID NO: 542), or CDR sequences having at most 1, 2 or 3 amino acid substitutions, insertions or deletions relative thereto. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a HC CDR1 comprising a sequence of SGDYYWS (SEQ ID NO: 438), a HC CDR2 comprising a sequence of YIYYSGSTYYNPSLKS (SEQ ID NO: 454), HC CDR3 comprising a sequence of CAREDVVKGAFDIW (SEQ ID NO: 533), a LC CDR1 comprising a sequence of RASQSISSYLN (SEQ ID NO: 535), a LC CDR2 comprising a sequence of AASSLQS (SEQ ID NO: 539), and a LC CDR3 comprising a sequence of QQSYSTPLT (SEQ ID NO: 542).

[0181] In some embodiments, the extracellular ligand binding domain of the first receptor comprises an scFv. In some embodiments, the scFv comprises a heavy chain comprising CDRs selected from the sequences of GYTMN (SEQ ID NO: 448), LITPYNGASSYNQKFRG (SEQ ID NO: 470) and GGYDGRGFDY (SEQ ID NO: 534). In some embodiments, the heavy chain comprises sequences of GYTMN (SEQ ID NO: 448), LITPYNGASSYNQKFRG(SEQ ID NO: 470) and GGYDGRGFDY (SEQ ID NO: 534). In some embodiments, the scFv comprising a light chain comprising CDRs selected from the sequences of SASSSVSYMH (SEQ ID NO: 538), DTSKLAS (SEQ ID NO: 541) and

QQWSGYPLT (SEQ ID NO: 545). In some embodiments, the light chain comprises sequences of SASSSVSYMH (SEQ ID NO: 538), DTSKLAS (SEQ ID NO: 541) and QQWSGYPLT (SEQ ID NO: 545).

[0182] Sequences of exemplary heavy and light chains of antigen binding domains that are specific to MSLN are set forth in Tables 3 and 4 below. Light chains paired with heavy chains in preferred embodiments are indicated at right in Table 3.

Table 2: Sequences of heavy chain variable fragments (VH)

#	SEQ ID NO	Heavy Chain (VH)	LC
1	216	EVQLVESGGGLVKPGGSLRLSCAASGFTFSNAWMSWVRQA PGKGLEWVGRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTL YLQMNSLKTEDTAVYYCTTDLPKLRNFHIWGQGTLVTVSS	A
2	217	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMHWVRQAP GKGLEYVSAISSNGGSTYYANSVKGRFTISRDNSKNTLYLQM GSLRAEDMAVYYCASLEYHGFRQYGLRYWHWGQGTLVTV SS	A
3	218	QLQLQESGSGLVKPSQTLSLTCAVSGGSISSGGYSWSWIRQP PGKGLEWIGYIYHSGSTYYNPSLKSRVTISVDRSKNQFSLKLS SVTAADTAVYYCASIKFWFAGINYFFPWGQGTLVTVSS	A
4	219	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMHWVRQA PGKGLVWVSRINSDGSSTSYADSVKGRFTISRDNAKNTLYLQ MNSLRAEDTAVYYCASGFLGMGSNFIWGQGTLVTVSS	A
5	220	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQH PGKGLEWIGYIYYSGSTYYNPSLKSLVTISVDTSKNQFSLKLS SVTAADTAVYYCASGDRARYFDLWGRGTLVTVSS	A
6	221	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMHWVRQA PGKGLVWVSRINSDGSSTSYADSVKGRFTISRDNAKNTLYLQ MNSLRAEDTAVYYCARYPRGYHQMVDAFDIWGQGTMVTV SS	A
7	222	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPP GKGLEWIGSIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSS VTAADTAVYYCARVRFLAARTTIPEANFLWGQGTLVTVSS	A
8	223	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAP GKGLEWVSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARVLSRARFDYWGQGTLVTVSS	A
9	224	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAP GKGLEWVSSISSSSSYIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARLRGRVFDPWGQGTLVTVSS	A
10	225	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPP GKGLEWIGSIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSS VTAADTAVYYCARIKFTSFLYVHGFLWGQGTLVTVSS	A
11	226	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYAMHWVRQ APGQRLEWMGWINAGNGNTKYSQKFQGRVTITRDTSASTA YMELSSLRSEDTAVYYCARGQRWLYLGGIRRHWGQGTLVT VSS	A

#	SEQ ID NO	Heavy Chain (VH)	LC
12	227	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPG KGLEWIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSV TAADTAVYYCAREWIPSRPYYFDYWGQGTLVTVSS	A
13	228	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQP PGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARESTGTGAFDIWGQGTMVTVSS	A
14	229	EVQLVESGGGVVRPGGSLRLSCAASGFTFDDYGMSWVRQA PGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKNSLYL QMNSLRAEDTALYHCARERYRRVLHWYFDLWGRGTLVTVS S	A
15	230	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQA TGQGLEWMGWMNPNSGNTGYAQKFQGRVTMTRNTSISTA YMELSSLRSEDTAVYYCAREPDAFDIWGQGTMVTVSS	A
16	231	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQP PGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCAREHMGTIPYYFDYWGQGTLVTVSS	A
17	232	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQP PGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCAREEFGYGDVLYWGQGTLVTVSS	A
18	233	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGDYYWSWIRQP PGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCAREDVVKGAFDIWGQGTMVTVSS	A
19	234	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAP GKGLEWVSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCAREDFSHKLGYFQHWGQGTLVTVSS	A
20	235	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARDYDYVWGQGTLVTVSS	A
21	236	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGDYYWSWIRQP PGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDRRDWDWFDPWGQGTLVTVSS	A
22	237	QVQLQESGPGLVKPSGTLSLTCAVSGGSISSSNWWSWVRQP PGKGLEWIGEIYHSGSTNYNPSLKSRVTISVDKSKNQFSLKLS SVTAADTAVYYCARDQQALKYRVDWGQGTLVTVSS	A
23	238	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAP GQGLEWMGWISAYNGNTNYAQKLQGRVTMTTDTSTSTAY MELRSLRSDDTAVYYCARDLTLGCFDYWGQGTLVTVSS	A
24	239	EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNYMSWVRQAP GKGLEWVSVIYSGGSTYYADSVKGRFTISRDNSKNTLYLQM NSLRAEDTAVYYCARDGSNSWYFDLWGRGTLVTVSS	A
25	240	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQA PGKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCARAFLFLSFSVWGQGTLVTVSS	A
26	241	EVQLVESGGVVVQPGGSLRLSCAASGFTFDDYTMHWVRQA PGKGLEWVSLISWDGGSTYYADSVKGRFTISRDNSKNSLYL QMNSLRTEDTALYYCAKGIFYSSKEDFDYWGQGTLVTVSS	A

#	SEQ ID NO	Heavy Chain (VH)	LC
27	242	EVQLVESGGVVVQPGGSLRLSCAASGFTFDDYTMHWVRQA PGKGLEWVSLISWDGGSTYYADSVKGRFTISRDNSKNSLYL QMNSLRTEDTALYYCAKDIWIFYSSNPKPTVYWGQGTLVTV SS	A
28	243	QVQLVQSGSELKKPGASVKVSCKASGYTFTSYAMNWVRQA PGQGLEWMGWINTNTGNPTYAQGFTGRFVFSFDTSVSTAYL QICSLKAEDTAVYYCARKDQTLTYGNWFDPWGQGTLVTVS S	A
29	244	QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGSYYWSWIRQP PGKGLEWIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDHYERGLYWGQGTLVTVSS	A
30	245	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARYMYNWYFDLWGRGTLVTVSS	B
31	246	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARDRRPAFDIWGQGTMVTVSS	B
32	247	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCAVHLKRRPYFDYWGQGTLVTVSS	C
33	248	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASVHKKPIFDYWGQGTLVTVSS	C
34	249	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASTSRRCTFQHWGQGTLVTVSS	C
35	250	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASTSPRPLFQHWGQGTLVTVSS	C
36	251	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASPYQVRGVYFDYWGQGTLVTVSS	C
37	252	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASPYKKRRTVFDYWGQGTLVTVSS	C
38	253	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASLQRGLALFQHWGQGTLVTVSS	C
39	254	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASILSVPYFDLWGRGTLVTVSS	C
40	255	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCASGWIRVPLRLPLFQHWGQGTLVTVSS	C

#	SEQ ID NO	Heavy Chain (VH)	LC
41	256	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARVTIFAIFDIWGQGTMVTVSS	C
42	257	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARVGRGFVHFDLWGRGTLVTVSS	C
43	259	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARTSRGLCVLFDYWGQGTLVTVSS	C
44	260	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARSGPSSYWYFDLWGRGTLVTVSS	C
45	261	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARNIYMGGIWFDPWGQGTLVTVSS	C
46	262	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARLTVRTGAFDIWGQGTMVTVSS	C
47	263	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARLRTAHLDFDLWGRGTLVTVSS	C
48	264	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARDLIFPVVFDYWGQGTLVTVSS	C
49	265	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARDGYRKYGYVFFDIWGQGTMVTVSS	C
50	266	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARDGRYRRFWHAFDIWGQGTMVTVSS	C
51	267	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAP GKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARAHIRGYFDLWGRGTLVTVSS	C
52	268	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCATWMGGGGRWYFDLWGRGTLVTVSS	C
53	269	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARTSRTTWYFDLWGRGTLVTVSS	C
54	270	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKWMGGGGRLYFDLWGRGTLVTVSS	C
55	271	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKWGGRLYWYFDLWGRGTLVTVSS	C

#	SEQ ID NO	Heavy Chain (VH)	LC
56	272	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKVIRQLWYFDLWGRGTLVTVSS	C
57	273	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKVFANSWYFDLWGRGTLVTVSS	C
58	274	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKVDRTTWYFDLWGRGTLVTVSS	C
59	275	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKRWGKDGPYWYFDLWGRGTLVTVS S	C
60	276	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKRRDSYGPYWYFDLWGRGTLVTVSS	C
61	277	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKNRPPPGYWYFDLWGRGTLVTVSS	C
62	278	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCAKGRRFSWYFDLWGRGTLVTVSS	C

Table 3: Sequences of light chain variable fragments (VL)

#	SEQ ID NO	Light Chain (VL)
A	279	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLT FGGGTKVEIK
B	280	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFPLT FGGGTKVEIK
C	281	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLI YDASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPLT FGGGTKVEIK
D	282	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLI YDASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNNYPLT FGGGTKVEIK

[0183] In some embodiments, the extracellular ligand binding domain of the first receptor comprises a variable heavy region (VH) sequence set forth in Table 3. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a VH sequence that has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least

94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VH set forth in Table 3. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a variable light region (VL) sequence set forth in Table 4. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a VL sequence that has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VL set forth set forth in Table 4.

[0184] In some embodiments, a the extracellular ligand binding domain of the first receptor comprises a VH that (i) comprises the HC CDR1, the HC CDR2, and the HC CDR3 sequences set forth in Table 2 (e.g., the HC CDR 1, the HC CDR2, and the HC CDR 3 of line #1, line #2, line #3, etc. of Table 2) and (ii) has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VH sequence set forth in Table 3. In some embodiments, extracellular ligand binding domain of the first receptor (i) comprises the LC CDR1, the LC CDR2, and the LC CDR3 sequences set forth in one line Table 2 (e.g., the LC CDR 1, the LC CDR2, and the LC CDR 3 of line A, line B, or line C of Table 2) and a VL sequence set forth in Table 4 and (ii) has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VL set forth set forth in Table 4.

[0185] In some embodiments, the extracellular ligand binding domain of the first receptor comprises (i) a VH sequence set forth in Table 3 or a VH sequence that has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VH set forth in Table 3, and (ii) a VL sequence set forth in Table 4 or a VL that has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VL set forth set forth in Table 4. In each case, the VH may be paired with any of the VLs, as the heavy chains and light chains share similarity, with routine testing to confirm desired expression and binding activity; however, the preferred pairing between Table 3 and Table 4 is indicated in the "LC" column of Table 3, corresponding to the # column of Table 4.

[0186] In some embodiments, the extracellular ligand binding domain of the first receptor comprises a VH sequence of SEQ ID NO: 233, or a sequence that has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity thereto. In some embodiments,

the extracellular ligand binding domain of the first receptor comprises a VH sequence of SEQ ID NO: 233.

[0187] In some embodiments, the extracellular ligand binding domain of the first receptor comprises a VL sequence of SEQ ID NO: 279, or a sequence that has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity thereto. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a VL sequence of SEQ ID NO: 279. In some embodiments, the extracellular ligand binding domain of the first receptor comprises a VH sequence of SEQ ID NO: 233, and a VL sequence of SEQ ID NO: 279, or sequences that have at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity thereto. In some embodiments the VH and VL are separated for a linker, for example a linker comprising a sequence of GGGGSGGGGSGGGGSGG (SEQ ID NO: 152). The VH and VL can be in any orientation, for example VH, linker, VL; or alternatively, VL, linker VH.

[0188] In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, or 6) amino acid residues in a CDR of the antigen binding domains provided herein are substituted with another amino acid. The substitution may be "conservative" in the sense of being a substitution within the same family of amino acids. The naturally occurring amino acids may be divided into the following four families and conservative substitutions will take place within those families: (1) amino acids with basic side chains: lysine, arginine, histidine; (2) amino acids with acidic side chains: aspartic acid, glutamic acid; (3) amino acids with uncharged polar side chains: asparagine, glutamine, serine, threonine, tyrosine; and (4) amino acids with nonpolar side chains: glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan, cysteine. By varying the amino acid sequence of the CDRs of an antibody by addition, deletion or substitution of amino acids, various effects such as increased binding affinity for the target antigen may be obtained.

Chimeric Antigen Receptors (CARs)

[0189] The disclosure provides a first, activator receptor and immune cells comprising same. In some embodiments, the first receptor is a chimeric antigen receptor.

[0190] The term "chimeric antigen receptors (CARs)" as used herein, may refer to artificial receptors derived from T-cell receptors and encompasses engineered receptors that graft an artificial specificity onto a particular immune effector cell. CARs may be employed to impart the specificity of a monoclonal antibody onto a T cell, thereby allowing a large number of specific T cells to be generated, for example, for use in adoptive cell therapy. In specific

embodiments, CARs direct specificity of the cell to a tumor associated antigen, for example. Exemplary CARs comprise an intracellular activation domain, a transmembrane domain, and an extracellular domain comprising a tumor associated antigen binding region. In some embodiments, CARs further comprise a hinge domain. In particular aspects, CARs comprise fusions of single-chain variable fragments (scFv) derived from monoclonal antibodies, fused to a CD3 transmembrane domain and endodomain. The specificity of other CAR designs may be derived from ligands of receptors (e.g., peptides). In certain cases, CARs comprise domains for additional co-stimulatory signaling, such as CD3, 4-1BB, FcR, CD27, CD28, CD137, DAP10, and/or OX40. In some cases, molecules can be co-expressed with the CAR, including co-stimulatory molecules, reporter genes for imaging, gene products that conditionally ablate the T cells upon addition of a pro-drug, homing receptors, cytokines, and cytokine receptors.

[0191] In some embodiments, the extracellular ligand binding domain of the first receptor is fused to the extracellular domain of a CAR.

[0192] In some embodiments, the CARs of the present disclosure comprise an extracellular hinge region. Incorporation of a hinge region can affect cytokine production from CAR-T cells and improve expansion of CAR-T cells *in vivo*. Exemplary hinges can be isolated or derived from IgD and CD8 domains, for example IgG1. In some embodiments, the hinge is isolated or derived from CD8α or CD28.

[0193] In some embodiments, the hinge is isolated or derived from CD8α or CD28. In some embodiments, the CD8α hinge comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 7). In some embodiments, the CD8α hinge comprises SEQ ID NO: 7. In some embodiments, the CD8α hinge consists essentially of SEQ ID NO: 7. In some embodiments, the CD8α hinge is encoded by a nucleotide sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of

ACCACGACGCCAGCGCCGCGACCACCAACACCGGCGCCCACCATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAG GCGTGCCGGCCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTTCGCCTGTGAT (SEQ ID NO: 8). In some embodiments, the CD8α hinge is encoded by SEQ ID NO: 8.

[0194] In some embodiments, the CD28 hinge comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of CTIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPLFPGPSKP (SEQ ID NO: 9). In some embodiments, the CD28 hinge comprises or consists essentially of

SEQ ID NO: 9. In some embodiments, the CD28 hinge is encoded by a nucleotide sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of TGTACCATTGAAGTTATGTATCCTCCTCCTTACCTAGACAATGAGAAGAGCAATGGAACCAT TATCCATGTGAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGGACCTTCTAAGCCC (SEQ ID NO: 10). In some embodiments, the CD28 hinge is encoded by SEQ ID NO: 10.

[0195] The CARs of the present disclosure can be designed to comprise a transmembrane domain that is fused to the extracellular domain of the CAR. In some embodiments, the transmembrane domain that naturally is associated with one of the domains in the CAR is used. For example, a CAR comprising a CD28 co-stimulatory domain might also use a CD28 transmembrane domain. In some instances, the transmembrane domain can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins to minimize interactions with other members of the receptor complex.

[0196] The transmembrane domain may be derived either from a natural or from a synthetic source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. Transmembrane regions may be isolated or derived from (i.e. comprise at least the transmembrane region(s) of) the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154, or from an immunoglobulin such as IgG4. Alternatively the transmembrane domain may be synthetic, in which case it will comprise predominantly hydrophobic residues such as leucine and valine. In some embodiments, a triplet of phenylalanine, tryptophan and valine will be found at each end of a synthetic transmembrane domain. Optionally, a short oligo- or polypeptide linker, preferably between 2 and 10 amino acids in length may form the linkage between the transmembrane domain and the cytoplasmic signaling domain of the CAR. A glycine-serine doublet provides a particularly suitable linker.

[0197] In some embodiments of the CARs of the disclosure, the CARs comprise a CD28 transmembrane domain. In some embodiments, the CD28 transmembrane domain comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of FWVLVVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO: 11). In some embodiments, the CD28 transmembrane domain comprises or consists essentially of SEQ ID NO: 11. In some embodiments, the CD28 transmembrane domain is encoded by a nucleotide sequence having

at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of TTCTGGGTGCTGGTCGTTGTGGGCGGCGTGCTGGCCTGCTACAGCCTGCTGGTGACAGTGGCCTTCATCATCTTT TGGGTG (SEQ ID NO: 12). In some embodiments, the CD28 transmembrane domain is encoded by SEQ ID NO: 12.

[0198] In some embodiments of the CARs of the disclosure, the CARs comprise an IL-2Rbeta transmembrane domain. In some embodiments, the IL-2Rbeta transmembrane domain comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of IPWLGHLLVGLSGAFGFIILVYLLI (SEQ ID NO: 13). In some embodiments, the IL-2Rbeta transmembrane domain comprises or consists essentially of SEQ ID NO: 13. In some embodiments, the IL-2Rbeta transmembrane domain is encoded by a nucleotide sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of ATTCCGTGGC TCGGCCACCT CCTCGTGGGC CTCAGCGGGG CTTTTGGCTT CATCATCTTA GTGTACTTGC TGATC (SEQ ID NO: 14). In some embodiments, the IL-2Rbeta transmembrane domain is encoded by SEQ ID NO: 14.

[0199] The cytoplasmic domain or otherwise the intracellular signaling domain of the CARs of the instant disclosure is responsible for activation of at least one of the normal effector functions of the immune cell in which the CAR has been placed. The term "effector function" refers to a specialized function of a cell. Thus the term "intracellular signaling domain" refers to the portion of a protein which transduces the effector function signal and directs the cell to perform a specialized function. While usually the entire intracellular signaling domain can be employed, in many cases it is not necessary to use the entire domain. To the extent that a truncated portion of the intracellular signaling domain is used, such truncated portion may be used in place of the intact chain as long as it transduces the effector function signal. In some cases, multiple intracellular domains can be combined to achieve the desired functions of the CAR-T cells of the instant disclosure. The term intracellular signaling domain is thus meant to include any truncated portion of one or more intracellular signaling domains sufficient to transduce the effector function signal.

[0200] Examples of intracellular signaling domains for use in the CARs of the instant disclosure include the cytoplasmic sequences of the T cell receptor (TCR) 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.

[0201] Accordingly, the intracellular domain of CARs of the instant disclosure comprises at least one cytoplasmic activation domain. In some embodiments, the intracellular activation domain ensures that there is T-cell receptor (TCR) signaling necessary to activate the effector functions of the CAR T-cell. In some embodiments, the at least one cytoplasmic activation is a CD247 molecule (CD3ζ) activation domain, a stimulatory killer immunoglobulin-like receptor (KIR) KIR2DS2 activation domain, or a DNAX-activating protein of 12 kDa (DAP12) activation domain.

[0202] In some embodiments, the CD3ζ activation domain comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of RVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQ EGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR (SEQ ID NO: 15).

[0203] In some embodiments, the CD3ζ activation domain comprises or consists essentially of SEQ ID NO: 15. In some embodiments, the CD3ζ activation domain is encoded by a nucleotide sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACAAGCAGGGCCAGAACCAGCTCTATAACGAGCTCAAT CTAGGACGAAGAGAGGAGTACGATGTTTTGGACAAGCGTAGAGGCCGGGACCCTGAGATGGGGGGAAAGCCGAGA AGGAAGAACCCTCAGGAAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGGAGGCCTACAGTGAGATTGGG ATGAAAGGCGAGCGCCGGAGGGGCAAGGGGCACGATGGCCTTTACCAGGGACTCAGTACAGCCACCAAGGACACC TACGACGCCCTTCACATGCAGGCCCTGCCCCCTCGC (SEQ ID NO: 16). In some embodiments, the CD3ζ activation domain is encoded by SEQ ID NO: 16).

[0204] It is known that signals generated through the TCR alone are often insufficient for full activation of the T cell and that a secondary or co-stimulatory signal is also required. Thus, T cell activation can be said to be mediated by two distinct classes of cytoplasmic signaling sequence: those that initiate antigen-dependent primary activation through the TCR (primary cytoplasmic signaling sequences) and those that act in an antigen-independent manner to provide a secondary or co-stimulatory signal (secondary cytoplasmic signaling sequences).

[0205] Primary cytoplasmic signaling sequences regulate primary activation of the TCR complex either in a stimulatory way, or in an inhibitory way. Primary cytoplasmic signaling sequences that act in a stimulatory manner may contain signaling motifs, which are known as

immunoreceptor tyrosine-based activation motifs or ITAMs. In some embodiments, the ITAM contains a tyrosine separated from a leucine or an isoleucine by any two other amino acids (YxxL/I (SEQ ID NO: 546)). In some embodiments, the cytoplasmic domain contains 1, 2, 3, 4 or 5 ITAMs. An exemplary ITAM containing cytoplasmic domain is the CD3ζ activation domain. Further examples of ITAM containing primary cytoplasmic signaling sequences that can be used in the CARs of the instant disclosure include those derived from TCRζ, FcRγ, FcRβ, CD3γ, CD3δ, CD3ε, CD3ζ, CD5, CD22, CD79a, CD79b, and CD66d.

[0206] In some embodiments, the CD3ζ activation domain comprising a single ITAM comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLHMQALPPR (SEQ ID NO: 17). In some embodiments, the CD3ζ activation domain comprises SEQ ID NO: 17. In some embodiments, the CD3ζ activation domain comprising a single ITAM consists essentially of an amino acid sequence of RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLHMQALPPR (SEQ ID NO: 17). In some embodiments, the CD3ζ activation domain comprising a single ITAM is encoded by a nucleotide sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of

AGAGTGAAGT TCAGCAGGAG CGCAGACGCC CCCGCGTACC AGCAGGGCCA GAACCAGCTC TATAACGAGC TCAATCTAGG ACGAAGAGAG GAGTACGATG TTTTGCACAT GCAGGCCCTG CCCCCTCGC (SEQ ID NO: 18). In some embodiments, the CD3ζ activation domain is encoded by SEQ ID NO: 18.

[0207] In some embodiments, the cytoplasmic domain of the CAR can be designed to comprise the CD3ζ signaling domain by itself or combined with any other desired cytoplasmic domain(s) useful in the context of the CAR of the instant disclosure. For example, the cytoplasmic domain of the CAR can comprise a CD3ζ chain portion and a co-stimulatory domain. The co-stimulatory domain refers to a portion of the CAR comprising the intracellular domain of a costimulatory molecule. A costimulatory molecule is a cell surface molecule other than an antigen receptor or its ligands that is required for an efficient response of lymphocytes to an antigen. Examples of such molecules include the co-stimulatory domain is selected from the group consisting of IL-2Rβ, Fc Receptor gamma (FcRγ), Fc Receptor beta (FcRβ), CD3g molecule gamma (CD3γ), CD3δ, CD3ε, CD5 molecule (CD5), CD22 molecule (CD22), CD79a molecule (CD79a), CD79b molecule (CD79b), carcinoembryonic antigen related cell adhesion molecule 3 (CD66d), CD27

molecule (CD27), CD28 molecule (CD28), TNF receptor superfamily member 9 (4-1BB), TNF receptor superfamily member 4 (OX40), TNF receptor superfamily member 8 (CD30), CD40 molecule (CD40), programmed cell death 1 (PD-1), inducible T cell costimulatory (ICOS), lymphocyte function-associated antigen-1 (LFA-1), CD2 molecule (CD2), CD7 molecule (CD7), TNF superfamily member 14 (LIGHT), killer cell lectin like receptor C2 (NKG2C) and CD276 molecule (B7-H3) c-stimulatory domains, or functional variants thereof. In some embodiments, the intracellular domains of CARs of the instant disclosure comprise at least one co-stimulatory domain. In some embodiments, the co-stimulatory domain is isolated or derived from CD28.

[0208] In some embodiments, the intracellular domains of CARs of the instant disclosure comprise at least one co-stimulatory domain. In some embodiments, the co-stimulatory domain is isolated or derived from CD28. In some embodiments, the CD28 co-stimulatory domain comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of RSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRS (SEQ ID NO: 19). In some embodiments, the CD28 co-stimulatory domain comprises or consists essentially of SEQ ID NO: 19. In some embodiments, the CD28 co-stimulatory domain is encoded by a nucleotide sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of AGGAGCAAGCGGAGCAGACTGCTGCACAGCGACTACATGAACATGACCCCCCGG AGGCCTGGCCCCACCCGGAAGCACTACCAGCCCTACGCCCCTCCCAGGGATTTCG CCGCCTACCGGAGC (SEQ ID NO: 20). In some embodiments, the CD28 co-stimulatory domain is encoded by SEQ ID NO: 20.

[0209] In some embodiments, the co-stimulatory domain is isolated or derived from 4-1BB. In some embodiments, the 4-1BB co-stimulatory domain comprises an amino acid sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 283). In some embodiments, the 4-1BB co-stimulatory domain comprises or consists essentially of KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 283). In some embodiments, the 4-1BB co-stimulatory domain s encoded by a nucleotide sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity or is identical to a sequence of AAACGGGGCAGAAAGAAACTCCTGTATATATTCAAACAACCATTTATGAGGCCA

GTACAAACTACTCAAGAGGAAGATGGCTGTAGCTGCCGATTTCCAGAAGAAGAA GAAGGAGGATGTGAACTG (SEQ ID NO: 284).

[0210] In some embodiments, the intracellular domain of the CAR comprises a CD28 co-stimulatory domain, a 4-1BB costimulatory domain, and a CD3ζ activation domain. In some embodiments, the intracellular domain of the CAR comprises a sequence of RSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPF MRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRR EEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGK GHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 285), or a sequence having at least 80% identity, at least 90% identity, at least 95% identity, at least 99% identity thereto.

[0211] The cytoplasmic domains within the cytoplasmic signaling portion of the CARs of the instant disclosure may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, for example between 2 and 10 amino acids in length may form the linkage. A glycine-serine doublet provides an example of a suitable linker. An exemplary linker comprises a sequence of GGGGSGGGGSGGGGSGG (SEQ ID NO: 152).

[0212] The cytoplasmic domains within the cytoplasmic signaling portion of the CARs of the instant disclosure may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, for example between 2 and 10 amino acids in length may form the linkage. A glycine-serine doublet provides an example of a suitable linker. Exemplary full length activator receptors of the disclosure are described in Table 20. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NOS: 286-347, as set forth in Table 20, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NOS: 286-347, as set forth in Table 20. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 288, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 297, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 301, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 302, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 303, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments,

the first activator receptor comprises a sequence of SEQ ID NO: 314, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 335, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 340, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the first activator receptor comprises a sequence of SEQ ID NO: 344, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0213] The cytoplasmic domains within the cytoplasmic signaling portion of the CARs of the instant disclosure may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, for example between 2 and 10 amino acids in length may form the linkage. A glycine-serine doublet provides an example of a suitable linker.

T Cell Receptors (TCRs)

[0214] The disclosure provides a first, activator receptor and immune cells comprising same. In some embodiments, the first receptor is a T cell receptor (TCR).

[0215] As used herein, a "TCR", sometimes also called a "TCR complex" or "TCR/CD3 complex" refers to a protein complex comprising a TCR alpha chain, a TCR beta chain, and one or more of the invariant CD3 chains (zeta, gamma, delta and epsilon), sometimes referred to as subunits. The TCR alpha and beta chains can be disulfide-linked to function as a heterodimer to bind to peptide-MHC complexes. Once the TCR alpha/beta heterodimer engages peptide-MHC, conformational changes in the TCR complex in the associated invariant CD3 subunits are induced, which leads to their phosphorylation and association with downstream proteins, thereby transducing a primary stimulatory signal. In an exemplary TCR complex, the TCR alpha and TCR beta polypeptides form a heterodimer, CD3 epsilon and CD3 delta form a heterodimer, CD3 epsilon and CD3 gamma for a heterodimer, and two CD3 zeta form a homodimer.

[0216] Any suitable ligand binding domain may be fused to an extracellular domain, hinge domain or transmembrane of the TCRs described herein. For example, the ligand binding domain can be an antigen binding domain of an antibody or TCR, or comprise an antibody fragment, a Vβ only domain, a linear antibody, a single-chain variable fragment (scFv), or a single domain antibody (sdAb).

[0217] In some embodiments, the ligand binding domain is fused to one or more extracellular domains or transmembrane domains of one or more TCR subunits. The TCR subunit can be TCR alpha, TCR beta, CD3 delta, CD3 epsilon, CD3 gamma or CD3 zeta. For example, the

ligand binding domain can be fused to TCR alpha, or TCR beta, or portions of the ligand binding can be fused to two subunits, for example portions of the ligand binding domain can be fused to both TCR alpha and TCR beta.

[0218] TCR subunits include TCR alpha, TCR beta, CD3 zeta, CD3 delta, CD3 gamma and CD3 epsilon. Any one or more of TCR alpha, TCR beta chain, CD3 gamma, CD3 delta, CD3 epsilon, or CD3 zeta, or fragments or derivative thereof, can be fused to one or more domains capable of providing a stimulatory signal of the disclosure, thereby enhancing TCR function and activity.

[0219] TCR transmembrane domains isolated or derived from any source are envisaged as within the scope of the disclosure. The transmembrane domain may be derived either from a natural or from a recombinant source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein.

[0220] In some embodiments, the transmembrane domain is capable of signaling to the intracellular domain(s) whenever the TCR complex has bound to a target. A transmembrane domain of particular use in this disclosure may include at least the transmembrane region(s) of *e.g.*, the alpha, beta or zeta chain of the TCR, CD3 delta, CD3 epsilon or CD3 gamma, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154.

[0221] In some embodiments, the transmembrane domain can be attached to the extracellular region of a polypeptide of the TCR, *e.g.*, the antigen binding domain of the TCR alpha or beta chain, via a hinge, *e.g.*, a hinge from a human protein. For example, the hinge can be a human immunoglobulin (Ig) hinge, *e.g.*, an IgG4 hinge, or a CD8a hinge. In some embodiments, the hinge is isolated or derived from CD8α or CD28.

[0222] In some embodiments, the extracellular ligand binding domain is attached to one or more transmembrane domains of the TCR. In some embodiments, the transmembrane domain comprises a TCR alpha transmembrane domain, a TCR beta transmembrane domain, or both. In some embodiments, the transmembrane comprises a CD3 zeta transmembrane domain.

[0223] A transmembrane domain can include one or more additional amino acids adjacent to the transmembrane region, e.g., one or more amino acid associated with the extracellular region of the protein from which the transmembrane was derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or up to 15 amino acids of the extracellular region) and/or one or more additional amino acids associated with the intracellular region of the protein from which the transmembrane protein is derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or up to 15 amino acids of the intracellular region).

[0224] In some embodiments, the transmembrane domain can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins, e.g., to minimize interactions with other members of the receptor complex.

[0225] When present, the transmembrane domain may be a natural TCR transmembrane domain, a natural transmembrane domain from a heterologous membrane protein, or an artificial transmembrane domain. The transmembrane domain may be a membrane anchor domain. Without limitation, a natural or artificial transmembrane domain may comprise a hydrophobic a-helix of about 20 amino acids, often with positive charges flanking the transmembrane segment. The transmembrane domain may have one transmembrane segment or more than one transmembrane segment. Prediction of transmembrane domains/segments may be made using publicly available prediction tools (e.g. TMHMM, Krogh et al. Journal of Molecular Biology 2001; 305(3):567-580; or TMpred, Hofmann & Stoffel Biol. Chem. Hoppe-Seyler 1993; 347: 166). Non-limiting examples of membrane anchor systems include platelet derived growth factor receptor (PDGFR) transmembrane domain, glycosylphosphatidylinositol (GPI) anchor (added post- translationally to a signal sequence) and the like.

[0226] In some embodiments, the transmembrane domain comprises a TCR alpha transmembrane domain. In some embodiments, the TCR alpha transmembrane domain comprises an amino acid sequence having at least 85% identity, at least 90% identity, at least 95% identity, at least 96% identity, at least 97% identity, at least 98% identity, at least 99% identity or is identical to a sequence of: VIGFRILLLKVAGFNLLMTLRLW (SEQ ID NO: 21). In some embodiments, the TCR alpha transmembrane domain comprises, or consists essentially of, SEQ ID NO: 21. In some embodiments, the TCR alpha transmembrane domain is encoded by a sequence of GTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGGCCGGGTTTAATCTGCTCATGA CGCTGCGGCTGTGG (SEQ ID NO: 22).

[0227] In some embodiments, the transmembrane domain comprises a TCR beta transmembrane domain. In some embodiments, the TCR beta transmembrane domain comprises an amino acid sequence having at least 85% identity, at least 90% identity, at least 95% identity, at least 96% identity, at least 97% identity, at least 98% identity, at least 99% identity or is identical to a sequence of: TILYEILLGKATLYAVLVSALVL (SEQ ID NO: 23). In some embodiments, the TCR beta transmembrane domain comprises, or consists

essentially of, SEQ ID NO: 23. In some embodiments, the TCR beta transmembrane domain is encoded by a sequence of ACCATCCTCTATGAGATCTTGCTAGGGAAGGCCACCTTGTATGCCGTGCTGGTCAGTGCCCTCGTGCTG (SEQ ID NO: 24).

[0228] TCRs of the disclosure can comprise one or more intracellular domains. Exemplary TCRs comprising intracellular domains for use in the instant disclosure are described in PCT/US2020/045250 filed on September 6, 2020, the contents of which are incorporated herein by reference. In some embodiments, the intracellular domain comprises one or more domains capable of providing a stimulatory signal to a transmembrane domain. In some embodiments, the intracellular domain comprises a first intracellular domain capable of providing a stimulatory signal and a second intracellular domain capable of providing a stimulatory signal. In other embodiments, the intracellular domain comprises a first, second and third intracellular domain capable of providing a stimulatory signal. The intracellular domains capable of providing a stimulatory signal are selected from the group consisting of a CD28 molecule (CD28) domain, a LCK proto-oncogene, Src family tyrosine kinase (Lck) domain, a TNF receptor superfamily member 9 (4-1BB) domain, a TNF receptor superfamily member 18 (GITR) domain, a CD4 molecule (CD4) domain, a CD8a molecule (CD8a) domain, a FYN proto-oncogene, Src family tyrosine kinase (Fyn) domain, a zeta chain of T cell receptor associated protein kinase 70 (ZAP70) domain, a linker for activation of T cells (LAT) domain, lymphocyte cytosolic protein 2 (SLP76) domain, (TCR) alpha, TCR beta, CD3 delta, CD3 gamma and CD3 epsilon intracellular domains.

[0229] In some embodiments, an intracellular domain comprises at least one intracellular signaling domain. An intracellular signaling domain generates a signal that promotes a function a cell, for example an immune effector function of a TCR containing cell, e.g., a TCR-expressing T-cell. In some embodiments, the intracellular domain of the first receptor of the disclosure includes at least one intracellular signaling domain. For example, the intracellular domains of CD3 gamma, delta or epsilon comprise signaling domains.

[0230] In some embodiments, the extracellular domain, transmembrane domain and intracellular domain are isolated or derived from the same protein, for example T-cell receptor (TCR) alpha, TCR beta, CD3 delta, CD3 gamma, CD3 epsilon or CD3 zeta.

[0231] Examples of intracellular domains for use in activator receptors of the disclosure include the cytoplasmic sequences of the TCR alpha, TCR beta, CD3 zeta, and 4-1BB, and the intracellular signaling 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 recombinant sequence that has the same functional capability.

[0232] In some embodiments, the intracellular signaling domain comprises a primary intracellular signaling domain. Exemplary primary intracellular signaling domains include those derived from the proteins responsible for primary stimulation, or antigen dependent stimulation.

[0233] In some embodiments, the intracellular domain comprises a CD3 delta intracellular domain, a CD3 epsilon intracellular domain, a CD3 gamma intracellular domain, a CD3 zeta intracellular domain, a TCR alpha intracellular domain or a TCR beta intracellular domain.

[0234] In some embodiments, the intracellular domain comprises a TCR alpha intracellular domain. In some embodiments, a TCR alpha intracellular domain comprises Ser-Ser. In some embodiments, a TCR alpha intracellular domain is encoded by a sequence of TCCAGC.

[0235] In some embodiments, the intracellular domain comprises a TCR beta intracellular domain. In some embodiments, the TCR beta intracellular domain comprises an amino acid sequence having at least 80% identity, at least 90% identity, or is identical to a sequence of: MAMVKRKDSR (SEQ ID NO: 25). In some embodiments, the TCR beta intracellular domain comprises, or consists essentially of SEQ ID NO: 25. In some embodiments, the TCR beta intracellular domain is encoded by a sequence of ATGGCCATGGTCAAGAGAAAGGATTCCAGA (SEQ ID NO: 26).

[0236] In some embodiments, the intracellular signaling domain comprises at least one stimulatory intracellular domain. In some embodiments, the intracellular signaling domain comprises a primary intracellular signaling domain, such as a CD3 delta, CD3 gamma and CD3 epsilon intracellular domain, and one additional stimulatory intracellular domain, for example a co-stimulatory domain. In some embodiments, the intracellular signaling domain comprises a primary intracellular signaling domain, such as a CD3 delta, CD3 gamma and CD3 epsilon intracellular domain, and two additional stimulatory intracellular domains.

[0237] Exemplary co-stimulatory intracellular signaling domains include those derived from proteins responsible for co-stimulatory signals, or antigen independent stimulation. Co-stimulatory molecules include, but are not limited to an MHC class I molecule, BTLA, a Toll ligand receptor, as well as DAP10, DAP12, CD30, LIGHT, OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18) 4-1BB (CD137, TNF receptor superfamily member 9), and CD28 molecule (CD28). A co-stimulatory protein can be represented in the following protein families: TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signaling lymphocytic activation molecules (SLAM proteins), and activating NK cell

receptors. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, GITR, CD30, CD40, ICOS, BAFFR, HVEM, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, a ligand that specifically binds with CD83, CD4, and the like. The co-stimulatory domain can comprise the entire intracellular portion, or the entire native intracellular signaling domain, of the molecule from which it is derived, or a functional variant thereof.

[0238] In some embodiments, the stimulatory domain comprises a co-stimulatory domain. In some embodiments, the co-stimulatory domain comprises a CD28 or 4-1BB co-stimulatory domain. CD28 and 4-1BB are well characterized co-stimulatory molecules required for full T cell activation and known to enhance T cell effector function. For example, CD28 and 4-1BB have been utilized in chimeric antigen receptors (CARs) to boost cytokine release, cytolytic function, and persistence over the first-generation CAR containing only the CD3 zeta signaling domain. Likewise, inclusion of co-stimulatory domains, for example CD28 and 4-1BB domains, in TCRs can increase T cell effector function and specifically allow co-stimulation in the absence of co-stimulatory ligand, which is typically down-regulated on the surface of tumor cells. In some embodiments, the stimulatory domain comprises a CD28 intracellular domain or a 4-1BB intracellular domain.

Inhibitory Receptors

[0239] The disclosure provides a second receptor, comprising an extracellular ligand binding domain specific to a non-target antigen that has been lost in a cancer cell, such as an allelic variant of a gene. The non-target allelic variant can be lost in the cancer cell through any mechanism, such as, without limitation, epigenetic changes that effect non-target allelic variant expression, mutations to the gene encoding the non-target allelic variant, disruption of cellular signaling that regulates expression of the non-target allelic variant, chromosome loss, partial or complete deletion of the genomic locus, gene silencing through modification of nucleic acids or heterochromatin, or loss of expression through other mechanisms. In variations of the compositions and methods disclosed herein, the cells or subject treated may exhibit a loss of expression of the non-target allelic variant because of non-genetic changes. Accordingly the disclosure provides compositions and methods for killing cells and/or treating subject lacking expression of the non-target antigen from any cause, including but not limited to, loss of heterozygosity.

[0240] The non-target antigen can be a protein, or an antigen peptide thereof in a complex with a major histocompatibility complex class I (MHC-I), where the non-target antigen

comprises a polymorphism. Because the non-target antigen is polymorphic, loss of a single copy of the gene encoding the non-target antigen, which may occur through loss of heterozygosity in a cancer cell, yields a cancer cell that retains the other polymorphic variant of gene, but has lost the non-target antigen. For example, a subject having HLA-A*02 and HLA-A*01 alleles at the HLA locus may have a cancer in which only the HLA-A*02 allele is lost. In such a subject, the HLA-A*01 protein remains present, but is not recognized by the inhibitory receptor of immune cells encountering the cancer cell, because the inhibitor receptor is designed to be specific to the HLA-A*02 (or other non-target antigen). In normal non-malignant cells, the HLA-A*02 (or other non-target antigen) is present and inhibits activation of the engineered immune cell. In cancer cells having loss of heterozygosity, the HLA-A*02 allelic variant (or other non-target antigen) is lost. Immune cells engineered to express the inhibitory receptor do not receive an inhibitory signal from the inhibitory receptor, as the inhibitory receptor only responds to the HLA-A*02 (or other non-target antigen), which is absent on cancer cells. By this mechanism, the immune cell is selectively activated, and selectively kills, cancer cells expressing MSLN but having lost HLA-A*02 (or another non-target antigen) due to loss-of-heterozygosity. HLA-A is used here as an example. Similar polymorphic variation occurs in the population at other MHC genes and in other non-MHC genes as well. Accordingly, the disclosure provides a second receptor, comprising an extracellular ligand binding domain specific to a non-target antigen selected from intercellular adhesion molecule 1 (ICAM1), catechol-O-methyltransferase (COMT), C-X-C motif chemokine ligand 16 (CXCL16), leucine rich repeat neuronal 4 (LRRN4) and uroplakin 3B (UPK3B), or an antigen peptide thereof in a complex with a major histocompatibility complex class I (MHC-I), wherein the non-target antigen may comprise a nonsynonymous, extracellular-domain polymorphism (e.g., in an extracellular domain of ICAM1, COMT, CXCL16), and immune cells comprising same. In some embodiments, the second receptor is an inhibitory chimeric antigen receptor. Alternatively, the non-target antigen may comprise a protein whose expression is lost in tumors, but present in key MSLN-expression normal tissues (e.g., LRRN4, UPK3B).

[0241] Exemplary inhibitory receptors are described in PCT/US2020/045228 filed on September 6, 2020, PCT/US2020/064607, filed on December 11, 2020, PCT/US2021/029907, filed on April 29, 2021 and PCT/US2020/059856 filed on November 10, 2020, the contents of each of which are incorporated herein by reference.

[0242] In some embodiments, the second receptor is humanized.

[0243] The disclosure provides a second receptor, which is an inhibitory receptor, comprising an extracellular ligand binding that can discriminate between single amino-acid variant alleles of a non-target antigen. This ability to discriminate between allelic variants of a non-target antigen allows the second receptor to inhibit activation of immune cells comprising the second receptor in the presence of non-target cells that express that the allele recognized by the ligand binding domain. However, activation of immune cells is not inhibited in the presence of target cells that have lost the allele, for example cancer cells that have lost one allele of a gene through loss of heterozygosity.

[0244] The disclosure provides a second receptor, which is an inhibitory receptor, comprising an extracellular ligand binding that can discriminate between different levels of expression of a non-target antigen. This allows the second receptor to inhibit activation of immune cells comprising the second receptor in the presence of non-target cells that express the ligand for the second receptor, but to allow activation of immune cells in the presence of cancer cells that express low levels, or have no expression, of the ligand for the second receptor.

Inhibitor Ligands

[0245] In some embodiments, the non-target antigen is not expressed by the target cells, and is expressed by non-target cells. In some embodiments, the non-target antigen is expressed by healthy cells, i.e. cells that are not cancer cells. In some embodiments, the target cells are a plurality of cancer cells that have lost expression of the non-target antigen through loss of heterozygosity (LOH). In some embodiments, the non-target cells are a plurality of healthy cells (*i.e.*, non-cancer cells), that express both the target and the non-target antigen.

[0246] Any cell surface molecule expressed by the non-target cells that is not expressed by target cells may be a suitable non-target antigen for the second receptor extracellular ligand binding domain. For example, a cell adhesion molecule, a cell-cell signaling molecule, an extracellular domain, a molecule involved in chemotaxis, a glycoprotein, a G protein-coupled receptor, a transmembrane, a receptor for a neurotransmitter or a voltage gated ion channel can be used as a non-target antigen.

In some embodiments, the target antigen is a peptide antigen of a cancer cell-specific antigen in a complex with a major histocompatibility complex class I (MHC-I).

[0247] In some embodiments, the non-target antigen is lost in the cancer cells due to loss of heterozygosity. Exemplary non-target antigens lost in cancer cells due to loss of heterozygosity include ICAM1, COMT and CXCL16. In some embodiments, the non-target antigen is selected from the group consisting of a polymorphic variant of ICAM1, COMT and CXCL16. IN some embodiments, the non-target antigen is an antigen peptide comprising a

polymorphic residue of ICAM1, COMT or CXCL16 in a complex with a major histocompatibility complex class I (MHC-I).

[0248] Non-target major histocompatibility complex class I MHC-I (or pMHC-I) antigens comprising any of HLA-A, HLA-B, HLA-C or HLA-E are envisaged as within the scope of the disclosure. In some embodiments, the non-target antigen comprises a Major Histocompatibility Complex (MHC) protein. In some embodiments, the MHC is MHC class I. In some embodiments, the MHC class I protein comprises a human leukocyte antigen (HLA) protein. In some embodiments, the non-target antigen comprises an allele of an HLA Class I protein selected from the group consisting of HLA-A, HLA-B, HLA-C, or HLA-E. In some embodiments, the HLA-A allele comprises HLA-A*01, HLA-A*02, HLA-A*03 or HLA-A*11. In some embodiments, the HLA-B allele comprises HLA-B*07. In some embodiments, the HLA-C allele comprises HLA-C*07.

[0249] In some embodiments, the non-target antigen comprises HLA-A. In some embodiments, the non-target antigen comprises an allele of HLA-A. in some embodiments, the allele of HLA-A comprises HLA-A*01, HLA-A*02, HLA-A*03 or HLA-A*11. In some embodiments, the non-target antigen comprises HLA-A*69. In some embodiments, the non-target antigen comprises a human leukocyte antigen A*02 allele (HLA-A*02).

[0250] In some embodiments, the non-target antigen comprises an allele of HLA-B. In some embodiments, the allele of HLA-B comprises HLA-B*07.

[0251] In some embodiments, the non-target antigen comprises HLA-C. In some embodiments, the HLA-C allele comprises HLA-C*07.

[0252] In some embodiments, the non-target antigen comprises ICAM1 or an antigen peptide thereof in a complex with MHC-I. Human ICAM1 is frequently lost through LOH in cancer cells.

[0253] A wild type Human ICAM1 is described in NCBI record number NP_000192.2the contents of which are incorporated by reference herein in their entirety. In some embodiments, ICAM1 comprises an amino acid sequence of:

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  1 MAPSSPRPAL PALLVLLGAL FPGPGNAQTS VSPSKVILPR GGSVLVTCST SCDQPKLLGI
 61 ETPLPKKELL LPGNNRKVYE LSNVQEDSQP MCYSNCPDGQ STAKTFLTVY WTPERVELAP
121 LPSWQPVGKN LTLRCQVEGG APRANLTVVL LRGEKELKRE PAVGEPAEVT TTVLVRRDHH
181 GANFSCRTEL DLRPQGLELF ENTSAPYQLQ TFVLPATPPQ LVSPRVLEVD TQGTVVCSLD
241 GLFPVSEAQV HLALGDQRLN PTVTYGNDSF SAKASVSVTA EDEGTQRLTC AVILGNQSQE
301 TLQTVTIYSF PAPNVILTKP EVSEGTEVTV KCEAHPRAKV TLNGVPAQPL GPRAQLLLKA
361 TPEDNGRSFS CSATLEVAGQ LIHKNQTREL RVLYGPRLDE RDCPGNWTWP ENSQQTPMCQ
421 AWGNPLPELK CLKDGTFPLP IGESVTVTRD LEGTYLCRAR STQGEVTRKV TVNVLSPRYE
481 IVIITVVAAA VIMGTAGLST YLYNRQRKIK KYRLQQAQKG TPMKPNTQAT PP (SEQ ID NO:
27).
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[0254] In some embodiments, ICAM1 comprises a sequence that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 27. Polymorphic residues of ICAM1 are marked as bold and underlined in SEQ ID NO: 27. For example, rs5498 is a polymorphism at position 469 of SEQ ID NO: 27, which can be a K or an E.

[0255] In some embodiments, the non-target antigen comprises a polymorphism of ICAM1. For example, the non-target antigen comprises a peptide derived from ICAM1 comprising a polymorphic residue of ICAM1. Polymorphic residues of ICAM1 include amino acid residue 469 of SEQ ID NO: 27. In some embodiments, the non-target antigen comprises a peptide of ICAM1 comprising amino acid 469 of SEQ ID NO: 27. In some embodiments, the non-target antigen comprises a K at position 469 of SEQ ID NO: 27. In some embodiments, the non-target antigen comprises an E at position 469 of SEQ ID NO: 27.

[0256] In some embodiments, the non-target antigen comprises an ICAM1 polymorphism with an K at position 469 of SEQ ID NO: 27, and the second receptor comprises a ligand binding domain with a higher affinity for an ICAM1 ligand with an K at position 469 of SEQ ID NO: 27 than for an ICAM1 ligand with an E at position 469 of SEQ ID NO: 27. In some embodiments, the non-target antigen comprises an ICAM1 polymorphism with an E at position 469 of SEQ ID NO: 27, and the second receptor comprises a ligand binding domain with a higher affinity for an ICAM1 ligand with an E at position 469 of SEQ ID NO: 27 than for an ICAM1 ligand with a K at position 469 of SEQ ID NO: 27..

[0257] In some embodiments, the non-target antigen comprises COMT or an antigen peptide thereof in a complex with MHC-I. Human COMT is frequently lost through LOH in cancer cells.

[0258] A wild type Human COMT is described in NCBI record number NP_000192.2, the contents of which are incorporated by reference herein in their entirety. In some embodiments, COMT comprises an amino acid sequence of:

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  1 MPEAPPLLLA AVLLGLVLLV VLLLLLRHWG WGLCLIGWNE FILQPIHNLL MGDTKEQRIL
 61 NHVLQHAEPG NAQSVLEAID TYCEQKEWAM NVGDKKGKIV DAVIQEHQPS VLLELGAYCG
121 YSAVRMARLL SPGARLITIE INPDCAAITQ RMVDFAGVKD KVTLVVGASQ DIIPQLKKKY
181 DVDTLDMVFL DHWKDRYLPD TLLLEECGLL RKGTVLLADN VICPGAPDFL AHVRGSSCFE
241 CTHYQSFLEY REVVDGLEKA IYKGPGSEAG P (SEQ ID NO: 28).
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[0259] In some embodiments, COMT comprises a sequence that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 28. Polymorphic residues of COMT are marked as bold and

underlined in SEQ ID NO: 28. For example, V158M is a polymorphism at position 158 of SEQ ID NO: 28, which can be a V or an M.

[0260] In some embodiments, the non-target antigen comprises a polymorphism of COMT. For example, the non-target antigen comprises a peptide derived from COMT comprising a polymorphic residue of COMT. Polymorphic residues of COMT 1 include amino acid residue 158 of SEQ ID NO: 28. In some embodiments, the non-target antigen comprises a peptide of COMT comprising amino acid 158 of SEQ ID NO: 28. In some embodiments, the non-target antigen comprises a V at position 158 of SEQ ID NO: 28. In some embodiments, the non-target antigen comprises an M at position 158 of SEQ ID NO: 28.

[0261] In some embodiments, the non-target antigen comprises a COMT polymorphism with a V at position 158 of SEQ ID NO: 28, and the second receptor comprises a ligand binding domain with a higher affinity for a COMT ligand with an V at position 158 of SEQ ID NO: 28 than for a COMT ligand with an M at position 158 of SEQ ID NO: 28. In some embodiments, the non-target antigen comprises a COMT polymorphism with a M at position 158 of SEQ ID NO: 28, and the second receptor comprises a ligand binding domain with a higher affinity for a COMT ligand with an M at position 158 of SEQ ID NO: 28 than for a COMT ligand with a V at position 158 of SEQ ID NO: 28.

[0262] In some embodiments, the non-target antigen comprises C-X-C motif chemokine ligand 16 (CXCL16) or an antigen peptide thereof in a complex with MHC-I. Human CXCL16 precursor is described in NCBI record number NP_001094282.1, the contents of which are incorporated by reference herein in their entirety. In some embodiments, CXCL16 comprises an amino acid sequence of:

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  1 MSGSQSEVAP SPQSPRSPEM GRDLRPGSRV LLLLLLLLLV YLTQPGNGNE GSVTGSCYCG
 61 KRISSDSPPS VQFMNRLRKH LRAYHRCLYY TRFQLLSWSV CGGNKDPWVQ ELMSCLDLKE
121 CGHAYSGIVA HQKHLLPTSP PISQASEGAS SDIHTPAQML LSTLQSTQRP TLPVGSLSSD
181 KELTRPNETT IHTAGHSLAA GPEAGENQKQ PEKNAGPTAR TSATVPVLCL LAIIFILTAA
241 LSYVLCKRRR GQSPQSSPDL PVHYIPVAPD SNT (SEQ ID NO: 29).
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[0263] In some embodiments, the non-target antigen comprises a polymorphism of CXCL16. For example, the non-target antigen comprises a peptide derived from CXCL16 comprising a polymorphic residue of CXCL16. Polymorphic residues of CXCL16 include positions 142 and 200 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising amino acid 142 or 200 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising an A at amino acid 200 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising a V at amino acid 200 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising an I

at amino acid 142 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising a T at amino acid 142 of SEQ ID NO: 29.

[0264] In some embodiments, the non-target antigen comprises a polymorphism of CXCL16. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising an A at amino acid 200 of SEQ ID NO: 29, and the second receptor comprises a ligand binding domain with a higher affinity for a CXCL16 ligand with an A at position 200 of SEQ ID NO: 29 than for a CXCL16 ligand with a V at position 200 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising a V at amino acid 200 of SEQ ID NO: 29, and the second receptor comprises a ligand binding domain with a higher affinity for a CXCL16 ligand with a V at position 200 of SEQ ID NO: 29 than for a CXCL16 ligand with an A at position 200 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising an I at amino acid 142 of SEQ ID NO: 29, and the second receptor comprises a ligand binding domain with a higher affinity for a CXCL16 ligand with an I at position 142 of SEQ ID NO: 29 than for a CXCL16 ligand with a T at position 142 of SEQ ID NO: 29. In some embodiments, the non-target antigen comprises a peptide of CXCL16 comprising a T at amino acid 142 of SEQ ID NO: 29, and the second receptor comprises a ligand binding domain with a higher affinity for a CXCL16 ligand with a T at position 142 of SEQ ID NO: 29 than for a CXCL16 ligand with an I at position 142 of SEQ ID NO: 29.

[0265] In some embodiments, the non-target antigen comprises HLA-A*01, HLA-A*02, HLA-A*03, HLA-A*11, HLA-B*07 or HLA-C*07. Various single variable domains that bind to or recognize the specified HLA alleles, for use in embodiments described herein, are described in Table 5. (complementarity determining regions underlined):

Table 5: HLA scFv binding domains

HLA-A*02 antigen binding domains	
DVLMTQTPLSLPVSL	GATGTTTTGATGACCCAAACTCCACTCTCCCTGCCT
GDQASISCRSSQSIVH	GTCAGTCTTGGAGATCAAGCCTCCATCTCTTGCAG
SNGNTYLEWYLQKP	ATCTAGTCAGAGCATTGTACATAGTAATGGAAACA
GQSPKLLIYKVSNRF	CCTATTTAGAATGGTACCTGCAGAAACCAGGCCAG
SGVPDRFSGSGSGTD	TCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCG
FTLKISRVEAEDLGV	ATTTTCTGGGGTCCCAGACAGGTTCAGTGGCAGTG
YYCFQGSHVPRTSGG	GATCAGGGACAGATTTCACACTCAAGATCAGTAGA
GTKLEIKGGGGSGGG	GTGGAGGCTGAGGATCTGGGAGTTTATTACTGCTT
GSGGGGSGGQVQLQ	TCAAGGTTCACATGTTCCTCGGACGTCCGGTGGAG
QSGPELVKPGASVRI	GCACCAAGCTGGAAATCAAAGGCGGAGGTGGAAG
SCKASGYTFTSYHIH	CGGAGGGGGAGGATCTGGCGGCGGAGGAAGCGGA
WVKQRPGQGLEWIG	GGCCAGGTCCAGCTGCAGCAGTCTGGACCTGAGCT
WIYPGNVNTEYNEK	GGTGAAGCCTGGGGCTTCAGTGAGGATATCCTGCA

FKGKATLTADKSSST AYMHLSSLTSEDSAV YFCAREEITYAMDY WGQGTSVTVSS (SEQ ID NO: 30)	AGGCTTCTGGCTACACCTTCACAAGTTACCATATA CATTGGGTGAAGCAGAGGCCTGGACAGGGACTTG AGTGGATTGGATGGATTTATCCTGGAAATGTTAAT ACTGAGTACAATGAGAAGTTCAAGGGCAAGGCCA CACTGACTGCAGACAAATCGTCCAGCACAGCCTAC ATGCACCTCAGCAGCCTGACCTCTGAGGACTCTGC GGTCTATTTCTGTGCCAGAGAGGAGATTACCTATG CTATGGACTACTGGGGTCAAGGAACCTCAGTCACC GTGTCCTCA (SEQ ID NO: 548)
QVQLVQSGAEVKKP GSSVKVSCKASGYTF TSYHIHWVRQAPGQ GLEWMGWIYPGNVN TEYNEKFKGKATITA DKSTSTAYMELSSLR SEDTAVYYCAREEIT YAMDYWGQGTTVT VSSGGGGSGGGGSG GGGSGGEIVLTQSPG TLSLSPGERATLSCRS SQSIVHSNGNTYLEW YQQKPGQAPRLLIYK VSNRFSGIPDRFSGSG SGTDFTLTISRLEPED FAVYYCFQGSHVPRT FGGGTKVEIK (SEQ ID NO: 31)	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAA GAAGCCTGGGTCCTCAGTGAAGGTTTCCTGCAAGG CTTCTGGATACACCTTCACTAGCTATCATATACATT GGGTGCGCCAGGCCCCCGGACAAGGGCTTGAGTG GATGGGATGGATCTACCCTGGCAATGTTAACACAG AATATAATGAGAAGTTCAAGGGCAAAGCCACCATT ACCGCGGACAAATCCACGAGCACAGCCTACATGG AGCTGAGCAGCCTGAGATCTGAAGACACGGCTGTG TATTACTGTGCGAGGGAGGAAATTACCTACGCTAT GGACTACTGGGGCCAGGGAACCACAGTCACCGTGT CCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGAGATTGTATTG ACCCAGAGCCCAGGCACCCTGAGCCTCTCTCCAGG AGAGCGGGCCACCCTCAGTTGTAGATCCAGTCAGA GTATTGTACACAGTAATGGGAACACCTATTTGGAA TGGTATCAGCAGAAACCAGGTCAAGCCCCAAGATT GCTCATCTACAAAGTCTCTAACAGATTTAGTGGTA TTCCAGACAGGTTCAGCGGTTCCGGAAGTGGTACT GATTTCACCCTCACGATCTCCAGGCTCGAGCCAGA AGATTTCGCCGTTTATTACTGTTTTCAAGGTTCACA TGTGCCGCGCACATTCGGTGGGGGTACTAAAGTAG AAATCAAA (SEQ ID NO: 549)
QVQLVQSGAEVKKP GSSVKVSCKASGYTF TSYHIHWVRQAPGQ GLEWMGWIYPGNVN TEYNEKFKGKATITA DKSTSTAYMELSSLR SEDTAVYYCAREEIT YAMDYWGQGTTVT VSSGGGGSGGGGSG GGGSGGDIVMTQTPL SLPVTPGEPASISCRS SQSIVHSNGNTYLEW YLQKPGQSPQLLIYK VSNRFSGVPDRFSGS GSGTDFTLKISRVEA EDVGVYYCFQGSHV PRTFGGGTKVEIK (SEQ ID NO: 32)	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAA GAAGCCTGGGTCCTCAGTGAAGGTTTCCTGCAAGG CTTCTGGATACACCTTCACTAGCTATCATATACATT GGGTGCGCCAGGCCCCCGGACAAGGGCTTGAGTG GATGGGATGGATCTACCCTGGCAATGTTAACACAG AATATAATGAGAAGTTCAAGGGCAAAGCCACCATT ACCGCGGACAAATCCACGAGCACAGCCTACATGG AGCTGAGCAGCCTGAGATCTGAAGACACGGCTGTG TATTACTGTGCGAGGGAGGAAATTACCTACGCTAT GGACTACTGGGGCCAGGGAACCACAGTCACCGTGT CCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGACATTGTAATG ACCCAGACCCCACTCAGCCTGCCCGTCACTCCAGG AGAGCCGGCCAGCATCAGTTGTAGATCCAGTCAGA GTATTGTACACAGTAATGGGAACACCTATTTGGAA TGGTATCTGCAGAAACCAGGTCAATCCCCACAATT GCTCATCTACAAAGTCTCTAACAGATTTAGTGGTG TACCAGACAGGTTCAGCGGTTCCGGAAGTGGTACT GATTTCACCCTCAAGATCTCCAGGGTCGAGGCAGA

	AGATGTCGGCGTTTATTACTGTTTTCAAGGTTCACA TGTGCCGCGCACATTCGGTGGGGGTACTAAAGTAG AAATCAAA (SEQ ID NO: 550)
EVQLVESGGGLVKP GGSLRLSCAASGYTF TSYHIHWVRQAPGK GLEWVGWIYPGNVN TEYNEKFKGRFTISR DDSKNTLYLQMNSL KTEDTAVYYCAREEI TYAMDYWGQGTTV TVSSGGGGSGGGGS GGGGSGGDIQMTQS PSSLSASVGDRVTITC RSSQSIVHSNGNTYL EWYQQKPGKAPKLL IYKVSNRFSGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCFQGSHV PRTFGGGTKVEIK (SEQ ID NO: 33)	GAGGTGCAGCTGGTGGAGTCTGGGGGTGGGCTGGT GAAGCCTGGGGGCTCACTGAGGCTTTCCTGCGCGG CTTCTGGATACACCTTCACTAGCTATCATATACATT GGGTGCGCCAGGCCCCCGGAAAAGGGCTTGAGTG GGTGGGATGGATCTACCCTGGCAATGTTAACACAG AATATAATGAGAAGTTCAAGGGCAGATTCACCATT AGCAGGGACGATTCCAAGAACACACTCTACCTGCA GATGAACAGCCTGAAAACTGAAGACACGGCTGTGT ATTACTGTGCGAGGGAGGAAATTACCTACGCTATG GACTACTGGGGCCAGGGAACCACAGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCT GGCGGCGGAGGAAGCGGAGGCGACATTCAAATGA CCCAGAGCCCATCCAGCCTGAGCGCATCTGTAGGT GACCGGGTCACCATCACTTGTAGATCCAGTCAGAG TATTGTACACAGTAATGGGAACACCTATTTGGAAT GGTATCAGCAGAAACCAGGTAAAGCCCCAAAATT GCTCATCTACAAAGTCTCTAACAGATTTAGTGGTG TACCAAGCAGGTTCAGCGGTTCCGGAAGTGGTACT GATTTCACCCTCACGATCTCCTCTCTCCAGCCAGAA GATTTCGCCACTTATTACTGTTTTCAAGGTTCACAT GTGCCGCGCACATTCGGTGGGGGTACTAAAGTAGA AATCAAA (SEQ ID NO: 551)
QVQLVQSGAEVKKP GSSVKVSCKASGYTF TSYHIHWVRQAPGQ GLEWIGWIYPGNVN TEYNEKFKGKATITA DESTNTAYMELSSLR SEDTAVYYCAREEIT YAMDYWGQGTLVT VSSGGGGSGGGGSG GGGSGGDIQMTQSPS TLSASVGDRVTITCR SSQSIVHSNGNTYLE WYQQKPGKAPKLLI YKVSNRFSGVPARFS GSGSGTEFTLTISSLQ PDDFATYYCFQGSH VPRTFGQGTKVEVK (SEQ ID NO: 34)	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAA GAAGCCTGGGTCCTCAGTGAAGGTTTCCTGCAAGG CTTCTGGATACACCTTCACTAGCTATCATATACATT GGGTGCGCCAGGCCCCCGGACAAGGGCTTGAGTG GATCGGATGGATCTACCCTGGCAATGTTAACACAG AATATAATGAGAAGTTCAAGGGCAAAGCCACCATT ACCGCGGACGAATCCACGAACACAGCCTACATGG AGCTGAGCAGCCTGAGATCTGAAGACACGGCTGTG TATTACTGTGCGAGGGAGGAAATTACCTACGCTAT GGACTACTGGGGCCAGGGAACCCTGGTCACCGTGT CCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGACATTCAAATG ACCCAGAGCCCATCCACCCTGAGCGCATCTGTAGG TGACCGGGTCACCATCACTTGTAGATCCAGTCAGA GTATTGTACACAGTAATGGGAACACCTATTTGGAA TGGTATCAGCAGAAACCAGGTAAAGCCCCAAAATT GCTCATCTACAAAGTCTCTAACAGATTTAGTGGTG TACCAGCCAGGTTCAGCGGTTCCGGAAGTGGTACT GAATTCACCCTCACGATCTCCTCTCTCCAGCCAGAT GATTTCGCCACTTATTACTGTTTTCAAGGTTCACAT GTGCCGCGCACATTCGGTCAGGGTACTAAAGTAGA AGTCAAA (SEQ ID NO: 552)
QVQLVQSGAEVKKP GSSVKVSCKASGYTF TSYHMHWVRQAPG	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAA GAAGCCTGGGTCCTCAGTGAAGGTTTCCTGCAAGG CTTCTGGATACACCTTCACTAGCTATCATATGCATT

QGLEWIGYIYPGNVN TEYNEKFKGKATLT ADKSTNTAYMELSSL RSEDTAVYFCAREEI TYAMDYWGQGTLV TVSSGGGGSGGGGS GGGGSGGDVQMTQS PSTLSASVGDRVTITC SSSQSIVHSNGNTYM EWYQQKPGKAPKLL IYKVSNRFSGVPDRF SGSGSGTEFTLTISSL QPDDFATYYCHQGS HVPRTFGQGTKVEV K (SEQ ID NO: 35)	GGGTGCGCCAGGCCCCCGGACAAGGGCTTGAGTG GATCGGATACATCTACCCTGGCAATGTTAACACAG AATATAATGAGAAGTTCAAGGGCAAAGCCACCCTT ACCGCGGACAAATCCACGAACACAGCCTACATGG AGCTGAGCAGCCTGAGATCTGAAGACACGGCTGTG TATTTCTGTGCGAGGGAGGAAATTACCTACGCTAT GGACTACTGGGGCCAGGGAACCCTGGTCACCGTGT CCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGACGTTCAAATG ACCCAGAGCCCATCCACCCTGAGCGCATCTGTAGG TGACCGGGTCACCATCACTTGTAGCTCCAGTCAGA GTATTGTACACAGTAATGGGAACACCTATATGGAA TGGTATCAGCAGAAACCAGGTAAAGCCCCAAAATT GCTCATCTACAAAGTCTCTAACAGATTTAGTGGTG TACCAGACAGGTTCAGCGGTTCCGGAAGTGGTACT GAATTCACCCTCACGATCTCCTCTCTCCAGCCAGAT GATTTCGCCACTTATTACTGTCATCAAGGTTCACAT GTGCCGCGCACATTCGGTCAGGGTACTAAAGTAGA AGTCAAA (SEQ ID NO: 553)
QVQLQQSGPELVKP GASVKMSCKASGYT FTSYHIQWVKQRPG QGLEWIGWIYPGDGS TQYNEKFKGKTTLT ADKSSSTAYMLLSSL TSEDSAIYFCAREGT YYAMDYWGQGTSV TVSSGGGGSGGGGS GGGGSGGDVLMTQT PLSLPVSLGDQVSISC RSSQSIVHSNGNTYL EWYLQKPGQSPKLLI YKVSNRFSGVPDRFS GSGSGTDFTLKISRV EAEDLGVYYCFQGS HVPRTFGGGTKLEIK (SEQ ID NO: 36)	CAGGTGCAGCTGCAGCAGTCTGGGCCTGAGCTGGT GAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGG CTTCTGGATACACCTTCACTAGCTATCATATCCAGT GGGTGAAGCAGAGGCCTGGACAAGGGCTTGAGTG GATCGGATGGATCTACCCTGGCGATGGTAGTACAC AGTATAATGAGAAGTTCAAGGGCAAAACCACCCTT ACCGCGGACAAATCCTCCAGCACAGCCTACATGTT GCTGAGCAGCCTGACCTCTGAAGACTCTGCTATCT ATTTCTGTGCGAGGGAGGGGACCTACTACGCTATG GACTACTGGGGCCAGGGAACCTCAGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCT GGCGGCGGAGGAAGCGGAGGCGATGTTTTGATGA CCCAGACTCCACTCTCCCTGCCTGTCTCTCTTGGAG ACCAAGTCTCCATCTCTTGTAGATCCAGTCAGAGT ATTGTACACAGTAATGGGAACACCTATTTAGAATG GTATCTGCAGAAACCAGGTCAGTCTCCAAAGTTGC TCATCTACAAAGTCTCTAACAGATTTAGTGGTGTA CCAGACAGGTTCAGCGGTTCCGGAAGTGGTACTGA TTTCACCCTCAAGATCTCGAGAGTGGAGGCTGAGG ATCTGGGAGTTTATTACTGTTTTCAAGGTTCACATG TGCCGCGCACATTCGGTGGAGGTACTAAACTGGAA ATCAAA (SEQ ID NO: 554)
QLQLQESGPGLVKPS ETLSLTCTVSGYTFTS YHIQWIRQPPGKGLE WIGWIYPGDGSTQY NEKFKGRATISVDTS KNQFSLNLDSVSAAD TAIYYCAREGTYYA MDYWGKGSTVTVSS GGGGSGGGGSGGGG	CAGCTGCAGCTGCAGGAGTCTGGGCCCGGGCTGGT GAAGCCTTCGGAAACGCTGAGCCTCACCTGCACGG TTTCTGGATACACCTTCACCAGCTATCATATCCAGT GGATCCGACAGCCCCCTGGAAAAGGGCTTGAGTGG ATCGGATGGATCTACCCTGGCGATGGTTCAACACA GTACAATGAGAAGTTCAAGGGCAGAGCCACGATT AGCGTGGACACATCCAAGAACCAATTCTCCCTGAA CCTGGACAGCGTGAGTGCTGCGGACACGGCCATTT ATTACTGTGCGAGAGAGGGAACTTACTACGCTATG

SGGDIQMTQSPSSLS ASVGDRVTITCRSSQ SIVHSNGNTYLEWY QQKPGKAPKLLIYKV SNRFSGVPSRFSGSGS GTDFTFTISSLQPEDI ATYYCFQGSHVPRTF GPGTKVDIK (SEQ ID NO: 37)	GACTACTGGGGCAAAGGGAGCACGGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCT GGCGGCGGAGGAAGCGGAGGCGACATCCAGATGA CCCAGAGCCCAAGCTCCCTGAGTGCGTCCGTGGGC GACCGCGTGACCATCACTTGCAGATCCTCTCAGTC CATCGTGCACTCCAACGGCAACACGTACCTCGAGT GGTACCAGCAGAAGCCCGGGAAGGCCCCGAAACT GCTCATCTACAAGGTGAGCAACCGGTTCTCCGGCG TCCCCAGCCGCTTCTCAGGGTCCGGCTCGGGGACG GATTTCACCTTCACGATTAGCAGCTTGCAGCCCGA AGACATCGCCACGTACTACTGCTTTCAGGGAAGTC ACGTGCCGCGTACCTTCGGGCCGGGCACGAAAGTG GATATTAAG (SEQ ID NO: 555)
EVQLVQSGAELKKP GSSVKVSCKASGYTF TSYHIQWVKQAPGQ GLEWIGWIYPGDGST QYNEKFKGKATLTV DKSTNTAYMELSSLR SEDTAVYYCAREGT YYAMDYWGQGTLV TVSSGGGGSGGGGS GGGGSGGDIQMTQS PSTLSASVGDRVTITC RSSQSIVHSNGNTYL EWYQQKPGKAPKLL IYKVSNRFSGVPSRFS GSGSGTDFTLTISSLQ PDDFATYYCFQGSH VPRTFGQGTKVEVK (SEQ ID NO: 38)	GAGGTGCAGCTGGTGCAGTCTGGGGCCGAGCTGAA GAAGCCTGGGTCCTCGGTGAAGGTGTCCTGCAAGG CTTCTGGATACACCTTCACCAGCTATCATATCCAGT GGGTAAAACAGGCCCCTGGACAAGGGCTTGAGTG GATCGGATGGATCTACCCTGGCGATGGTTCAACAC AGTACAATGAGAAGTTCAAGGGCAAAGCCACGCTT ACCGTGGACAAATCCACGAACACAGCCTACATGGA GCTGAGCAGCCTGAGATCTGAGGACACGGCCGTAT ATTACTGTGCGAGAGAGGGAACTTACTACGCTATG GACTACTGGGGCCAAGGGACCCTGGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCT GGCGGCGGAGGAAGCGGAGGCGACATCCAGATGA CCCAGAGCCCATCCACCCTGAGTGCGTCCGTGGGC GACCGCGTGACCATCACTTGCAGATCCTCTCAGTC CATCGTGCACTCCAACGGCAACACGTACCTCGAGT GGTACCAGCAGAAGCCCGGGAAGGCCCCGAAACT GCTCATCTACAAGGTGAGCAACCGGTTCTCCGGCG TCCCCAGCCGCTTCTCAGGGTCCGGCTCGGGGACG GATTTCACCCTCACGATTAGCAGCTTGCAGCCCGA TGACTTCGCCACGTACTACTGCTTTCAGGGAAGTC ACGTGCCGCGTACCTTCGGGCAGGGCACGAAAGTG GAAGTTAAG (SEQ ID NO: 556)
QVQLVQSGAEVKKP GSSVKVSCKASGYTF TSYHIQWVRQAPGQ GLEWMGWIYPGDGS TQYNEKFKGRVTITA DKSTSTAYMELSSLR SEDTAVYYCAREGT YYAMDYWGQGTTV TVSSGGGGSGGGGS GGGGSGGEIVLTQSP GTLSLSPGERATLSC RSSQSIVHSNGNTYL EWYQQKPGQAPRLLI YKVSNRFSGIPDRFS GSGSGTDFTLTISRLE	CAGGTGCAGCTGGTGCAGTCTGGGGCCGAGGTGAA GAAGCCTGGGTCCTCGGTGAAGGTGTCCTGCAAGG CTTCTGGATACACCTTCACCAGCTATCATATCCAGT GGGTACGACAGGCCCCTGGACAAGGGCTTGAGTG GATGGGATGGATCTACCCTGGCGATGGTTCAACAC AGTACAATGAGAAGTTCAAGGGCAGAGTCACGATT ACCGCGGACAAATCCACGAGCACAGCCTACATGG AGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTA TATTACTGTGCGAGAGAGGGAACTTACTACGCTAT GGACTACTGGGGCCAAGGGACCACGGTCACCGTGT CCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGAGATCGTCCTG ACCCAGAGCCCAGGGACCCTGAGTTTGTCCCCGGG CGAGCGCGCGACCCTCAGTTGCAGATCCTCTCAGT CCATCGTGCACTCCAACGGCAACACGTACCTCGAG

PEDFAVYYCFQGSH VPRTFGGGTKVEIK (SEQ ID NO: 39)	TGGTACCAGCAGAAGCCCGGGCAGGCCCCGCGACT GCTCATCTACAAGGTGAGCAACCGGTTCTCCGGCA TCCCCGACCGCTTCTCAGGGTCCGGCTCGGGGACG GATTTCACCCTCACGATTAGCCGCTTGGAGCCCGA AGACTTCGCCGTGTACTACTGCTTTCAGGGAAGTC ACGTGCCGCGTACCTTCGGGGGGGGCACGAAAGTG GAAATTAAG (SEQ ID NO: 557)
QVTLKQSGAEVKKP GSSVKVSCTASGYTF TSYHVSWVRQAPGQ GLEWLGRIYPGDGST QYNEKFKGKVTITAD KSMDTSFMELTSLTS EDTAVYYCAREGTY YAMDLWGQGTLVT VSSGGGGSGGGGSG GGGSGGEIVLTQSPG TLSLSPGERATLSCRS SQSIVHSNGNTYLAW YQQKPGQAPRLLISK VSNRFSGVPDRFSGS GSGTDFTLTISRLEPE DFAVYYCQQGSHVP RTFGGGTKVEIK (SEQ ID NO: 40)	CAGGTGACCCTGAAGCAGTCTGGGGCCGAGGTGA AGAAGCCTGGGTCCTCGGTGAAGGTGTCCTGCACG GCTTCTGGATACACCTTCACCAGCTATCATGTCAGC TGGGTACGACAGGCCCCTGGACAAGGGCTTGAGTG GTTGGGAAGGATCTACCCTGGCGATGGTTCAACAC AGTACAATGAGAAGTTCAAGGGCAAAGTCACGATT ACCGCGGACAAATCCATGGACACATCCTTCATGGA GCTGACCAGCCTGACATCTGAGGACACGGCCGTAT ATTACTGTGCGAGAGAGGGAACTTACTACGCTATG GACCTCTGGGGCCAAGGGACCCTGGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCT GGCGGCGGAGGAAGCGGAGGCGAGATCGTCCTGA CCCAGAGCCCAGGGACCCTGAGTTTGTCCCCGGGC GAGCGCGCGACCCTCAGTTGCAGATCCTCTCAGTC CATCGTGCACTCCAACGGCAACACGTACCTCGCGT GGTACCAGCAGAAGCCCGGGCAGGCCCCGCGACT GCTCATCTCCAAGGTGAGCAACCGGTTCTCCGGCG TCCCCGACCGCTTCTCAGGGTCCGGCTCGGGGACG GATTTCACCCTCACGATTAGCCGCTTGGAGCCCGA AGACTTCGCCGTGTACTACTGCCAACAGGGAAGTC ACGTGCCGCGTACCTTCGGGGGGGGCACGAAAGTG GAAATTAAG (SEQ ID NO: 558)
QVQLVQSGAEVKKP GASVKVSCKASGYT FTSYHMHWVRQAPG QRLEWMGWIYPGDG STQYNEKFKGKVTIT RDTSASTAYMELSSL RSEDTAVYYCAREG TYYAMDYWGQGTL VTVSSGGGGSGGGG SGGGGSGGDIVMTQ TPLSLPVTPGEPASIS CRSSQSIVHSNGNTY LDWYLQKPGQSPQL LIYKVSNRFSGVPDR FSGSGSGTDFTLKISR VEAEDVGVYYCMQ GSHVPRTFGGGTKVE IK (SEQ ID NO: 41)	CAGGTGCAGCTGGTGCAGTCTGGGGCCGAGGTGAA GAAGCCTGGGGCCTCGGTGAAGGTGTCCTGCAAGG CTTCTGGATACACCTTCACCAGCTATCATATGCACT GGGTACGACAGGCCCCTGGACAAAGGCTTGAGTG GATGGGATGGATCTACCCTGGCGATGGTTCAACAC AGTACAATGAGAAGTTCAAGGGCAAAGTCACGATT ACCCGGGACACATCCGCGAGCACAGCCTACATGGA GCTGAGCAGCCTGAGATCTGAGGACACGGCCGTAT ATTACTGTGCGAGAGAGGGAACTTACTACGCTATG GACTACTGGGGCCAAGGGACCCTGGTCACCGTGTC CTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATCT GGCGGCGGAGGAAGCGGAGGCGACATCGTCATGA CCCAGACCCCACTGTCCCTGCCTGTGACCCCGGGC GAGCCCGCGAGCATCAGTTGCAGATCCTCTCAGTC CATCGTGCACTCCAACGGCAACACGTACCTCGACT GGTACCTGCAGAAGCCCGGGCAGTCCCCGCAACTG CTCATCTACAAGGTGAGCAACCGGTTCTCCGGCGT CCCCGACCGCTTCTCAGGGTCCGGCTCGGGGACGG ATTTCACCCTCAAGATTAGCCGCGTGGAGGCCGAA GACGTCGGCGTGTACTACTGCATGCAGGGAAGTCA

	CGTGCCGCGTACCTTCGGGGGGGGCACGAAAGTGG AAATTAAG (SEQ ID NO: 559)
HLA-B*07 antigen binding domains	
1.10_scFv	QVQLQESGPGLVKPSQTLSLTCTVSGYSITSGYSWHW IRQPPGKGLEWIGYIHFSGSTHYHPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARGGVVSHYAMDCW GQGTTVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPS SLSASVGDRVTITCRASENIYSNLAWYQQKPGKAPKL LIYAATYLPDGVPSRFSGSGSGTDFTLTISSLQPEDFA TYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 560)
1.9_scFv	EVQLVESGGGLVKPGGSLRLSCAASGYSITSGYSWH WVRQAPGKGLEWVSYIHFSGSTHYHPSLKSRFTISRD NAKNSLYLQMNSLRAEDTAVYYCARGGVVSHYAM DCWGQGTTVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSVSASVGDRVTITCRASENIYSNLAWYQQKPGK APKLLIYAATYLPDGVPSRFSGSGSGTDFTLTISSLQP EDFATYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 561)
1.8_scFv	EVQLVESGGGLVKPGGSLRLSCAASGYSITSGYSWH WVRQAPGKGLEWVGYIHFSGSTHYHPSLKSRFTISRD DSKNTLYLQMNSLKTEDTAVYYCARGGVVSHYAMD CWGQGTTVTVSSGGGGSGGGGSGGGGSGGEIVLTQS PATLSLSPGERATLSCRASENIYSNLAWYQQKPGQAP RLLIYAATYLPDGIPARFSGSGSGTDFTLTISSLEPEDF AVYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 562)
1.7_scFv	QVQLQQSGPGLVKPSQTLSLTCAISGYSITSGYSWHW IRQSPSRGLEWLGYIHFSGSTHYHPSLKSRITINPDTSK NQFSLQLNSVTPEDTAVYYCARGGVVSHYAMDCWG QGTTVTVSSGGGGSGGGGSGGGGSGGEIVLTQSPAT LSLSPGERATLSCRASENIYSNLAWYQQKPGQAPRLL IYAATYLPDGIPARFSGSGSGTDFTLTISRLEPEDFAVY YCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 563)
1.6_scFv	EVQLVESGGGLVKPGGSLRLSCAASGYSITSGYSWH WVRQAPGKGLEWVGYIHFSGSTHYHPSLKSRFTISRD DSKNTLYLQMNSLKTEDTAVYYCARGGVVSHYAMD CWGQGTTVTVSSGGGGSGGGGSGGGGSGGDIQMTQ SPSSVSASVGDRVTITCRASENIYSNLAWYQQKPGKA PKLLIYAATYLPDGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 564)
1.5_scFv	EVQLVESGGGLVQPGGSLRLSCAASGYSITSGYSWH WVRQAPGKGLEWVSYIHFSGSTHYHPSLKSRFTISRD NSKNTLYLQMNSLRAEDTAVYYCARGGVVSHYAM DCWGQGTTVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASENIYSNLAWYQQKPGK APKLLIYAATYLPDGVPSRFSGSGSGTDFTLTISSLQP EDFATYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 565)
1.4_scFv	EVQLVESGGGLVKPGGSLRLSCAASGYSITSGYSWH WVRQAPGKGLEWVGYIHFSGSTHYHPSLKSRFTISRD

	DSKNTLYLQMNSLKTEDTAVYYCARGGVVSHYAMD CWGQGTTVTVSSGGGGSGGGGSGGGGSGGDIQMTQ SPSSLSASVGDRVTITCRASENIYSNLAWYQQKPGKA PKLLIYAATYLPDGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 566)
1.3_scFv	QVQLQQWGAGLLKPSETLSLTCAVYGYSITSGYSWH WIRQPPGKGLEWIGYIHFSGSTHYHPSLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARGGVVSHYAMDC WGQGTTVTVSSGGGGSGGGGSGGGGSGGDIQMTQS PSSLSASVGDRVTITCRASENIYSNLAWYQQKPGKAP KLLIYAATYLPDGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 567)
1.2_scFv	QVQLQESGPGLVKPSQTLSLTCTVSGYSITSGYSWHW IRQHPGKGLEWIGYIHFSGSTHYHPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARGGVVSHYAMDCW GQGTTVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPS SLSASVGDRVTITCRASENIYSNLAWYQQKPGKAPKL LIYAATYLPDGVPSRFSGSGSGTDFTLTISSLQPEDFA TYYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 568)
1.1_scFv	QVQLQQSGPGLVKPSQTLSLTCAISGYSITSGYSWHW IRQSPSRGLEWLGYIHFSGSTHYHPSLKSRITINPDTSK NQFSLQLNSVTPEDTAVYYCARGGVVSHYAMDCWG QGTTVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPSS LSASVGDRVTITCRASENIYSNLAWYQQKPGKAPKLL IYAATYLPDGVPSRFSGSGSGTDFTLTISSLQPEDFAT YYCQHFWVTPYTFGGGTKVEIK (SEQ ID NO: 569)
HLA-A*11 antigen binding domains	
QVQLQESGPGLVKPS QTLSLTCTVSGGSISS GGGYYWSWIRQPPGK GLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCARHYYYYS MDVWGKGTTVTVSS GGGGSGGGGSGGGG SGGDIQMTQSPSSLS ASVGDRVTITCRASQ SISSYLNWYQQKPGK APKLLIYAASSLQSG VPSRFSGSGSGTDFT LTISSLQPEDFATYYC QQSYSTPLTFGGGTK VEIK (SEQ ID NO: 114)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGT GAAACCCAGCCAGACCCTGAGCCTGACCTGCACAG TGTCCGGCGGCTCGATCAGCAGCGGCGGCTACTAC TGGTCCTGGATCAGACAGCCCCCTGGCAAGGGCCT GGAATGGATCGGCTACATCTACTACAGCGGCAGCA CCTACTACAACCCCAGCCTGAAGTCCAGAGTGACC ATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCT GAAGCTGAGCAGCGTGACAGCCGCCGACACCGCT GTGTATTACTGTGCGAGACACTACTACTACTACTCC ATGGACGTCTGGGGCAAAGGGACCACGGTCACCGT GTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGA TCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGA TGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAG GAGACAGAGTCACCATCACTTGCCGGGCAAGTCAG AGCATTAGCAGCTATTTAAATTGGTATCAGCAGAA ACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTG CATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC AGTGGCAGTGGATCTGGGACAGATTTCACTCTCAC CATCAGCAGTCTGCAACCTGAAGATTTTGCAACTT ACTACTGTCAACAGAGTTACAGTACCCCTCTCACTT

	TCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 123)
QITLKESGPTLVKPT QTLTLTCTFSGFSLST SGVGVGWIRQPPGK ALEWLALIYWNDDK RYSPSLKSRLTITKDT SKNQVVLTMTNMDP VDTATYYCAHRHMR LSCFDYWGQGTLVT VSSGGGGSGGGGSG GGGSGGDIQMTQSPS SLSASVGDRVTITCR ASQSISSYLNWYQQK PGKAPKLLIYAASSL QSGVPSRFSGSGSGT DFTLTISSLQPEDFAT YYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 115)	CAGATCACCCTGAAAGAGTCCGGCCCCACCCTGGT GAAACCCACCCAGACCCTGACCCTGACATGCACCT TCAGCGGCTTCAGCCTGAGCACCTCTGGCGTGGGC GTGGGCTGGATCAGACAGCCTCCCGGCAAGGCCCT GGAATGGCTGGCCCTGATCTACTGGAACGACGACA AGCGGTACAGCCCCAGCCTGAAGTCCCGGCTGACC ATCACCAAGGACACCTCGAAGAACCAGGTGGTGCT GACCATGACAAACATGGACCCCGTGGACACCGCCA CATATTACTGTGCACACAGACACATGCGTTTAAGC TGTTTTGACTACTGGGGCCAGGGAACCCTGGTCAC CGTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGA GGATCTGGCGGCGGAGGAAGCGGAGGCGACATCC AGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTG TAGGAGACAGAGTCACCATCACTTGCCGGGCAAGT CAGAGCATTAGCAGCTATTTAAATTGGTATCAGCA GAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATG CTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGG TTCAGTGGCAGTGGATCTGGGACAGATTTCACTCT CACCATCAGCAGTCTGCAACCTGAAGATTTTGCAA CTTACTACTGTCAACAGAGTTACAGTACCCCTCTCA CTTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 124)
QVQLVQSGAEVKKP GASVKVSCKASGYT FTSYAMHWVRQAPG QRLEWMGWINAGN GNTKYSQKFQGRVTI TRDTSASTAYMELSS LRSEDTAVYYCARE GNGANPDAFDIWGQ GTMVTVSSGGGGSG GGGSGGGGSGGDIQ MTQSPSSLSASVGDR VTITCRASQSISSYLN WYQQKPGKAPKLLI YAASSLQSGVPSRFS GSGSGTDFTLTISSLQ PEDFATYYCQQSYST PLTFGGGTKVEIK (SEQ ID NO: 116)	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCCTGCAAGG CCAGCGGCTACACCTTCACCAGCTACGCCATGCAC TGGGTTCGACAGGCCCCTGGCCAGAGACTGGAATG GATGGGCTGGATCAACGCCGGCAACGGCAACACC AAGTACAGCCAGAAATTCCAGGGCAGAGTGACCA TCACCCGGGACACCAGCGCCAGCACCGCCTACATG GAACTGAGCAGCCTGCGGAGCGAGGACACCGCTG TGTATTACTGTGCGAGAGAAGGAAATGGTGCCAAC CCTGATGCTTTTGATATCTGGGGCCAAGGGACAAT GGTCACCGTGTCCTCAGGCGGAGGTGGAAGCGGA GGGGGAGGATCTGGCGGCGGAGGAAGCGGAGGCG ACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTG CATCTGTAGGAGACAGAGTCACCATCACTTGCCGG GCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTA TCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA TCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCA TCAAGGTTCAGTGGCAGTGGATCTGGGACAGATTT CACTCTCACCATCAGCAGTCTGCAACCTGAAGATT TTGCAACTTACTACTGTCAACAGAGTTACAGTACC CCTCTCACTTTCGGCGGCGGAACAAAGGTGGAGAT CAAG (SEQ ID NO: 125)
EVQLVESGGGLVQP GGSLRLSCAASGFTF SSYDMHWVRQATG KGLEWVSAIGTAGD	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGG TGCAGCCTGGCGGCAGCCTGAGACTGTCTTGCGCC GCCAGCGGCTTCACCTTCAGCAGCTACGACATGCA CTGGGTCCGCCAGGCCACCGGCAAGGGACTGGAAT

TYYPGSVKGRFTISR ENAKNSLYLQMNSL RAGDTAVYYCARDL PGSYWYFDLWGRGT LVTVSSGGGGSGGG GSGGGGSGGDIQMT QSPSSLSASVGDRVTI TCRASQSISSYLNWY QQKPGKAPKLLIYAA SSLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 117)	GGGTGTCCGCCATCGGCACAGCCGGCGACACTTAC TACCCCGGCAGCGTGAAGGGCCGGTTCACCATCAG CAGAGAGAACGCCAAGAACAGCCTGTACCTGCAG ATGAACAGCCTTCGAGCCGGCGATACCGCCGTGTA TTACTGTGCAAGAGATCTCCCTGGTAGCTACTGGT ACTTCGATCTCTGGGGCCGTGGCACCCTGGTCACT GTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGACATCCA GATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGT AGGAGACAGAGTCACCATCACTTGCCGGGCAAGTC AGAGCATTAGCAGCTATTTAAATTGGTATCAGCAG AAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGC TGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGT TCAGTGGCAGTGGATCTGGGACAGATTTCACTCTC ACCATCAGCAGTCTGCAACCTGAAGATTTTGCAAC TTACTACTGTCAACAGAGTTACAGTACCCCTCTCAC TTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 126)
QVQLQESGPGLVKPS QTLSLTCTVSGGSISS GGYYWSWIRQPPGK GLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCARHYYYYY LDVWGKGTTVTVSS GGGGSGGGGSGGGG SGGDIQMTQSPSSLS ASVGDRVTITCRASQ SISSYLNWYQQKPGK APKLLIYAASSLQSG VPSRFSGSGSGTDFT LTISSLQPEDFATYYC QQSYSTPLTFGGGTK VEIK (SEQ ID NO: 118)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGT GAAACCCAGCCAGACCCTGAGCCTGACCTGCACAG TGTCCGGCGGCTCGATCAGCAGCGGCGGCTACTAC TGGTCCTGGATCAGACAGCCCCCTGGCAAGGGCCT GGAATGGATCGGCTACATCTACTACAGCGGCAGCA CCTACTACAACCCCAGCCTGAAGTCCAGAGTGACC ATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCT GAAGCTGAGCAGCGTGACAGCCGCCGACACCGCT GTGTATTACTGTGCGAGACACTACTACTACTACTA CCTGGACGTCTGGGGCAAAGGGACCACGGTCACCG TGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGG ATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAG ATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTA GGAGACAGAGTCACCATCACTTGCCGGGCAAGTCA GAGCATTAGCAGCTATTTAAATTGGTATCAGCAGA AACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCT GCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTT CAGTGGCAGTGGATCTGGGACAGATTTCACTCTCA CCATCAGCAGTCTGCAACCTGAAGATTTTGCAACT TACTACTGTCAACAGAGTTACAGTACCCCTCTCACT TTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 127)
EVQLVESGGGLVQP GGSLRLSCAASGFTF SSYWMHWVRQAPG KGLVWVSRINSDGSS TSYADSVKGRFTISR DNAKNTLYLQMNSL RAEDTAVYYCCLGV LLYNWFDPWGQGTL VTVSSGGGGSGGGG SGGGGSGGDIQMTQ	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGG TGCAGCCTGGCGGCAGCCTGAGACTGTCTTGCGCC GCCAGCGGCTTCACCTTCAGCAGCTACTGGATGCA CTGGGTCCGCCAGGCCCCTGGCAAGGGACTGGTCT GGGTGTCTCGAATCAACAGCGACGGCAGCAGCACC AGCTACGCCGACAGCGTGAAGGGCCGGTTCACCAT CAGCCGGGACAACGCCAAGAACACCCTGTACCTGC AGATGAACAGCCTGCGGGCCGAGGACACCGCCGT GTATTACTGTTGTTTGGGTGTTTTATTATACAACTG GTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCG

SPSSLSASVGDRVTIT CRASQSISSYLNWYQ QKPGKAPKLLIYAAS SLQSGVPSRFSGSGS GTDFTLTISSLQPEDF ATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 119)	TGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGG ATCTGGCGGCGGAGGAAGCGGAGGCGACATCCAG ATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTA GGAGACAGAGTCACCATCACTTGCCGGGCAAGTCA GAGCATTAGCAGCTATTTAAATTGGTATCAGCAGA AACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCT GCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTT CAGTGGCAGTGGATCTGGGACAGATTTCACTCTCA CCATCAGCAGTCTGCAACCTGAAGATTTTGCAACT TACTACTGTCAACAGAGTTACAGTACCCCTCTCACT TTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 128)
QVQLQESGPGLVKPS QTLSLTCTVSGGSISS GGGYYWSWIRQPPGK GLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCARHYYYY MDVWGKGTTVTVSS GGGGSGGGGSGGGG SGGDIQMTQSPSSLS ASVGDRVTITCRASQ SISSYLNWYQQKPGK APKLLIYAASSLQSG VPSRFSGSGSGTDFT LTISSLQPEDFATYYC QQSYSTPLTFGGGTK VEIK (SEQ ID NO: 120)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGT GAAACCCAGCCAGACCCTGAGCCTGACCTGCACAG TGTCCGGCGGCTCGATCAGCAGCGGCGGCTACTAC TGGTCCTGGATCAGACAGCCCCCTGGCAAGGGCCT GGAATGGATCGGCTACATCTACTACAGCGGCAGCA CCTACTACAACCCCAGCCTGAAGTCCAGAGTGACC ATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCT GAAGCTGAGCAGCGTGACAGCCGCCGACACCGCT GTGTATTACTGTGCGAGACACTACTACTACTACAT GGACGTCTGGGGCAAAGGGACCACGGTCACCGTGT CCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGATC TGGCGGCGGAGGAAGCGGAGGCGACATCCAGATG ACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGCAAGTCAGAG CATTAGCAGCTATTTAAATTGGTATCAGCAGAAAC CAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCA TCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAG TGGCAGTGGATCTGGGACAGATTTCACTCTCACCA TCAGCAGTCTGCAACCTGAAGATTTTGCAACTTAC TACTGTCAACAGAGTTACAGTACCCCTCTCACTTTC GGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 129)
QITLKESGPTLVKPT QTLTLTCTFSGFSLST SGVGVGWIRQPPGK ALEWLALIYWNDDK RYSPSLKSRLTITKDT SKNQVVLTMTNMDP VDTATYYCAHKTTS FYFDYWGQGTLVTV SSGGGGSGGGGSGG GGSGGDIQMTQSPSS LSASVGDRVTITCRA SQSISSYLNWYQQKP GKAPKLLIYAASSLQ SGVPSRFSGSGSGTD FTLTISSLQPEDFATY YCQQSYSTPLTFGGG	CAGATCACCCTGAAAGAGTCCGGCCCCACCCTGGT GAAACCCACCCAGACCCTGACCCTGACATGCACCT TCAGCGGCTTCAGCCTGAGCACCTCTGGCGTGGGC GTGGGCTGGATCAGACAGCCTCCCGGCAAGGCCCT GGAATGGCTGGCCCTGATCTACTGGAACGACGACA AGCGGTACAGCCCCAGCCTGAAGTCCCGGCTGACC ATCACCAAGGACACCTCGAAGAACCAGGTGGTGCT GACCATGACAAACATGGACCCCGTGGACACCGCCA CATATTACTGTGCACACAAAACGACGTCGTTTTAC TTTGACTACTGGGGCCAGGGAACCCTGGTCACCGT GTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAGGA TCTGGCGGCGGAGGAAGCGGAGGCGACATCCAGA TGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAG GAGACAGAGTCACCATCACTTGCCGGGCAAGTCAG AGCATTAGCAGCTATTTAAATTGGTATCAGCAGAA ACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTG

TKVEIK (SEQ ID NO: 121)	CATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC AGTGGCAGTGGATCTGGGACAGATTTCACTCTCAC CATCAGCAGTCTGCAACCTGAAGATTTTGCAACTT ACTACTGTCAACAGAGTTACAGTACCCCTCTCACTT TCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 130)
QVQLQESGPGLVKPS QTLSLTCTVSGGSISS GGGYYWSWIRQPPGK GLEWIGYIYYSGSTY YNPSLKSRVTISVDTS KNQFSLKLSSVTAAD TAVYYCARHYYYYY MDVWGKGTTVTVSS GGGGSGGGGSGGGG SGGDIQMTQSPSSLS ASVGDRVTITCRASQ SISSYLNWYQQKPGK APKLLIYAASSLQSG VPSRFSGSGSGTDFT LTISSLQPEDFATYYC QQSYSTPLTFGGGTK VEIK (SEQ ID NO: 122)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCTGGT GAAACCCAGCCAGACCCTGAGCCTGACCTGCACAG TGTCCGGCGGCTCGATCAGCAGCGGCGGCTACTAC TGGTCCTGGATCAGACAGCCCCCTGGCAAGGGCCT GGAATGGATCGGCTACATCTACTACAGCGGCAGCA CCTACTACAACCCCAGCCTGAAGTCCAGAGTGACC ATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCT GAAGCTGAGCAGCGTGACAGCCGCCGACACCGCT GTGTATTACTGTGCGAGACACTACTACTACTACTA CATGGACGTCTGGGGCAAAGGGACCACGGTCACC GTGTCCTCAGGCGGAGGTGGAAGCGGAGGGGGAG GATCTGGCGGCGGAGGAAGCGGAGGCGACATCCA GATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGT AGGAGACAGAGTCACCATCACTTGCCGGGCAAGTC AGAGCATTAGCAGCTATTTAAATTGGTATCAGCAG AAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGC TGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGT TCAGTGGCAGTGGATCTGGGACAGATTTCACTCTC ACCATCAGCAGTCTGCAACCTGAAGATTTTGCAAC TTACTACTGTCAACAGAGTTACAGTACCCCTCTCAC TTTCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 131)
HLA-C*07 antigen binding domains	
C7-45	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEW VSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA VSFDWFDPWGQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPS SLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 570)
C7-44	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR ERSISPYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQM TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQ SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEI K (SEQ ID NO: 571)
C7-43	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGKGLEWI GSIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDS VIWYWFDPWGQGTLVTVSSGGGGSGGGGSGGGGSGGQSVLTQPPS ASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPKLLIYSNNQRPSG VPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGWVFGGGTK LTVL (SEQ ID NO: 572)
C7-42	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EEILPRLSYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQM

	TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 573)
C7-41	QVQLVQSGSELKKPGASVKVSCKASGYTFTSYAMNWVRQAPGQGLEWMGWINTNTGNPTYAQGFTGRFVFSFDTSVSTAYLQICSLKAEDTAVYYCARGGRAHSSWYFDLWGRGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 574)
C7-40	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDRIKILPRLGYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 575)
C7-39	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTVIHYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 576)
C7-38	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDVIVEVFLSYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 577)
C7-37	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDIFIHYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 578)
C7-36	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGTFYSYSPYYFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 579)
C7-35	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREWIKILPRLGYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 580)
C7-34	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDRSLYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 581)

C7-33	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DKILAPNYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQM TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQ SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEI K (SEQ ID NO: 582)
C7-32	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EKSWKYFYYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 583)
C7-31	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR ENTSTIPYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQ MTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASS LQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 584)
C7-30	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EDVDKNTSTIYYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSG GDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY AASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 585)
C7-29	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEW VSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR DGGDIVSSSAIYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGGSGGAI QLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYDAS SLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPLTFGGGTK VEIK (SEQ ID NO: 586)
C7-28	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DLILPPYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQM TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQ SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEI K (SEQ ID NO: 587)
C7-27	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR ETWIKILPRYYYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGG DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGG TKVEIK (SEQ ID NO: 588)
C7-26	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DLSRYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 589)
C7-25	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEW VSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR EHIVLCFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPSS

	LSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYPLTFGGGTKVEIK (SEQ ID NO: 590)
C7-24	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DKILPRPYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQ MTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASS LQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 591)
C7-23	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEW MGWISAYNGNTNYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVY YCARGSNEYFQHWGQGTLVTVSSGGGGSGGGGSGGGGSGGQSALTQ PPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVS KRPSGVPDRFSGSKSGNTASLTVSGLQAEDEADYYCSSYAGSNNWVFG GGTKLTVL (SEQ ID NO: 592)
C7-22	QVQLVQSGSELKKPGASVKVSCKASGYTFTSYAMNWVRQAPGQGLE WMGWINTNTGNPTYAQGFTGRFVFSFDTSVSTAYLQICSLKAEDTAVY YCARGTSYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 593)
C7-21	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EEIVEVFYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQM TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQ SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEI K (SEQ ID NO: 594)
C7-20	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEW VSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA KVDDYYFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPS SLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 595)
C7-19	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMHWVRQAPGKGLV WVSRINSDGSSTSYADSVKGRFTISRDNAKNTLYLQMNSLRAEDTAVYY CAWSTNILLSYTKAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 596)
C7-18	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DKTYYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 597)
C7-17	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EKYFHDKYFHDYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSG GDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY AASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 598)

C7-16	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DTSVYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 599)
C7-15	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EKILPYYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQM TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQ SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEI K (SEQ ID NO: 600)
C7-14	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEW VSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAI QWIYIYINPRGFIFLHDAFDIWGQGTMVTVSSGGGGSGGGGSGGGGS GGQSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPK LLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSL NGWVFGGGTKLTVL (SEQ ID NO: 601)
C7-13	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPSRGLE WLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVY YCAKEDVDFHHDAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 602)
C7-12	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EGVDKNTSTIYYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSG GDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY AASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGG GTKVEIK (SEQ ID NO: 603)
C7-11	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEW VSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR DRRGYFDLWGRGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPSS LSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYPLTFGGGTKVEIK (SEQ ID NO: 604)
C7-10	EVQLVQSGAEVKKPGATVKISCKVSGYTFTDYYMHWVQQAPGKGLEW MGLVDPEDGETIYAEKFQGRVTITADTSTDTAYMELSSLRSEDTAVYYC ATGIHVDIRSMEDWFDPWGQGTLVTVSSGGGGSGGGGSGGGGSGG DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGG TKVEIK (SEQ ID NO: 605)
C7-9	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DIGTSYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQMTQ SPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 606)
C7-8	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EVVEVFLYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQ

	MTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASS LQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 607)
C7-7	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DLYYYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 608)
C7-6	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR ESWKYFYPRGSIFIHYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGG SGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKL LIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTF GGGTKVEIK (SEQ ID NO: 609
C7-5	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DRIVEVFYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQM TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQ SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEI K (SEQ ID NO: 610)
C7-4	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR EKYFHDWLYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 611)
C7-3	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPPGKGLE WIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR DLVDKNTSYYYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTK VEIK (SEQ ID NO: 612)
C7-2	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEW MGWISAYNGNTNYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVY YCARVQNEYFQHWGQGTLVTVSSGGGGSGGGGSGGGGSGGGQSALT QPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEV SKRPSGVPDRFSGSKSGNTASLTVSGLQAEDEADYYCSSYAGSNNWVF GGGTKLTVL (SEQ ID NO: 613)
C7-1	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEW VSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAT ANWFDPWGQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPSSV SASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFPLTFGGGTKVEIK (SEQ ID NO: 614)
HLA-A*03 scFv Sequences	
15	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTM TTDTSTSTAYMELRSLRSDDTAVYYCARERVSQRGA FDIWGQGTMVTVSSGGGGSGGGGSGGGGSGGDIQM TQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPG

	KAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQP EDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 615)
16	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNW VRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISRD NAKNSLYLQMNSLRAEDTAVYYCARGNPDKDPFDY WGQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQS PSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDF ATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 616)
17	QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGSYYWS WIRQPPGKGLEWIGYIYYSGSTNYNPSLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARDFYCTNWYFDL WGRGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQS PSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDF ATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 617)
18	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWI RQPPGKGLEWIGYIYYSGSTNYNPSLKSRVTISVDTSK NQFSLKLSSVTAADTAVYYCARESSSGSYWYFDLWG RGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPSS LSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLL IYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATY YCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 618)
19	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGW VRQMPGKGLEWMGIIYPGDSDTRYSPSFQGQVTISAD KSISTAYLQWSSLKASDTAMYYCARDSGYKYNLYY YYYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSG GDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWY QQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 619)
20	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTM TTDTSTSTAYMELRSLRSDDTAVYYCARGGDLSHYY YYYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGQ TVVTQEPSLTVSPGGTVTLTCASSTGAVTSGYYPNWF QQKPGQAPRALIYSTSNKHSWTPARFSGSLLGGKAA LTLSGVQPEDEAEYYCLLYYGGAQWVFGGGTKLTV L (SEQ ID NO: 620)
21	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTM TTDTSTSTAYMELRSLRSDDTAVYYCARENRRYNSC YYFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQK PGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 621)
22	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTM

	TTDTSTSTAYMELRSLRSDDTAVYYCARGGDLSHYY YYLDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGQT VVTQEPSLTVSPGGTVTLTCASSTGAVTSGYYPNWF QQKPGQAPRALIYSTSNKHSWTPARFSGSLLGGKAA LTLSGVQPEDEAEYYCLLYYGGAQWVFGGGTKLTV L (SEQ ID NO: 622)
23	EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNYMSW VRQAPGKGLEWVSVIYSGGSTYYADSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCARATLLSLSYDAF DIWGQGTMVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGK APKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 623)
24	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTM TTDTSTSTAYMELRSLRSDDTAVYYCARGGDLSHYY YMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGQT VVTQEPSLTVSPGGTVTLTCASSTGAVTSGYYPNWF QQKPGQAPRALIYSTSNKHSWTPARFSGSLLGGKAA LTLSGVQPEDEAEYYCLLYYGGAQWVFGGGTKLTV L (SEQ ID NO: 624)
25	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGW VRQMPGKGLEWMGIIYPGDSDTRYSPSFQGQVTISAD KSISTAYLQWSSLKASDTAMYYCARERDRWFDPWG QGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPSS LSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLL IYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATY YCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 625)
26	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTM TTDTSTSTAYMELRSLRSDDTAVYYCARETPPSLGAF DIWGQGTMVTVSSGGGGSGGGGSGGGGSGGQSALT QPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHP GKAPKLMIYEVSKRPSGVPDRFSGSKSGNTASLTVSG LQAEDEADYYCSSYAGSNNWVFGGGTKLTVL (SEQ ID NO: 626)
27	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWG WIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCAREAYCLSDSYWYF DLWGRGTLVTVSSGGGGSGGGGSGGGGSGGQSVLT QPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPG TAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQ SEDEADYYCAAWDDSLNGWVFGGGTKLTVL (SEQ ID NO: 627)
28	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWS WIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARESWKYFYPRGY MDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQ MTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKP

	GKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 628)
HLA-A*01 scFv Sequences	
A1-9	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTM TTDTSTSTAYMELRSLRSDDTAVYYCARGGWTAWY YYMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGQ TVVTQEPSLTVSPGGTVTLTCASSTGAVTSGYYPNWF QQKPGQAPRALIYSTSNKHSWTPARFSGSLLGGKAA LTLSGVQPEDEAEYYCLLYYGGAQWVFGGGTKLTV L (SEQ ID NO: 629)
A1-8	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNW VRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISRD NAKNSLYLQMNSLRAEDTAVYYCARAKYYYMDVW GKGTTVTVSSGGGGSGGGGSGGGGSGGQSVLTQPPS ASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPK LLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDE ADYYCAAWDDSLNGWVFGGGTKLTVL (SEQ ID NO: 630)
A1-7	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWS WIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARDQVDKNTYYYY MDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQ MTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKP GKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 631)
A1-6	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSW IRQAPGKGLEWVSYISSSGSTIYYADSVKGRFTISRDN AKNSLYLQMNSLRAEDTAVYYCARACQLAEYFQHW GQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPS SVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFA TYYCQQANSFPLTFGGGTKVEIK (SEQ ID NO: 632)
A1-5	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWS WIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARDRVDKNTSYYY MDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGDIQ MTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKP GKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 633)
A1-4	QVQLQESGPGLVKPSDTLSLTCAVSGYSISSSNWWG WIRQPPGKGLEWIGYIYYSGSTYYNPSLKSRVTMSVD TSKNQFSLKLSSVTAVDTAVYYCARRVQLKLVHWF DPWGQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMT QSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGK APKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPE

	DFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 634)
A1-3	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINW VRQATGQGLEWMGWMNPNSGNTGYAQKFQGRVT MTRNTSISTAYMELSSLRSEDTAVYYCATYYDYVTV FYFQHWGQGTLVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQK PGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 635)
A1-2	QLQLQESGSGLVKPSQTLSLTCAVSGGSISSGGYSWS WIRQPPGKGLEWIGYIYHSGSTYYNPSLKSRVTISVD RSKNQFSLKLSSVTAADTAVYYCARESYPSFYAFDIW GQGTMVTVSSGGGGSGGGGSGGGGSGGDIQMTQSP SSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFA TYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 636)
A1-1	QITLKESGPTLVKPTQTLTLTCTFSGFSLSTSGVGVGW IRQPPGKALEWLALIYWNDDKRYSPSLKSRLTITKDT SKNQVVLTMTNMDPVDTATYYCAHSNMWSYSLND YYFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGDI QMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQK PGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO: 637)

[0266] In some embodiments, the ligand binding domain of the second, inhibitory receptor comprises an scFv. In some embodiments, the scFv binds to HLA-A*01, HLA-A*02, HLA-A*3, HLA-A*11, HLA-B*07 or HLA-C*07, and comprises a sequence selected from the group of sequences set forth in Table 5, or a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the scFv binds to HLA-A*01, HLA-A*02, HLA-A*3, HLA-A*11, HLA-B*07 or HLA-C*07, and comprises a sequence selected from the group of sequences set forth in Table 5. In some embodiments, the non-target antigen comprises HLA-A*01, and the non-target extracellular ligand binding domain of the second receptor comprises an HLA-A*01 scFv sequence set forth in Table 5, or a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the non-target antigen comprises HLA-A*02, and the non-target extracellular ligand binding domain of the second receptor comprises an HLA-A*02 scFv sequence set forth in Table 5, or a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the non-target antigen comprises HLA-A*03, and the non-target extracellular ligand binding domain of the second receptor comprises an HLA-

A*03 scFv sequence set forth in Table 5, or a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the non-target antigen comprises HLA-A*11, and the non-target extracellular ligand binding domain of the second receptor comprises an HLA-A*11 scFv sequence set forth in Table 5, or a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the non-target antigen comprises HLA-B*07, and the non-target extracellular ligand binding domain of the second receptor comprises an HLA-B*07 scFv sequence set forth in Table 5, or a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the non-target antigen comprises HLA-C*07, and the non-target extracellular ligand binding domain of the second receptor comprises an HLA-C*07 scFv sequence set forth in Table 5, or a sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0267] Exemplary heavy chain and light chain CDRs (CDR-H1, CDR-H2 and CDR-H3, or CDR-L1, CDR-L2 and CDR-L3, respectively) for HLA-A*01, HLA-A*02, HLA-A*03, HLA-A*11, HLA-B*07 and HLA-C*07 ligand binding domains are shown in Table 6 below.

Table 6: CDRs corresponding to HLA antigen binding domains

CDR-L1	**CDR-L2**	**CDR-L3**	**CDR-H1**	**CDR-H2**	**CDR-H3**
RSSQSIVH SNGNTYL E (SEQ ID NO: 42)	KVSNRFS GVPDR (SEQ ID NO: 43)	FQGSHVP RT (SEQ ID NO: 44)	ASGYTFTS YHIH (SEQ ID NO: 45)	WIYPGNV NTEYNEK FKGK (SEQ ID NO: 46)	EEITYAM DY (SEQ ID NO: 47)
RSSQSIVH SNGNTYL D (SEQ ID NO: 48)	KVSNRFS GVPDR (SEQ ID NO: 49)	MQGSHVP RT (SEQ ID NO: 50)	SGYTFTSY HMH (SEQ ID NO: 51)	WIYPGDG STQYNEK FKG (SEQ ID NO: 52)	EGTYYAM DY (SEQ ID NO: 53)
HLA-A*03 CDRs					
RASQSISSYL N (SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYGIS (SEQ ID NO: 657)	WISAYNGNT NYAQKLQG (SEQ ID NO: 676)	ERVSQRGAF DI (SEQ ID NO: 693)

RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYSMN (SEQ ID NO: 658)	YISSSSSTIYY ADSVKG (SEQ ID NO: 677)	GNPDKDPF DY (SEQ ID NO: 694)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGSYYWS (SEQ ID NO: 659)	YIYYSGSTNY NPSLKS (SEQ ID NO: 678)	DFYCTNWYF DL (SEQ ID NO: 695)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYYWS (SEQ ID NO: 660)	YIYYSGSTNY NPSLKS (SEQ ID NO: 678)	ESSSGSYWY FDL (SEQ ID NO: 696)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYWIG (SEQ ID NO: 661)	IIYPGDSDTR YSPSFQG (SEQ ID NO: 679)	DSGYKYNLY YYYYYMDV (SEQ ID NO: 697)
ASSTGAVTS GYYPN (SEQ ID NO: 639)	STSNKHS (SEQ ID NO: 646)	LLYYGGAQ WV (SEQ ID NO: 651)	SYGIS (SEQ ID NO: 657)	WISAYNGNT NYAQKLQG (SEQ ID NO: 676)	GGDLSHYYY YMDV (SEQ ID NO: 698)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYGIS (SEQ ID NO: 657)	WISAYNGNT NYAQKLQG (SEQ ID NO: 676)	ENRRYNSCY YFDY (SEQ ID NO: 699)
ASSTGAVTS GYYPN (SEQ ID NO: 639)	STSNKHS (SEQ ID NO: 646)	LLYYGGAQ WV (SEQ ID NO: 651)	SYGIS (SEQ ID NO: 657)	WISAYNGNT NYAQKLQG (SEQ ID NO: 676)	GGDLSHYYY YLDV (SEQ ID NO: 700)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SNYMS (SEQ ID NO: 662)	VIYSGGSTYY ADSVKG	ATLLSLSYDA FDI (SEQ ID NO: 701)

				(SEQ ID NO: 680)	
ASSTGAVTS GYYPN (SEQ ID NO: 639)	STSNKHS (SEQ ID NO: 646)	LLYYGGAQ WV (SEQ ID NO: 651)	SYGIS (SEQ ID NO: 657)	WISAYNGNT NYAQKLQG (SEQ ID NO: 676)	GGDLSHYYY MDV (SEQ ID NO: 702)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYWIG (SEQ ID NO: 661)	IIYPGDSDTR YSPSFQG (SEQ ID NO: 679)	ERDRWFDP (SEQ ID NO: 703)
TGTSSDVGG YNYVS (SEQ ID NO: 640)	EVSKRPS (SEQ ID NO: 647)	SSYAGSNN WV (SEQ ID NO: 652)	SYGIS (SEQ ID NO: 657)	WISAYNGNT NYAQKLQG (SEQ ID NO: 676)	ETPPSLGAF DI (SEQ ID NO: 704)
SGSSSNIGS NTVN (SEQ ID NO: 641)	SNNQRPS (SEQ ID NO: 648)	AAWDDSLN GWV (SEQ ID NO: 653)	SSSYYWG (SEQ ID NO: 663)	SIYYSGSTYY NPSLKS (SEQ ID NO: 681)	EAYCLSDSY WYFDL (SEQ ID NO: 705)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	ESWKYFYPR GYMDV (SEQ ID NO: 706)
HLA-B*07 CDRs					
RASENIYSNL A (SEQ ID NO: 642)	AATYLPD (SEQ ID NO: 649)	QHFWVTPY T (SEQ ID NO: 654)	SGYSWH (SEQ ID NO: 665)	YIHFSGSTHY HPSLKS (SEQ ID NO: 683)	GGVVSHYA MDC (SEQ ID NO: 707)
HLA-C*07 CDRs					
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYAMS (SEQ ID NO: 668)	AISGSGGSTY YADSVKG	SFDWFDP (SEQ ID NO: 708)

				(SEQ ID NO: 686)	
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	ERSISPYYYY YMDV (SEQ ID NO: 709)
SGSSSNIGS NTVN (SEQ ID NO: 641)	SNNQRPS (SEQ ID NO: 648)	AAWDDSLN GWV (SEQ ID NO: 653)	SSSYYWG (SEQ ID NO: 663)	SIYYSGSTYY NPSLKS (SEQ ID NO: 681)	DSVIWYWF DP (SEQ ID NO: 710)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	EEILPRLSYYY YMDV (SEQ ID NO: 711)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYAMN (SEQ ID NO: 669)	WINTNTGN PTYAQGFTG (SEQ ID NO: 687)	GGRAHSSW YFDL (SEQ ID NO: 712)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DRIKILPRLG YYYYMDV (SEQ ID NO: 713)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DTVIHYYYY MDV (SEQ ID NO: 714)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DVIVEVFLSY YYYMDV (SEQ ID NO: 715)

RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DIFIHYYYYM DV (SEQ ID NO: 716)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYSMN (SEQ ID NO: 658)	YISSSSSTIYY ADSVKG (SEQ ID NO: 677)	DGTFYSYSPY YFDY (SEQ ID NO: 717)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	EWIKILPRLG YYYYMDV (SEQ ID NO: 718)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DRSLYYYYY MDV (SEQ ID NO: 719)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DKILAPNYYY YMDV (SEQ ID NO: 720)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	EKSWKYFYY YYYYMDV (SEQ ID NO: 721)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	ENTSTIPYYY YYMDV (SEQ ID NO: 722)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS	EDVDKNTST IYYYYYYMD

				(SEQ ID NO: 682)	V (SEQ ID NO: 723)
RASQGISSALA (SEQ ID NO: 643)	DASSLES (SEQ ID NO: 55)	QQFNSYPLT (SEQ ID NO: 60)	DYYMS (SEQ ID NO: 670)	YISSSGSTIYY ADSVKG (SEQ ID NO: 688)	DGGDIVSSS AIYWYFDL (SEQ ID NO: 724)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DLILPPYYYY YMDV (SEQ ID NO: 725)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	ETWIKILPRY YYYYYYMDV (SEQ ID NO: 726)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DLSRYYYYY MDV (SEQ ID NO: 727)
RASQGISSWLA (SEQ ID NO: 644)	AASSLQS (SEQ ID NO: 645)	QQYNSYPLT (SEQ ID NO: 655)	SYSMN (SEQ ID NO: 658)	YISSSSSTIYY ADSVKG (SEQ ID NO: 677)	EHIVLCFDY (SEQ ID NO: 728)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DKILPRPYYY YYMDV (SEQ ID NO: 729)
TGTSSDVGGYNYVS (SEQ ID NO: 640)	EVSKRPS (SEQ ID NO: 647)	SSYAGSNNWV (SEQ ID NO: 652)	SYGIS (SEQ ID NO: 657)	WISAYNGNTNYAQKLQG (SEQ ID NO: 676)	GSNEYFQH (SEQ ID NO: 730)

RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYAMN (SEQ ID NO: 669)	WINTNTGN PTYAQGFTG (SEQ ID NO: 687)	GTSYWYFDL (SEQ ID NO: 731)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	EEIVEVFYYY YMDV (SEQ ID NO: 732)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYAMS (SEQ ID NO: 668)	AISGSGGSTY YADSVKG (SEQ ID NO: 686)	VDDYYFDY (SEQ ID NO: 733)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYWMH (SEQ ID NO: 667)	RINSDGSSTS YADSVKG (SEQ ID NO: 685)	STNILLSYTK AFDI (SEQ ID NO: 734)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DKTYYYYYY MDV (SEQ ID NO: 735)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	EKYFHDKYF HDYYYYYM DV (SEQ ID NO: 736)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DTSVYYYYY MDV (SEQ ID NO: 737)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS	EKILPYYYYY YMDV (SEQ ID NO: 738)

				(SEQ ID NO: 682)	
SGSSSNIGS NTVN (SEQ ID NO: 641)	SNNQRPS (SEQ ID NO: 648)	AAWDDSLN GWV (SEQ ID NO: 653)	SYSMN (SEQ ID NO: 658)	YISSSSSTIYY ADSVKG (SEQ ID NO: 677)	QWIYIYINPR GFIFLHDAF DI (SEQ ID NO: 739)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SNSAAWN (SEQ ID NO: 671)	RTYYRSKWY NDYAVSVKS (SEQ ID NO: 689)	EDVDFHHD AFDI (SEQ ID NO: 740)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	EGVDKNTST IYYYYYYMD V (SEQ ID NO: 741)
RASQGISSW LA (SEQ ID NO: 644)	AASSLQS (SEQ ID NO: 645)	QQYNSYPLT (SEQ ID NO: 655)	SYSMN (SEQ ID NO: 658)	YISSSSSTIYY ADSVKG (SEQ ID NO: 677)	DRRGYFDL (SEQ ID NO: 742)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	DYYMH (SEQ ID NO: 672)	LVDPEDGETI YAEKFQG (SEQ ID NO: 690)	GIHVDIRSM EDWFDP (SEQ ID NO: 743)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	DIGTSYYYY MDV (SEQ ID NO: 744)
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYY NPSLKS (SEQ ID NO: 682)	EVVEVFLYYY YYMDV (SEQ ID NO: 745)

RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	DLYYYYYYYMDV (SEQ ID NO: 746)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	ESWKYFYPRGSIFIHYYYYMDV (SEQ ID NO: 747)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	DRIVEVFYYYYMDV (SEQ ID NO: 748)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	EKYFHDWLYYYYYMDV (SEQ ID NO: 749)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	DLVDKNTSYYYYYMDV (SEQ ID NO: 750)
TGTSSDVGGYNYVS (SEQ ID NO: 640)	EVSKRPS (SEQ ID NO: 647)	SSYAGSNNWV (SEQ ID NO: 652)	SYGIS (SEQ ID NO: 657)	WISAYNGNTNYAQKLQG (SEQ ID NO: 676)	VQNEYFQH (SEQ ID NO: 751)
RASQGISSWLA (SEQ ID NO: 644)	AASSLQS (SEQ ID NO: 645)	QQANSFPLT (SEQ ID NO: 656)	DYYMS (SEQ ID NO: 670)	YISSSGSTIYYADSVKG (SEQ ID NO: 688)	ANWFDP (SEQ ID NO: 752)
HLA-A*01 CDRs					

ASSTGAVTSGYYPN (SEQ ID NO: 639)	STSNKHS (SEQ ID NO: 646)	LLYYGGAQWV (SEQ ID NO: 651)	SYGIS (SEQ ID NO: 657)	WISAYNGNTNYAQKLQG (SEQ ID NO: 676)	GGWTAWYYYMDV (SEQ ID NO: 753)
SGSSSNIGSNTVN (SEQ ID NO: 641)	SNNQRPS (SEQ ID NO: 648)	AAWDDSLNGWV (SEQ ID NO: 653)	SYSMN (SEQ ID NO: 658)	YISSSSSTIYYADSVKG (SEQ ID NO: 677)	AKYYYMDV (SEQ ID NO: 754)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	DQVDKNTYYYYMDV (SEQ ID NO: 755)
RASQGISSWLA (SEQ ID NO: 644)	AASSLQS (SEQ ID NO: 645)	QQANSFPLT (SEQ ID NO: 656)	DYYMS (SEQ ID NO: 670)	YISSSGSTIYYADSVKG (SEQ ID NO: 688)	ACQLAEYFQH (SEQ ID NO: 756)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYYWS (SEQ ID NO: 664)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	DRVDKNTSYYYMDV (SEQ ID NO: 757)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SSNWWG (SEQ ID NO: 673)	YIYYSGSTYYNPSLKS (SEQ ID NO: 682)	RVQLKLVHWFDP (SEQ ID NO: 758)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SYDIN (SEQ ID NO: 674)	WMNPNSGNTGYAQKFQG (SEQ ID NO: 691)	YYDYVTVFYFQH (SEQ ID NO: 759)
RASQSISSYLN(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	SGGYSWS (SEQ ID NO: 675)	YIYHSGSTYYNPSLKS	ESYPSFYAFDI (SEQ ID NO: 760)

				(SEQ ID NO: 692)	
RASQSISSYL N(SEQ ID NO: 638)	AASSLQS (SEQ ID NO: 645)	QQSYSTPLT (SEQ ID NO: 650)	TSGVGVG (SEQ ID NO: 666)	LIYWNDDKR YSPSLKS (SEQ ID NO: 684)	SNMWSYSL NDYYFDY (SEQ ID NO: 761)

[0268] In some embodiments, the non-target antigen comprises HLA-A. In some embodiments, the ligand binding domain of the second, inhibitory receptor comprises an HLA-A*01, HLA-A*02, HLA-A*03 or HLA-A*11 ligand binding domain comprising CDR sequences as set forth in Table 6 or Table 7.

[0269] In some embodiments, the non-target antigen comprises HLA-B. In some embodiments, the ligand binding domain of the second, inhibitory receptors comprises an HLA-B*07 ligand binding domain comprising CDR sequences as set forth in Table 6.

[0270] In some embodiments, the non-target antigen comprises HLA-C. In some embodiments, the ligand binding domain of the second, inhibitory receptors comprises an HLA-C*07 ligand binding domain comprising CDR sequences as set forth in Table 6.

[0271] In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds an allelic variant of an HLA-A, HLA-B, or HLA-C protein. In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*01, HLA-A*02, HLA-A*03, HLA-A*11, HLA-B*07, or HLA-C*07.

[0272] In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*01. In some embodiments, the extracellular ligand binding domain of the second receptor comprises HLA-A*01 complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 6; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the HLA-A*01 CDRs of Table 6.

[0273] In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*02. In some embodiments, the extracellular ligand binding domain of the second receptor comprises HLA-A*02 complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 6; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the HLA-A*02 CDRs of Table 6.

[0274] In some embodiments, the extracellular ligand binding domain of the second receptor comprises complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 of SEQ ID NOS: 103-108 or of SEQ ID NOS: 109-114; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of SEQ ID NOS: 103-108 or SEQ ID NOS: 109-114.

[0275] In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*03. In some embodiments, the extracellular ligand binding domain of the second receptor comprises HLA-A*03 complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 6; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the HLA-A*03 CDRs of Table 6.

[0276] In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*11. In some embodiments, the extracellular ligand binding domain of the second receptor comprises HLA-A*11 complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 7; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the HLA-A*11 CDRs of Table 7.

[0277] In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-B*07. In some embodiments, the extracellular ligand binding domain of the second receptor comprises HLA-B*07 complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 6; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the HLA-B*07 CDRs of Table 6.

[0278] In some embodiments, the extracellular ligand binding domain of the second receptor specifically binds to HLA-C*07. In some embodiments, the extracellular ligand binding domain of the second receptor comprises HLA-C*07 complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 6; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the HLA-C*07 CDRs of Table 6.

[0279] In further embodiments of any of the ligand binding domains, each CDR sequence may have 1, 2, 3 or more substitutions, insertions, or deletions. CDR sequences may tolerate substitutions, deletions, or insertions. Using sequence alignment tools, routine experimentation, and known assays, those of skill in the art may generate and test variant

sequences having 1, 2, 3, or more substitutions, insertions, or deletions in CDR sequences without undue experimentation.

[0280] In some embodiments, the non-target antigen comprising HLA-A*02, and the ligand binding domain of the second receptor comprises an HLA-A*02 ligand binding domain. In some embodiments, the ligand binding domain binds HLA-A*02 independent of the peptide in a pMHC complex comprising HLA-A*02. In some embodiments, the HLA-A*02 ligand binding domain comprises an scFv domain. In some embodiments, the HLA-A*02 ligand binding domain comprises a sequence of any one of SEQ ID NOs: 30-41. In some embodiments, the HLA-A*02 ligand binding domain comprises a sequence at least 90%, at least 95%, at least 97% or at least 99% identical to a sequence of any one of SEQ ID NOs: 30-41.

[0281] In some embodiments, the non-target antigen comprises HLA-A*02, and the extracellular ligand binding domain of the second receptor comprises a sequence of SEQ ID NO: 30, or a sequence having at least 90%, at least 95%, at least 97%, or at least 99% identity thereto. In some embodiments, the non-target antigen comprises HLA-A*02, and the extracellular ligand binding domain of the second receptor comprises a sequence of SEQ ID NO: 30.

[0282] In some embodiments, the non-target antigen comprises HLA-A*02, and the extracellular ligand binding domain of the second receptor comprises a VL comprising a sequence of DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSN RFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYYCFQGSHVPRTSGGGTKLEIK (SEQ ID NO: 762), or a sequence having at least 90%, at least 95%, at least 97%, or at least 99% identity thereto. In some embodiments, the extracellular ligand binding domain of the second receptor comprises a VH comprising a sequence of QVQLQQSGPELVKPGASVRISCKASGYTFTSYHIHWVKQRPGQGLEWIGWIYPGNV NTEYNEKFKGKATLTADKSSSTAYMHLSSLTSEDSAVYFCAREEITYAMDYWGQGT SVTVSS (SEQ ID NO: 763), or a sequence having at least 90%, at least 95%, at least 97%, or at least 99% identity thereto. In some embodiments, the VH and VL are separated by a linker, for example GGGGSGGGGSGGGGSGG (SEQ ID NO: 152). In some embodiments, the VH and VL are ordered, from N to C terminal, VH, linker and VL. In some embodiments, the VH and VL are ordered, from N to C terminal, VL, linker and VH.

[0283] In some embodiments, the HLA-A*02 scFv comprises the complementarity determined regions (CDRs) of any one of SEQ ID NOS: 42-53. In some embodiments, the

scFv comprises a sequence at least 95% identical to any one of SEQ ID NOS: 42-53. In some embodiments, the scFv comprises a sequence identical to any one of SEQ ID NOS: 42-53. In some embodiments, the heavy chain of the antigen binding domain comprises the heavy chain CDRs of any one of SEQ ID NOS: 42-53, and wherein the light chain of the antigen binding domain comprises the light chain CDRs of any one of SEQ ID NOS: 42-53. In some embodiments, the HLA-A*02 antigen binding domain comprises a heavy chain and a light chain, and the heavy chain comprises CDRs selected from SEQ ID NOs: 45-47 and 51-53 and the light chain comprises CDRs selected from SEQ ID NOs: 42-44 and 48-50.

[0284] In some embodiments, the HLA-A*02 antigen binding domain comprises a heavy chain and a light chain, and the heavy chain comprises a sequence at least 95% identical to the heavy chain portion of any one of SEQ ID NOS: 30-41, and the light chain comprises a sequence at least 95% identical to the light chain portion of any one of SEQ ID NOS: 30-41.

[0285] In some embodiments, the heavy chain comprises a sequence identical to the heavy chain portion of any one of SEQ ID NOS: 30-41, and wherein the light chain of comprises a sequence identical to the light chain portion of any one of SEQ ID NOS: 30-41.

[0286] In some embodiments, the non-target antigen comprises HLA-A*01, and the extracellular ligand binding domain of the second receptor comprises an HLA-A*01 ligand binding domain. In some embodiments, the HLA-A*01 ligand binding domain comprises an scFv domain comprising a sequence selected from the group of sequences set forth in Table 5, or a sequence at least 90%, at least 95% or at least 99% identical to thereto. In some embodiments, the HLA-A*01 scFv comprises HLA-A*1 CDR sequences as set forth in Table 6.

[0287] In some embodiments, the non-target antigen comprises HLA-A*03, and the extracellular ligand binding domain of the second receptor comprises an HLA-A*03 ligand binding domain. In some embodiments, the HLA-A*03 ligand binding domain comprises an scFv domain comprising a sequence selected from the group of sequences set forth in Table 5, or a sequence at least 90%, at least 95% or at least 99% identical to thereto. In some embodiments, the HLA-A*03 scFv comprises HLA-A*03 CDR sequences as set forth in Table 6.

[0288] In some embodiments, the non-target antigen comprises HLA-A*11, and the extracellular ligand binding domain of the second receptor comprises an HLA-A*11 ligand binding domain. In some embodiments, the HLA-A*11 ligand binding domain comprises an scFv domain comprising a sequence selected from the group of sequences set forth in Table 5, or a sequence at least 90%, at least 95% or at least 99% identical to thereto. In some

embodiments, the HLA-A*11 scFv comprises HLA-A*11 CDR sequences as set forth in Table 7.

[0289] In some embodiments, the non-target antigen comprises HLA-B*07, and the extracellular ligand binding domain of the second receptor comprises an HLA-B*07 ligand binding domain. In some embodiments, the HLA-B*07 ligand binding domain comprises an scFv domain comprising a sequence selected from the group of sequences set forth in Table 5, or a sequence at least 90%, at least 95% or at least 99% identical to thereto. In some embodiments, the HLA-B*07 scFv comprises HLA-B*07 CDR sequences as set forth in Table 6.

[0290] In some embodiments, the non-target antigen comprises HLA-C*07, and the extracellular ligand binding domain of the second receptor comprises an HLA-C*07 ligand binding domain. In some embodiments, the HLA-C*07 ligand binding domain comprises an scFv domain comprising a sequence selected from the group of sequences set forth in Table 5, or a sequence at least 90%, at least 95% or at least 99% identical to thereto. In some embodiments, the HLA-C*07 scFv comprises HLA-C*07 CDR sequences as set forth in Table 6.

[0291] In some embodiments, the non-target antigen comprises HLA-A*11. Various single variable domains known in the art or disclosed herein that bind to and recognize HLA-A*11 are suitable for use in embodiments. Such scFvs include, for example and without limitation, the following mouse and humanized scFv antibodies that bind HLA-A*11 in a peptide-independent way shown in Table 5 supra.

[0292] Exemplary heavy chain and light chain CDRs (CDR-H1, CDR-H2 and CDR-H3, or CDR-L1, CDR-L2 and CDR-L3, respectively) for HLA-A*11 ligand binding domains are shown in Table 7 below. Any of the VH CDRs in Table 7 and may be combined with the VL CDRs disclosed in Table 7.

Table 7: Exemplary anti-HLA-A*11 CDR Sequences

CDR H1	**CDR H2**	**CDR H3**
SGGYYWS (SEQ ID NO: 92)	YIYYSGSTYYNPSLKS (SEQ ID NO: 97)	HYYYYYMDV (SEQ ID NO: 105)
TSGVGVG (SEQ ID NO: 93)	LIYWNDDKRYSPSLKS (SEQ ID NO: 98)	KTTSFYFDY (SEQ ID NO: 106)
SGGYYWS (SEQ ID NO: 92)	YIYYSGSTYYNPSLKS (SEQ ID NO: 97)	HYYYYMDV (SEQ ID NO: 104)
SYWMH (SEQ ID NO: 96)	RINSDGSSTSYADSVKG (SEQ ID NO: 101)	GVLLYNWFDP (SEQ ID NO: 110)

SGGYYWS (SEQ ID NO: 92)	YIYYSGSTYYNPSLKS (SEQ ID NO: 97)	HYYYYYLDV (SEQ ID NO: 103)
SYDMH (SEQ ID NO: 95)	AIGTAGDTYYPGSVKG (SEQ ID NO: 100)	DLPGSYWYFDL (SEQ ID NO: 109)
SYAMH (SEQ ID NO: 94)	WINAGNGNTKYSQKFQ G (SEQ ID NO: 99)	EGNGANPDAFDI (SEQ ID NO: 108)
TSGVGVG (SEQ ID NO: 93)	LIYWNDDKRYSPSLKS (SEQ ID NO: 98)	RHMRLSCFDY (SEQ ID NO: 107)
SGGYYWS (SEQ ID NO: 92)	YIYYSGSTYYNPSLKS (SEQ ID NO: 97)	HYYYYSMDV (SEQ ID NO: 102)
CDR1 LC	**CDR2 LC**	**CDR3 LC**
RASQSISSYLN (SEQ ID NO: 111)	AASSLQS (SEQ ID NO: 112)	QQSYSTPLT (SEQ ID NO: 113)

[0293] In some embodiments, the non-target antigen comprising HLA-A*11, and the ligand binding domain of the second receptor comprises an HLA-A*11 ligand binding domain. In some embodiments, the ligand binding domain binds HLA-A*11 independent of the peptide in a pMHC complex comprising HLA-A*11. In some embodiments, the HLA-A*11 ligand binding domain comprises an scFv domain. In some embodiments, the HLA-A*11 ligand binding domain comprises a sequence of any one of SEQ ID NOs: 114-122. In some embodiments, the HLA-A*11 ligand binding domain comprises a sequence at least 90%, at least 95% or at least 99% identical to a sequence of any one of SEQ ID NOs: 114-122.

[0294] In some embodiments, the HLA-A*11 scFv comprises the complementarity determined regions (CDRs) of any one of SEQ ID NOS: 114-122. In some embodiments, the scFv comprises a sequence at least 95% identical to any one of SEQ ID NOS: 114-122. In some embodiments, the scFv comprises a sequence identical to any one of SEQ ID NOS: 114-122. In some embodiments, the heavy chain of the antigen binding domain comprises the heavy chain CDRs of any one of SEQ ID NOS: 132-140, and wherein the light chain of the antigen binding domain comprises the light chain CDRs of SEQ ID NO: 141. In some embodiments, the HLA-A*11 antigen binding domain comprises a heavy chain and a light chain, and the heavy chain comprises one, two, or three CDRs selected from SEQ ID NOs: 92-110 and the light chain comprises one, two or three CDRs selected from SEQ ID NOs: 111-113.

[0295] Exemplary heavy and light chain sequences for HLA-A*11 antigen binding domains are provided in Table 8, below. In some embodiments, the HLA-A*11 antigen binding domain comprises a heavy chain and a light chain, and the heavy chain comprises a sequence at least 95% identical to the heavy chain portion of any one of SEQ ID NOS: 132-140, and the light chain comprises a sequence at least 95% identical to the light chain portion of SEQ ID NO: 141.

[0296] In some embodiments, the heavy chain comprises a sequence identical to the heavy chain portion of any one of SEQ ID NOS: 114-122, and wherein the light chain of comprises a sequence identical to the light chain portion of any one of SEQ ID NOS: 114-122.

Table 8: Exemplary anti-HLA-A*11 heavy and light chain sequences

scFv	Protein Sequence	DNA Sequence
	Heavy Chain Sequences	
9	QVQLQESGPGL VKPSQTLSLTCT VSGGSISSGGYY WSWIRQPPGKG LEWIGYIYYSGS TYYNPSLKSRV TISVDTSKNQFS LKLSSVTAADT AVYYCARHYY YYSMDVWGKG TTVTVSS (SEQ ID NO: 132)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCT GGTGAAACCCAGCCAGACCCTGAGCCTGACCT GCACAGTGTCCGGCGGCTCGATCAGCAGCGGC GGCTACTACTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCT ACTACAGCGGCAGCACCTACTACAACCCCAGC CTGAAGTCCAGAGTGACCATCAGCGTGGACAC CAGCAAGAACCAGTTCAGCCTGAAGCTGAGCA GCGTGACAGCCGCCGACACCGCTGTGTATTAC TGTGCGAGACACTACTACTACTACTCCATGGA CGTCTGGGGCAAAGGGACCACGGTCACCGTGT CCTCA (SEQ ID NO: 142)
8	QITLKESGPTLV KPTQTLTLTCTF SGFSLSTSGVGV GWIRQPPGKAL EWLALIYWNDD KRYSPSLKSRLT ITKDTSKNQVV LTMTNMDPVDT ATYYCAHRHM RLSCFDYWGQG TLVTVSS (SEQ ID NO: 133)	CAGATCACCCTGAAAGAGTCCGGCCCCACCCT GGTGAAACCCACCCAGACCCTGACCCTGACAT GCACCTTCAGCGGCTTCAGCCTGAGCACCTCT GGCGTGGGCGTGGGCTGGATCAGACAGCCTCC CGGCAAGGCCCTGGAATGGCTGGCCCTGATCT ACTGGAACGACGACAAGCGGTACAGCCCCAGC CTGAAGTCCCGGCTGACCATCACCAAGGACAC CTCGAAGAACCAGGTGGTGCTGACCATGACAA ACATGGACCCCGTGGACACCGCCACATATTAC TGTGCACACAGACACATGCGTTTAAGCTGTTTT GACTACTGGGGCCAGGGAACCCTGGTCACCGT GTCCTCA (SEQ ID NO: 143)
7	QVQLVQSGAEV KKPGASVKVSC KASGYTFTSYA MHWVRQAPGQ RLEWMGWINA GNGNTKYSQKF QGRVTITRDTSA STAYMELSSLRS EDTAVYYCARE	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGT GAAGAAACCTGGCGCCTCCGTGAAGGTGTCCT GCAAGGCCAGCGGCTACACCTTCACCAGCTAC GCCATGCACTGGGTTCGACAGGCCCCTGGCCA GAGACTGGAATGGATGGGCTGGATCAACGCCG GCAACGGCAACACCAAGTACAGCCAGAAATTC CAGGGCAGAGTGACCATCACCCGGGACACCAG CGCCAGCACCGCCTACATGGAACTGAGCAGCC TGCGGAGCGAGGACACCGCTGTGTATTACTGT

scFv	Protein Sequence	DNA Sequence
	GNGANPDAFDI WGQGTMVTVS S (SEQ ID NO: 134)	GCGAGAGAAGGAAATGGTGCCAACCCTGATGC TTTTGATATCTGGGGCCAAGGGACAATGGTCA CCGTGTCCTCA (SEQ ID NO: 144)
6	EVQLVESGGGL VQPGGSLRLSC AASGFTFSSYD MHWVRQATGK GLEWVSAIGTA GDTYYPGSVKG RFTISRENAKNS LYLQMNSLRAG DTAVYYCARDL PGSYWYFDLW GRGTLVTVSS (SEQ ID NO: 135)	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCC TGGTGCAGCCTGGCGGCAGCCTGAGACTGTCT TGCGCCGCCAGCGGCTTCACCTTCAGCAGCTA CGACATGCACTGGGTCCGCCAGGCCACCGGCA AGGGACTGGAATGGGTGTCCGCCATCGGCACA GCCGGCGACACTTACTACCCCGGCAGCGTGAA GGGCCGGTTCACCATCAGCAGAGAGAACGCCA AGAACAGCCTGTACCTGCAGATGAACAGCCTT CGAGCCGGCGATACCGCCGTGTATTACTGTGC AAGAGATCTCCCTGGTAGCTACTGGTACTTCG ATCTCTGGGGCCGTGGCACCCTGGTCACTGTGT CCTCA (SEQ ID NO: 145)
5	QVQLQESGPGL VKPSQTLSLTCT VSGGSISSGGYY WSWIRQPPGKG LEWIGYIYYSGS TYYNPSLKSRV TISVDTSKNQFS LKLSSVTAADT AVYYCARHYY YYYLDVWGKG TTVTVSS (SEQ ID NO: 136)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCT GGTGAAACCCAGCCAGACCCTGAGCCTGACCT GCACAGTGTCCGGCGGCTCGATCAGCAGCGGC GGCTACTACTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCT ACTACAGCGGCAGCACCTACTACAACCCCAGC CTGAAGTCCAGAGTGACCATCAGCGTGGACAC CAGCAAGAACCAGTTCAGCCTGAAGCTGAGCA GCGTGACAGCCGCCGACACCGCTGTGTATTAC TGTGCGAGACACTACTACTACTACTACCTGGA CGTCTGGGGCAAAGGGACCACGGTCACCGTGT CCTCA (SEQ ID NO: 146)
4	EVQLVESGGGL VQPGGSLRLSC AASGFTFSSYW MHWVRQAPGK GLVWVSRINSD GSSTSYADSVK GRFTISRDNAKN TLYLQMNSLRA EDTAVYYCCLG VLLYNWFDPW GQGTLVTVSS (SEQ ID NO: 137)	GAAGTGCAGCTGGTGGAAAGCGGCGGAGGCC TGGTGCAGCCTGGCGGCAGCCTGAGACTGTCT TGCGCCGCCAGCGGCTTCACCTTCAGCAGCTA CTGGATGCACTGGGTCCGCCAGGCCCCTGGCA AGGGACTGGTCTGGGTGTCTCGAATCAACAGC GACGGCAGCAGCACCAGCTACGCCGACAGCGT GAAGGGCCGGTTCACCATCAGCCGGGACAACG CCAAGAACACCCTGTACCTGCAGATGAACAGC CTGCGGGCCGAGGACACCGCCGTGTATTACTG TTGTTTGGGTGTTTTATTATACAACTGGTTCGA CCCCTGGGGCCAGGGAACCCTGGTCACCGTGT CCTCA (SEQ ID NO: 147)
3	QVQLQESGPGL VKPSQTLSLTCT VSGGSISSGGYY WSWIRQPPGKG LEWIGYIYYSGS TYYNPSLKSRV TISVDTSKNQFS LKLSSVTAADT AVYYCARHYY	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCT GGTGAAACCCAGCCAGACCCTGAGCCTGACCT GCACAGTGTCCGGCGGCTCGATCAGCAGCGGC GGCTACTACTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCT ACTACAGCGGCAGCACCTACTACAACCCCAGC CTGAAGTCCAGAGTGACCATCAGCGTGGACAC CAGCAAGAACCAGTTCAGCCTGAAGCTGAGCA GCGTGACAGCCGCCGACACCGCTGTGTATTAC

scFv	Protein Sequence	DNA Sequence
	YYMDVWGKGT TVTVSS (SEQ ID NO: 138)	TGTGCGAGACACTACTACTACTACATGGACGT CTGGGGCAAAGGGACCACGGTCACCGTGTCCT CA (SEQ ID NO: 148)
2	QITLKESGPTLV KPTQTLTLTCTF SGFSLSTSGVGV GWIRQPPGKAL EWLALIYWNDD KRYSPSLKSRLT ITKDTSKNQVV LTMTNMDPVDT ATYYCAHKTTS FYFDYWGQGTL VTVSS (SEQ ID NO: 139)	CAGATCACCCTGAAAGAGTCCGGCCCCACCCT GGTGAAACCCACCCAGACCCTGACCCTGACAT GCACCTTCAGCGGCTTCAGCCTGAGCACCTCT GGCGTGGGCGTGGGCTGGATCAGACAGCCTCC CGGCAAGGCCCTGGAATGGCTGGCCCTGATCT ACTGGAACGACGACAAGCGGTACAGCCCCAGC CTGAAGTCCCGGCTGACCATCACCAAGGACAC CTCGAAGAACCAGGTGGTGCTGACCATGACAA ACATGGACCCCGTGGACACCGCCACATATTAC TGTGCACACAAAACGACGTCGTTTTACTTTGAC TACTGGGGCCAGGGAACCCTGGTCACCGTGTC CTCA (SEQ ID NO: 149)
1	QVQLQESGPGL VKPSQTLSLTCT VSGGSISSGGYY WSWIRQPPGKG LEWIGYIYYSGS TYYNPSLKSRV TISVDTSKNQFS LKLSSVTAADT AVYYCARHYY YYYMDVWGKG TTVTVSS (SEQ ID NO: 140)	CAGGTGCAGCTGCAGGAAAGCGGCCCTGGCCT GGTGAAACCCAGCCAGACCCTGAGCCTGACCT GCACAGTGTCCGGCGGCTCGATCAGCAGCGGC GGCTACTACTGGTCCTGGATCAGACAGCCCCC TGGCAAGGGCCTGGAATGGATCGGCTACATCT ACTACAGCGGCAGCACCTACTACAACCCCAGC CTGAAGTCCAGAGTGACCATCAGCGTGGACAC CAGCAAGAACCAGTTCAGCCTGAAGCTGAGCA GCGTGACAGCCGCCGACACCGCTGTGTATTAC TGTGCGAGACACTACTACTACTACTACATGGA CGTCTGGGGCAAAGGGACCACGGTCACCGTGT CCTCA (SEQ ID NO: 150)
Light Chain Sequence		
1-9	DIQMTQSPSSLS ASVGDRVTITCR ASQSISSYLNWY QQKPGKAPKLLI YAASSLQSGVPS RFSGSGSGTDFT LTISSLQPEDFA TYYCQQSYSTP LTFGGGTKVEIK (SEQ ID NO: 141)	GACATCCAGATGACCCAGTCTCCATCCTCCCTG TCTGCATCTGTAGGAGACAGAGTCACCATCAC TTGCCGGGCAAGTCAGAGCATTAGCAGCTATT TAAATTGGTATCAGCAGAAACCAGGGAAAGCC CCTAAGCTCCTGATCTATGCTGCATCCAGTTTG CAAAGTGGGGTCCCATCAAGGTTCAGTGGCAG TGGATCTGGGACAGATTTCACTCTCACCATCA GCAGTCTGCAACCTGAAGATTTTGCAACTTACT ACTGTCAACAGAGTTACAGTACCCCTCTCACTT TCGGCGGCGGAACAAAGGTGGAGATCAAG (SEQ ID NO: 151)

Differentially Expressed Inhibitor Ligands

[0297] The disclosure provides inhibitor ligands (non-target antigens) that are differentially expressed between cancer cells and normal cells.

[0298] Activation of the inhibitory receptor is mediated by the presence of the non-target antigen on the surface of a cell. A cell that expresses the non-target antigen will activate the inhibitory receptor based on the level of expression of the non-target antigen. In some

embodiments, the non-target antigen is expressed by both target and non-target cells. However, in these embodiments, the non-target antigen is expressed by non-target cells at a higher level than the target cells. The higher levels of non-target antigen expressed by the non-target cells activate the inhibitory receptor, thereby preventing activation of the immune cell. In contrast, the lower levels of non-target antigen expressed by the target are not sufficient to activate the inhibitory receptor, leading to activation of the immune cell.

[0299] In alternative embodiments, the non-target antigen is expressed by non-target cells but not by target cells. In the absence of expression of the non-target antigen, the target cells activate the target receptor, thereby activating the immune cells.

[0300] Differential expression can be determined by any techniques known in the art used to measure expression. These include, *inter alia*, techniques for measuring mRNA and/or protein levels of a target gene in a cell. Methods of measuring protein levels in samples include immunohistochemistry, enzyme-linked immunosorbent assays (ELISA), and analytical methods such as liquid chromatography-mass spectrometry (LC-MS). Methods of measuring mRNA levels include real time quantitative reverse transcription PCR (qRT-PCR), as well as high throughput sequencing. Expression differences can be observed between, for example, a normal cell and a diseased cell, for example a cancer cell.

[0301] Activation of the inhibitory receptor by a non-target antigen can occur according to various modalities known in the art. Activation of the inhibitory receptor by a non-target antigen can be determined by methods known in the art. For example, the level of downstream intracellular signaling in a cell expressing the inhibitory receptor can be measured through the use of a reporter gene.

[0302] Without wishing to be bound by theory, whether or not expression of a non-target antigen inhibits activation of an immune cell via activation of the inhibitory receptor can occur according to the ratio of the non-target antigen to the inhibitor receptor. The expression levels of the non-target antigen and the inhibitory receptor, and the ratio thereof, can be determined by methods known in the art, including, *inter alia*, immunohistochemistry and fluorescence activated cell sorting (FACS). Analysis of the expression levels of the non-target antigen on target and non-target cells can be used to predict selective targeting of the immune cells expressing the inhibitory receptor. Low or no expression of the non-target antigen on a target or non-target cell can indicate, for example, that the inhibitory receptor will not be activated in an immune cell of the disclosure.

[0303] Alternatively, or in addition, and without wishing to be bound by theory, inhibition of immune cell activation by a non-target antigen via activation of the inhibitory receptor can

depend on the affinity of the non-target antigen for the inhibitory receptor. Methods of measuring affinity are known in the art, and include, inter alia, enzyme-linked immunosorbent assay or radioimmunoassay methods.

[0304] Alternatively, or in addition, and without wishing to be bound by theory, inhibition of immune cell activation by a non-target antigen via activation of the inhibitory receptor can occur according to cross talk between the inhibitory receptor and the activator receptor, leading to down-regulation of the activity of the activator receptor. For example, activation of the inhibitory receptor by the non-target antigen can lead to reduced expression of the activator receptor on the surface of the immune cell.

[0305] In some embodiments, the non-target antigen is expressed at a lower level in a target cell than a normal cell. In some embodiments, the non-target antigen is expressed by healthy cells, *i.e.* cells that are not cancer cells. In some embodiments, the non-target antigen expression level is at least about 10 times less, at least about 30 times less, at least about 50 times less, at least about 70 times less, at least about 90 times less, at least about 100 times less, at least about 110 times less, at least about 150 times less, at least about 200 times less, at least about 250 times less, at least about 300 times less, at least about 350 times less, at least about 400 times less, at least about 450 times less, at least about 500 times less, at least about 600 times less, at least about 700 times less, at least about 800 times less, at least about 900 times less or at least about 1000 times less in the target cell than in the non-target cell. In some embodiments, the non-target antigen expression level is about 10 times less, about 30 times less, about 50 times less, about 70 times less, about 90 times less, about 100 times less, or about 110 times less than the plurality of healthy cells. In some embodiments, the non-target antigen expression level is at least about 5 times less in the plurality of cancer cells than in the plurality of healthy cells. In some embodiments, the non-target antigen expression level is at least about 5 times less in a target cell than a non-target cell. In some embodiments, the target cells are a plurality of cancer cells that have low or no expression of the non-target antigen.

[0306] Any cell surface molecule expressed by the non-target cells that is not expressed by target cells (or expressed at a low level) may be a suitable non-target antigen for the second receptor extracellular ligand binding domain. For example, a cell adhesion molecule, a cell-cell signaling molecule, an extracellular domain, a molecule involved in chemotaxis, a glycoprotein, a G protein-coupled receptor, a transmembrane protein, a receptor for a neurotransmitter or a voltage gated ion channel can be used as a non-target antigen.

[0307] In some embodiments, the non-target antigen is selected from the group consisting of leucine rich repeat neuronal 4 (LRRN4) and uroplakin B3 (UPKB3), or a peptide antigen of any of these in a complex with a major histocompatibility complex class I (MHC-I). In some embodiments, the non-target antigen is LRRN4 or a peptide antigen thereof in a complex with MHC-I. In some embodiments, the non-target antigen is UPKB3 or a peptide antigen thereof in a complex with MHC-I.

[0308] In some embodiments, the target antigen is a peptide antigen of a cancer cell-specific antigen in a complex with a major histocompatibility complex class I (MHC-I).

[0309] Non-target MHC-I (pMHC) antigens comprising any of HLA-A, HLA-B or HLA-C are envisaged as within the scope of the disclosure. In some embodiments, the non-target antigen comprises HLA-A. In some embodiments, the non-target antigen comprises HLA-B. In some embodiments, the non-target antigen comprises HLA-C.

[0310] Non-target antigens comprise proteins that have low or no expression in cancer cells, for example lung cancer cells, but are expressed in normal tissues, such as normal lung tissue.

[0311] In some embodiments, the non-target antigen comprises LRRN4 or an antigen peptide thereof in a complex with MHC-I. A human LRRN4 is described in NCBI record number NP_689824.2, the contents of which are incorporated by reference herein in their entirety. In some embodiments, LRRN4 comprises an amino acid sequence of:

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  1 MRQTLPLLLL TVLRPSWADP PQEKVPLFRV TQQGPWGSSG SNATDSPCEG LPAADATALT
 61 LANRNLERLP GCLPRTLRSL DASHNLLRAL STSELGHLEQ LQVLTLRHNR IAALRWGPGG
121 PAGLHTLDLS YNQLAALPPC TGPALSSLRA LALAGNPLRA LQPRAFACFP ALQLLNLSCT
181 ALGRGAQGGI AEAAFAGEDG APLVTLEVLD LSGTFLERVE SGWIRDLPKL TSLYLRKMPR
241 LTTLEGDIFK MTPNLQQLDC QDSPALASVA THIFQDTPHL QVLLFQNCNL SSFPPWTLDS
301 SQVLSINLFG NPLTCSCDLS WLLTDAKRTV LSRAADTMCA PAAGSSGPFS ASLSLSQLPG
361 VCQSDQSTTL GASHPPCFNR STYAQGTTVA PSAAPATRPA GDQQSVSKAP NVGSRTIAAW
421 PHSDAREGTA PSTTNSVAGH SNSSVFPRAA STTRTQHRGE HAPELVLEPD ISAASTPLAS
481 KLLGPFPTSW DRSISSPQPG QRTHATPQAP NPSLSEGEIP VLLLDDYSEE EEGRKEEVGT
541 PHQDVPCDYH PCKHLQTPCA ELQRRWRCRC PGLSGEDTIP DPPRLQGVTE TTDTSALVHW
601 CAPNSVVHGY QIRYSAEGWA GNQSVVGVIY ATARQHPLYG LSPGTTYRVC VLAANRAGLS
661 QPRSSGWRSP CAAFTTKPSF ALLLSGLCAA SGLLLASTVV LSACLCRRGQ TLGLQRCDTH
721 LVAYKNPAFD DYPLGLQTVS (SEQ ID NO: 75).
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[0312] In some embodiments, LRRN4 comprises a sequence that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 75. In some embodiments, LRRN4 comprises a sequence identical to SEQ ID NO: 75.

[0313] In some embodiments, the non-target antigen comprises UPK3B or an antigen peptide thereof in a complex with MHC-I. All isoforms of UPK3B are envisaged as within the scope of the instant disclosure. A human UPK3B isoform a precursor is described in NCBI record number NP_085047.1, the contents of which are incorporated by reference herein in their

entirety. In some embodiments, UPK3B isoform a precursor comprises an amino acid sequence of:

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  1 MGLPWGQPHL GLQMLLLALN CLRPSLSLGE WGSWMDASSQ TQGAGGPAGV IGPWAPAPLR
 61 LGEAAPGTPT PVSVAHLLSP VATELVPYTP QITAWDLEGK VTATTFSLEQ PRCVFDGLAS
121 ASDTVWLVVA FSNASRGFQN PETLADIPAS PQLLTDGHYM TLPLSPDQLP CGDPMAGSGG
181 APVLRVGHDH GCHQQPFCNA PLPGPGPYRE DPRIHRHLAR AAKWQHDRHY LHPLFSGRPP
241 TLGLLGSLYH ALLQPVVAGG GPGAAADRLL HGQALHDPPH PTQRGRHTAG GLQAWPGPPP
301 QPQPLAWPLC MGLGEMGRRE (SEQ ID NO: 76).
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[0314] A human UPK3B isoform b precursor is described in NCBI record number NP_872625.1, the contents of which are incorporated by reference herein in their entirety. In some embodiments, UPK3B isoform b precursor comprises an amino acid sequence of:

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  1 MGLPWGQPHL GLQMLLLALN CLRPSLSLEL VPYTPQITAW DLEGKVTATT FSLEQPRCVF
 61 DGLASASDTV WLVVAFSNAS RGFQNPETLA DIPASPQLLT DGHYMTLPLS PDQLPCGDPM
121 AGSGGAPVLR VGHDHGCHQQ PFCNAPLPGP GPYRVKFLLM DTRGSPRAET KWSDPITLHQ
181 GKTPGSIDTW PGRRSGSMIV ITSILSSLAG LLLLAFLAAS TMRFSSLWWP EEAPEQLRIG
241 SFMGKRYMTH HIPPSEAATL PVGCKPGLDP LPSLSP (SEQ ID NO: 77).
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[0315] A human UPK3B isoform c precursor is described in NCBI record number NP_872624.1, the contents of which are incorporated by reference herein in their entirety. In some embodiments, UPK3B isoform c precursor comprises an amino acid sequence of:

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  1 MGLPWGQPHL GLQMLLLALN CLRPSLSLEL VPYTPQITAW DLEGKVTATT FSLEQPRCVF
 61 DGLASASDTV WLVVAFSNAS RGFQNPETLA DIPASPQLLT DGHYMTLPLS PDQLPCGDPM
121 AGSGGAPVLR VGHDHGCHQQ PFCNAPLPGP GPYREDPRIH RHLARAAKWQ HDRHYLHPLF
181 SGRPPTLGLL GSLYHALLQP VVAGGGPGAA ADRLLHGQAL HDPPHPTQRG RHTAGGLQAW
241 PGPPPQPQPL AWPLCMGLGE MGRRE (SEQ ID NO: 78).
```

[0316] A human UPK3B isoform d precursor is described in NCBI record number NP_001334613.1, the contents of which are incorporated by reference herein in their entirety. In some embodiments, UPK3B isoform c precursor comprises an amino acid sequence of:

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  1 MGLPWGQPHL GLQMLLLALN CLRPSLSLEL VPYTPQITAW DLEGKVTATT FSLEQPRCVF
 61 DGLASASDTV WLVVAFSNAS RGFQNPETLA DIPASPQLLT DGHYMTLPLS PDQLPCGDPM
121 AGSGGAPVLR VGHDHGCHQQ PFCNAPLPGP GPYRVKFLLM DTRGSPRAET KWSDPITLHQ
181 GKTPGSIDTW PGRRSGSMIV ITSILSSLAG LLLLAFLAAS TMRFSSLWWP EEAPEQLRIG
241 SFMGKRYMTH HIPPREAATL PVGCKPGLDP LPSLSP (SEQ ID NO: 79).
```

[0317] In some embodiments, UPKB3 comprises a sequence or subsequence that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to any one of SEQ ID NOs: 76-79. In some embodiments, UPKB3 comprises a sequence or subsequence identical to SEQ ID NOs: 76-79.

Inhibitory Chimeric Antigen Receptors

[0318] The disclosure provides a second receptor that is an inhibitory chimeric antigen receptor. The inhibitory receptor may comprise an extracellular ligand binding domain that

binds to and recognizes the non-target antigen or a peptide derivative thereof in a MHC-I complex.

[0319] The term "inhibitory receptor" as used herein refers to a ligand-binding domain that is fused to an intracellular signaling domain capable of transducing an inhibitory signal that inhibits or suppresses the immune activity of an immune cell. Inhibitory receptors have immune cell inhibitory potential, and are distinct and distinguishable from CARs, which are receptors with immune cell activating potential. For example, CARs are activating receptors as they include intracellular stimulatory and/or co-stimulatory domains. Inhibitory receptors are inhibiting receptors that contain intracellular inhibitory domains.

[0320] As used herein "inhibitory signal" refers to signal transduction or changes in protein expression in an immune cell resulting in suppression of an immune response (e.g., decrease in cytokine production or reduction of immune cell activation). Inhibition or suppression of an immune cell can selective and/or reversible, or not selective and/or reversible.

[0321] Inhibitory receptors of the disclosure may comprise an extracellular ligand binding domain. Any type of ligand binding domain that can regulate the activity of a receptor in a ligand dependent manner is envisaged as within the scope of the instant disclosure. Inhibitory receptors are responsive to non-target antigens (*e.g.* HLA-A*02). For example, when a non-target antigen (*e.g.* HLA-A*02) binds to or contacts the inhibitory receptor, the inhibitory receptor is responsive and activates an inhibitory signal in the immune cell expressing the inhibitory receptor upon binding of the non-target antigen by the extracellular ligand binding domain of the inhibitory receptor.

[0322] Inhibitory receptors of the disclosure may comprise an extracellular ligand binding domain. Any type of ligand binding domain that can regulate the activity of a receptor in a ligand dependent manner is envisaged as within the scope of the instant disclosure.

[0323] In some embodiments, the ligand binding domain is an antigen binding domain. Exemplary antigen binding domains include, *inter alia*, scFv, SdAb, Vβ-only domains, and TCR antigen binding domains derived from the TCR α and β chain variable domains.

[0324] Any type of antigen binding domain is envisaged as within the scope of the instant disclosure.

[0325] In some embodiments, the extracellular ligand binding domain of the second receptor is an scFv.

[0326] In some embodiments, the extracellular ligand binding domain of the second receptor binds to and recognizes a polymorphic variant of intercellular adhesion molecule 1 (ICAM1), catechol-O-methyltransferase (COMT), C-X-C motif chemokine ligand 16 (CXCL16),

leucine rich repeat neuronal 4 (LRRN4) and uroplakin 3B UPK3B, or an antigen peptide thereof in a complex with a major histocompatibility complex class I (MHC-I), or HLA-A*02. In some embodiments, the extracellular ligand binding domain of the second receptor is an scFv.

[0327] In some embodiments, the extracellular ligand binding domain of the second receptor is fused to the extracellular domain of an inhibitory receptor.

[0328] In some embodiments, the inhibitory receptors of the present disclosure comprise an extracellular hinge region. Exemplary hinges can be isolated or derived from IgD and CD8 domains, for example IgG1. In some embodiments, the hinge is isolated or derived from CD8α or CD28.

[0329] The inhibitory receptors of the present disclosure can be designed to comprise a transmembrane domain that is fused to the extracellular domain of the inhibitory receptor. In some instances, the transmembrane domain can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins to minimize interactions with other members of the receptor complex.

[0330] The transmembrane domain may be derived either from a natural or from a synthetic source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. Transmembrane regions may be isolated or derived from (i.e. comprise at least the transmembrane region(s) of) the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154, or from an immunoglobulin such as IgG4. Alternatively the transmembrane domain may be synthetic, in which case it will comprise predominantly hydrophobic residues such as leucine and valine. In some embodiments, a triplet of phenylalanine, tryptophan and valine will be found at each end of a synthetic transmembrane domain. Optionally, a short oligo- or polypeptide linker, preferably between 2 and 10 amino acids in length may form the linkage between the transmembrane domain and the intracellular domain of the inhibitory receptor. A glycine-serine doublet provides a particularly suitable linker.

[0331] The disclosure provides an inhibitory receptor comprising an intracellular domain. The intracellular domain of the inhibitory receptors of the instant disclosure is responsible for inhibiting activation of the immune cells comprising the inhibitory receptor, which would otherwise be activated in response to activation signals by the first receptor. In some embodiments, the inhibitory intracellular domain comprises an immunoreceptor tyrosine-

based inhibitory motif (ITIM). In some embodiments, the inhibitory intracellular domain comprising an ITIM can be isolated or derived from an immune checkpoint inhibitor such as CTLA-4 and PD-1. CTLA-4 and PD-1 are immune inhibitory receptors expressed on the surface of T cells, and play a pivotal role in attenuating or terminating T cell responses.

[0332] In some embodiments, an inhibitory intracellular domain is isolated from human tumor necrosis factor related apoptosis inducing ligand (TRAIL) receptor and CD200 receptor 1. In some embodiments, the TRAIL receptor comprises TR10A, TR10B or TR10D.

[0333] In some embodiments, an inhibitory intracellular domain is isolated from phosphoprotein membrane anchor with glycosphingolipid microdomains 1 (PAG1). In some embodiments, an inhibitory intracellular domain is isolated from leukocyte immunoglobulin like receptor B1 (LILRB1).

[0334] In some embodiments, the inhibitory domain is isolated or derived from a human protein, for example a human TRAIL receptor, CTLA-4, PD-1, PAG1 or LILRB1 protein.

[0335] In some embodiments, the inhibitory domain comprises an intracellular domain, a transmembrane or a combination thereof. In some embodiments, the inhibitory domain comprises an intracellular domain, a transmembrane domain, a hinge region or a combination thereof.

[0336] In some embodiments, the inhibitory domain is isolated or derived from killer cell immunoglobulin like receptor, three Ig domains and long cytoplasmic tail 2 (KIR3DL2), killer cell immunoglobulin like receptor, three Ig domains and long cytoplasmic tail 3 (KIR3DL3), leukocyte immunoglobulin like receptor B1 (LIR1, also called LIR-1 and LILRB1), programmed cell death 1 (PD-1), Fc gamma receptor IIB (FcgRIIB), killer cell lectin like receptor K1 (NKG2D), CTLA-4, a domain containing a synthetic consensus ITIM, a ZAP70 SH2 domain (e.g., one or both of the N and C terminal SH2 domains), or ZAP70 KI_K369A (kinase inactive ZAP70).

[0337] In some embodiments, the inhibitory domain is isolated or derived from a human protein.

[0338] In some embodiments, the second, inhibitory receptor comprises an inhibitory domain. In some embodiments, the second, inhibitory receptor comprises an inhibitory intracellular domain and/or an inhibitory transmembrane domain. In some embodiments, the inhibitory intracellular domain is fused to an intracellular domain of an inhibitory receptor. In some embodiments, the inhibitory intracellular domain is fused to the transmembrane domain of an inhibitory receptor.

[0339] In some embodiments, the second, inhibitory receptor comprises a cytoplasmic domain, a transmembrane domain, and an extracellular domain or a portion thereof isolated or derived isolated or derived from the same protein, for example an ITIM containing protein. In some embodiments, the second, inhibitory receptor comprises a hinge region isolated or derived from isolated or derived from the same protein as the intracellular domain and/or transmembrane domain, for example an ITIM containing protein.

[0340] In some embodiments, the second receptor is a TCR comprising an inhibitory domain (an inhibitory TCR). In some embodiments, the inhibitory TCR comprises an inhibitory intracellular domain and/or an inhibitory transmembrane domain. In some embodiments, the inhibitory intracellular domain is fused to the intracellular domain of TCR alpha, TCR beta, CD3 delta, CD3 gamma or CD3 epsilon or a portion thereof a TCR. In some embodiments, the inhibitory intracellular domain is fused to the transmembrane domain of TCR alpha, TCR beta, CD3 delta, CD3 gamma or CD3 epsilon.

In some embodiments, the second receptor is a TCR comprising an inhibitory domain (an inhibitory TCR). In some embodiments, the inhibitory domain is isolated or derived from LILRB1.

LILRB1 Inhibitory receptors

[0341] The disclosure provides a second, inhibitory receptor comprising a LILRB1 inhibitory domain, and optionally, a LILRB1 transmembrane and/or hinge domain, or functional variants thereof. The inclusion of the LILRB1 transmembrane domain and/or the LILRB1 hinge domain in the inhibitory receptor may increase the inhibitory signal generated by the inhibitory receptor compared to a reference inhibitory receptor having another transmembrane domain or another hinge domains. The second, inhibitory receptor comprising the LILRB1 inhibitory domain may be a CAR or TCR, as described herein. Any suitable ligand binding domain, as described herein, may be fused to the LILRB1-based second, inhibitory receptors.

[0342] Leukocyte immunoglobulin-like receptor subfamily B member 1 (LILRB1), also known as Leukocyte immunoglobulin-like receptor B1, as well as ILT2, LIR1, MIR7, PIRB, CD85J, ILT-2 LIR-1, MIR-7 and PIR-B, is a member of the leukocyte immunoglobulin-like receptor (LIR) family. The LILRB1 protein belongs to the subfamily B class of LIR receptors. These receptors contain two to four extracellular immunoglobulin domains, a transmembrane domain, and two to four cytoplasmic immunoreceptor tyrosine-based inhibitory motifs (ITIMs). The LILRB1 receptor is expressed on immune cells, where it binds to MHC class I molecules on antigen-presenting cells and transduces a negative signal that

inhibits stimulation of an immune response. LILRB1 is thought to regulate inflammatory responses, as well as cytotoxicity, and to play a role in limiting auto-reactivity. Multiple transcript variants encoding different isoforms of LILRB1 exist, all of which are contemplated as within the scope of the instant disclosure.

[0343] In some embodiments of the inhibitory receptors described herein, the inhibitory receptor comprises one or more domains isolated or derived from LILRB1. In some embodiments of the receptors having one or more domains isolated or derived from LILRB1, the one or more domains of LILRB1 comprise an amino acid sequence that is at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or is identical to a sequence or subsequence of SEQ ID NO: 54. In some embodiments, the one or more domains of LILRB1 comprise an amino acid sequence that is identical to a sequence or subsequence of SEQ ID NO: 54. In some embodiments, the one or more domains of LILRB1 consist of an amino acid sequence that is at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or is identical to a sequence or subsequence of SEQ ID NO: 54. In some embodiments, the one or more domains of LILRB1 consist of an amino acid sequence that is identical to a sequence or subsequence of SEQ ID NO: 54.

[0344] In some embodiments of the receptors having one or more domains isolated or derived from LILRB1, the one or more domains of LILRB1 are encoded by a polynucleotide sequence that is at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or is identical to a sequence or subsequence of SEQ ID NO: 55.

[0345] In some embodiments of the receptors having one or more domains of LILRB1, the one or more domains of LILRB1 are encoded by a polynucleotide sequence that is identical to a sequence or subsequence of SEQ ID NO: 55.

[0346] In various embodiments, an inhibitory receptor is provided, comprising a polypeptide, wherein the polypeptide comprises one or more of: an LILRB1 hinge domain or functional variant thereof; an LILRB1 transmembrane domain or a functional variant thereof; and an LILRB1 intracellular domain or an intracellular domain comprising at least one, or at least two immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0347] As used herein an "immunoreceptor tyrosine-based inhibitory motif" or "ITIM" refers to a conserved sequence of amino acids with a consensus sequence of S/I/V/LxYxxI/V/L (SEQ ID NO: 547), or the like, that is found in the cytoplasmic tails of many inhibitory receptors of the immune system. After ITIM-possessing inhibitory receptors interact with

their ligand, the ITIM motif is phosphorylated, allowing the inhibitory receptor to recruit other enzymes, such as the phosphotyrosine phosphatases SHP-1 and SHP-2, or the inositol-phosphatase called SHIP.

[0348] In some embodiments, the polypeptide comprises an intracellular domain comprising at least one immunoreceptor tyrosine-based inhibitory motif (ITIM), at least two ITIMs, at least 3 ITIMs, at least 4 ITIMs, at least 5 ITIMs or at least 6 ITIMs. In some embodiments, the intracellular domain has 1, 2, 3, 4, 5, or 6 ITIMs.

[0349] In some embodiments, the polypeptide comprises an intracellular domain comprising at least one ITIM selected from the group of ITIMs consisting of NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0350] In further particular embodiments, the polypeptide comprises an intracellular domain comprising at least two immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0351] In some embodiments, the intracellular domain comprises both ITIMs NLYAAV (SEQ ID NO: 56) and VTYAEV (SEQ ID NO: 57). In some embodiments, the intracellular domain comprises a sequence at least 95% identical to SEQ ID NO: 60. In some embodiments, the intracellular domain comprises or consists essentially of a sequence identical to SEQ ID NO: 60.

[0352] In some embodiments, the intracellular domain comprises both ITIMs VTYAEV (SEQ ID NO: 57) and VTYAQL (SEQ ID NO: 58). In some embodiments, the intracellular domain comprises a sequence at least 95% identical to SEQ ID NO: 61. In some embodiments, the intracellular domain comprises or consists essentially of a sequence identical to SEQ ID NO: 61.

[0353] In some embodiments, the intracellular domain comprises both ITIMs VTYAQL (SEQ ID NO: 58) and SIYATL (SEQ ID NO: 59). In some embodiments, the intracellular domain comprises a sequence at least 95% identical to SEQ ID NO: 62. In some embodiments, the intracellular domain comprises or consists essentially of a sequence identical to SEQ ID NO: 62.

[0354] In some embodiments, the intracellular domain comprises the ITIMs NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), and VTYAQL (SEQ ID NO: 58). In some embodiments, the intracellular domain comprises a sequence at least 95% identical to SEQ

ID NO: 63. In some embodiments, the intracellular domain comprises or consists essentially of a sequence identical to SEQ ID NO: 63.

[0355] In some embodiments, the intracellular domain comprises the ITIMs VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59). In some embodiments, the intracellular domain comprises a sequence at least 95% identical to SEQ ID NO: 64. In some embodiments, the intracellular domain comprises or consists essentially of a sequence identical to SEQ ID NO: 64.

[0356] In some embodiments, the intracellular domain comprises the ITIMs NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59). In some embodiments, the intracellular domain comprises a sequence at least 95% identical to SEQ ID NO: 65. In some embodiments, the intracellular domain comprises or consists essentially of a sequence identical to SEQ ID NO: 65.

[0357] In some embodiments, the intracellular domain comprises a sequence at least 95% identical to the LILRB1 intracellular domain (SEQ ID NO: 70). In some embodiments, the intracellular domain comprises or consists essentially of a sequence identical to the LILRB1 intracellular domain (SEQ ID NO: 70).

[0358] LILRB1 intracellular domains or functional variants thereof of the disclosure can have at least 1, at least 2, at least 4, at least 4, at least 5, at least 6, at least 7, or at least 8 ITIMs. In some embodiments, the LILRB1 intracellular domain or functional variant thereof has 2, 3, 4, 5, or 6 ITIMs.

[0359] In particular embodiments, the intracellular domain comprises two, three, four, five, or six immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0360] In particular embodiments, the intracellular domain comprises at least three immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0361] In particular embodiments, the intracellular domain comprises three immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0362] In particular embodiments, the intracellular domain comprises four immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from

NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0363] In particular embodiments, the intracellular domain comprises five immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0364] In particular embodiments, the intracellular domain comprises six immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0365] In particular embodiments, the intracellular domain comprises at least seven immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0366] The LILRB1 protein has four immunoglobulin (Ig) like domains termed D1, D2, D3 and D4. In some embodiments, the LILRB1 hinge domain comprises an LILRB1 D3D4 domain or a functional variant thereof. In some embodiments, the LILRB1 D3D4 domain comprises a sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or identical to SEQ ID NO: 66. In some embodiments, the LILRB1 D3D4 domain comprises or consists essentially of SEQ ID NO: 66.

[0367] In some embodiments, the polypeptide comprises the LILRB1 hinge domain or functional variant thereof. In embodiments, the LILRB1 hinge domain or functional variant thereof comprises a sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical or identical to SEQ ID NO: 73, SEQ ID NO: 66, or SEQ ID NO: 67. In embodiments, the LILRB1 hinge domain or functional variant thereof comprises a sequence at least 95% identical to SEQ ID NO: 73, SEQ ID NO: 66, or SEQ ID NO: 67.

[0368] In some embodiments, the LILRB1 hinge domain comprises a sequence identical to SEQ ID NO: 73, SEQ ID NO: 66, or SEQ ID NO: 67.

[0369] In some embodiments, the LILRB1 hinge domain consists essentially of a sequence identical to SEQ ID NO: 73, SEQ ID NO: 66, or SEQ ID NO: 67.

[0370] In some embodiments, the transmembrane domain is a LILRB1 transmembrane domain or a functional variant thereof. In some embodiments, the LILRB1 transmembrane domain or a functional variant thereof comprises a sequence at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical or at least 99% to SEQ ID NO:

74. In some embodiments, the LILRB1 transmembrane domain or a functional variant thereof comprises a sequence at least 95% identical to SEQ ID NO: 74. In some embodiments, the LILRB1 transmembrane domain comprises a sequence identical to SEQ ID NO: 74. In embodiments, the LILRB1 transmembrane domain consists essentially of a sequence identical to SEQ ID NO: 74.

[0371] In some embodiments, the transmembrane domain can be attached to the extracellular region of the second, inhibitory receptor, *e.g.*, the antigen binding domain or ligand binding domain, via a hinge, *e.g.*, a hinge from a human protein. For example, in some embodiments, the hinge can be a human immunoglobulin (Ig) hinge, *e.g.*, an IgG4 hinge, a CD8a hinge or an LILRB1 hinge.

[0372] In some embodiments, the second, inhibitory receptor comprises an inhibitory domain. In some embodiments, the second, inhibitory receptor comprises an inhibitory intracellular domain and/or an inhibitory transmembrane domain. In some embodiments, the inhibitory domain is isolated or derived from LILR1B.

Inhibitory Receptors Comprising Combinations of LILRB1 Domains

[0373] In some embodiments, the LILRB1-based inhibitory receptors of the disclosure comprise more than one LILRB1 domain or functional equivalent thereof. For example, in some embodiments, the inhibitory receptor comprises an LILRB1 transmembrane domain and intracellular domain, or an LILRB1 hinge domain, transmembrane domain and intracellular domain.

[0374] In particular embodiments, the inhibitory receptor comprises an LILRB1 hinge domain or functional variant thereof, and the LILRB1 transmembrane domain or a functional variant thereof. In some embodiments, the polypeptide comprises a sequence at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical, at least 99% identical or identical to SEQ ID NO: 68. In some embodiments, the polypeptide comprises a sequence at least 95% identical to SEQ ID NO: 68. In some embodiments, the polypeptide comprises a sequence identical to SEQ ID NO: 68.

[0375] In further embodiments, the inhibitory receptor comprises: the LILRB1 transmembrane domain or a functional variant thereof, and an LILRB1 intracellular domain and/or an intracellular domain comprising at least one immunoreceptor tyrosine-based inhibitory motif (ITIM), wherein the ITIM is selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59). In some embodiments, the polypeptide comprises the LILRB1 transmembrane domain or a functional variant thereof, and an LILRB1 intracellular domain and/or an intracellular domain

comprising at least two ITIM, wherein each ITIM is independently selected from NLYAAV (SEQ ID NO: 56), VTYAEV (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0376] In some embodiments, the inhibitory receptor comprises a LILRB1 transmembrane domain and intracellular domain. In some embodiments, the polypeptide comprises a sequence at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical, at least 99% identical or identical to SEQ ID NO: 69. In some embodiments, the polypeptide comprises a sequence at least 95% identical to SEQ ID NO: 69. In some embodiments, the polypeptide comprises a sequence identical to SEQ ID NO: 69.

[0377] In preferred embodiments, the inhibitory receptor comprises: an LILRB1 hinge domain or functional variant thereof; an LILRB1 transmembrane domain or a functional variant thereof; and an LILRB1 intracellular domain and/or an intracellular domain comprising at least two immunoreceptor tyrosine-based inhibitory motifs (ITIMs), wherein each ITIM is independently selected from LYAAV (SEQ ID NO: 56), VTYAE (SEQ ID NO: 57), VTYAQL (SEQ ID NO: 58), and SIYATL (SEQ ID NO: 59).

[0378] In some embodiments, the inhibitory receptor comprises a sequence at least 95% identical to SEQ ID NO: 71 or SEQ ID NO: 72, or at least 99% identical to SEQ ID NO: 71 or SEQ ID NO: 72, or identical to SEQ ID NO: 71 or SEQ ID NO: 72.

[0379] In some embodiments, the polypeptide comprises a sequence at least 99% identical to SEQ ID NO: 68, or at least 99% identical to SEQ ID NO: 68, or identical to SEQ ID NO: 68.

[0380] In some embodiments, the polypeptide comprises a sequence at least 99% identical to SEQ ID NO: 69, or at least 99% identical to SEQ ID NO: 69, or identical to SEQ ID NO: 69.

Table 9: Polypeptide sequences for illustrative LILRB1-based inhibitory receptors

Name	Sequence
LILRB1	MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVITQ GSPVTLRCQGGQETQEYRLYREKKTALWITRIPQELVKKG QFPIPSITWEHAGRYRCYYGSDTAGRSESSDPLELVVTGA YIKPTLSAQPSPVVNSGGNVILQCDSQVAFDGFSLCKEGED EHPQCLNSQPHARGSSRAIFSVGPVSPSRRWWYRCYAYDS NSPYEWSLPSDLLELLVLGVSKKPSLSVQPGPIVAPEETLT LQCGSDAGYNRFVLYKDGERDFLQLAGAQPQAGLSQANF TLGPVSRSYGGQYRCYGAHNLSSEWSAPSDPLDILIAGQF YDRVSLSVQPGPTVASGENVTLLCQSQGWMQTFLLTKEG

	AADDPWRLRSTYQSQKYQAEFPMGPVTSAHAGTYRC**YGSQSSKPYLLTHPSDPLEL**VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEEN**LYAAV**KHTQPEDGVEMDTRSPHDEDPQA**VTYAEV**KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQD**VTYAQ**LHSLTLRREATEPPPSQEGPSPAVP**SIYAT**LAIHPSQEGPSPAVPSIYATLAIH SEQ ID NO: 54
LILRB1 hinge-transmembrane-intracellular domain	**YGSQSSKPYLLTHPSDPLEL**VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLG**VVIGILVAVILLLLLLLLLFLIL**RHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIH SEQ ID NO: 71
LILRB1 hinge-transmembrane-intracellular domain (w/o YGSQSSKPYLLTHPSDPLEL (SEQ ID NO: 66))	VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLG**VVIGILVAVILLLLLLLLLFLIL**RHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIH SEQ ID NO: 72
LILRB1 hinge domain	**YGSQSSKPYLLTHPSDPLEL**VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLG SEQ ID NO: 73
LILRB1 transmembrane domain	**VVIGILVAVILLLLLLLLLFLIL** SEQ ID NO: 74
LILRB1 intracellular domain	RHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQM

	DTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPA VPSIYATLAIH SEQ ID NO: 70
ITIM1	NLYAAV SEQ ID NO: 56
ITIM2	VTYAEV SEQ ID NO: 57
ITIM3	VTYAQL SEQ ID NO: 58
ITIM4	SIYATL SEQ ID NO: 59
ITIM1-2	**NLYAAV**KHTQPEDGVEMDTRSPHDEDPQA**VTYAEV** SEQ ID NO: 60
ITIM2-3	**VTYAEV**KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQ MDTEAAASEAPQD**VTYAQL** SEQ ID NO: 61
ITIM3-4	**VTYAQL**HSLTLRREATEPPPSQEGPSPAVP**SIYATL** SEQ ID NO: 62
ITIM1-3	**NLYAAV**KHTQPEDGVEMDTRSPHDEDPQA**VTYAEV**KHS RPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEA PQD**VTYAQL** SEQ ID NO: 63
ITIM2-4	**VTYAEV**KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQ MDTEAAASEAPQD**VTYAQL**HSLTLRREATEPPPSQEGPSP AVP**SIYATL** SEQ ID NO: 64
ITIM1-4	**NLYAAV**KHTQPEDGVEMDTRSPHDEDPQA**VTYAEV**KHS RPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEA PQD**VTYAQL**HSLTLRREATEPPPSQEGPSPAVP**SIYATL** SEQ ID NO: 65
D3D4 domain	**YGSQSSKPYLLTHPSDPLEL** SEQ ID NO: 66

Short hinge	VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRH LG SEQ ID NO: 67
Hinge (iTIM hinge)	YGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGP EDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 81)
Short hinge 2	VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRH LGV (SEQ ID NO: 82)
Long hinge 1	AGSGGSGGSGGSPVPSTPPTPSPSTPPTPSPSGGSGNSSGSG GSPVPSTPPTPSPSTPPTPSPSASV (SEQ ID NO: 83)
Long hinge 2	AGSGGSGGSGGSPVPSTPPTNSSSTPPTPSPSPVPSTPPTNSS STPPTPSPSPVPSTPPTNSSSTPPTPSPSASV (SEQ ID NO: 84)
2X short hinge	VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRH VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRH LGV SEQ ID NO: 91
Hinge (truncated)	TTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 90)
Hinge-transmembrane	**YGSQSSKPYLLTHPSDPLEL**VVSGPSGGPSSPTTGPTSTSG PEDQPLTPTGSDPQSGLGRHLG**VVIGILVAVILLLLLLLLL FLIL** SEQ ID NO: 68
Transmembrane-intracellular domain.	**VVIGILVAVILLLLLLLLLFLIL**RHRRQGKHWTSTQRKA DFQHPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVK HTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMAS PPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYA QLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIH SEQ ID NO: 69

[0381] Exemplary inhibitory receptors of the disclosure comprise the scFv specific to any of HLA-A, HLA-B or HLA-C non-target antigens, the sequences of which are set forth in Table 5, fused to the N terminus a LILRB1 hinge, transmembrane and intracellular domain. In some embodiments, the LILRB1 hinge comprises a sequence of SEQ ID NO: 73, the LILRB1 transmembrane domain comprises a sequence of SEQ ID NO: 74, and the LILRB1 intracellular domain comprises a sequence of SEQ ID NO: 70. For example, the second,

inhibitory receptor comprises an scFv sequence of Table 5 fused to the N terminus of SEQ ID NO: 71.

[0382] As a further example, the non-target antigen comprises HLA-A*02, and the second inhibitory receptor comprises a sequence of:
DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTL
KISRVEAEDLGVYYCFQGSHVPRTSGGGTKLEIKGGGGSGGGGSGGGGSGGQVQLQQSGPELVKPGASVRISCKA
SGYTFTSYHIHWVKQRPGQGLEWIGWIYPGNVNTEYNEKFKGKATLTADKSSSTAYMHLSSLTSEDSAVYFCAREEI
TYAMDYWGQGTSVTVSSYGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLG
RHLGVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENLY
AAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAAS
EAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 348), or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the non-target antigen comprises HLA-A*02 and the second inhibitory receptor comprises a sequence of SEQ ID NO: 348.

Polynucleotides and Vectors

[0383] The disclosure provides polynucleotides encoding the sequence(s) of the first and second receptors of the disclosure. The disclosure provides immune cells comprising the polynucleotides and vectors described herein.

[0384] In some embodiments, the sequence of the first and/or second receptor is operably linked to a promoter. In some embodiments, the sequence encoding the first receptor is operably linked to a first promoter, and the sequence encoding the second receptor is operably linked to a second promoter.

[0385] The disclosure provides vectors comprising the polynucleotides described herein.

[0386] In some embodiments, the first receptor is encoded by a first vector and the second receptor is encoded by a second vector. In some embodiments, both receptors are encoded by a single vector. In some embodiments, the first and/or second vector comprises an shRNA, for example a B2M shRNA.

[0387] In some embodiments, both receptors are encoded by a single vector. In some embodiments the vector comprises an shRNA, for example a B2M shRNA.

[0388] In some embodiments, the first and second receptors are encoded by a single vector. Methods of encoding multiple polypeptides using a single vector will be known to persons of ordinary skill in the art, and include, *inter alia*, encoding multiple polypeptides under control of different promoters, or, if a single promoter is used to control transcription of multiple

polypeptides, use of sequences encoding internal ribosome entry sites (IRES) and/or self-cleaving peptides. Exemplary self-cleaving peptides include T2A, P2A, E2A and F2A self-cleaving peptides. In some embodiments, the T2A self-cleaving peptide comprises a sequence of EGRGSLLTCGDVEENPGP (SEQ ID NO: 764). In some embodiments, the P2A self-cleaving peptide comprises a sequence of ATNFSLLKQAGDVEENPGP (SEQ ID NO: 765). In some embodiments, the E2A self-cleaving peptide comprises a sequence of QCTNYALLKLAGDVESNPGP (SEQ ID NO: 766). In some embodiments, the F2A self-cleaving peptide comprises a sequence of VKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 767). In some embodiments, the T2A self-cleaving peptide comprises a sequence of EGRGSLLTCGDVEENPGP (SEQ ID NO: 764). Any of the foregoing can also include an N terminal GSG linker. For example, a T2A self-cleaving peptide can also comprise a sequence of GSGEGRGSLLTCGDVEENPGP (SEQ ID NO: 351), which can be encoded by a sequence of GGATCCGGAGAGGGCAGAGGCAGCCTGCTGACATGTGGCGACGTGGAAGAGAACCCTGGCCCC (SEQ ID NO: 768).

[0389] In some embodiments, the vector is an expression vector, i.e. for the expression of the first and/or second receptor in a suitable cell.

[0390] Vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity.

[0391] The expression of natural or synthetic nucleic acids encoding receptors is typically achieved by operably linking a nucleic acid encoding the receptor or portions thereof to a promoter, and incorporating the construct into an expression vector. The vectors can be suitable for replication and integration eukaryotes. Typical cloning vectors contain transcription and translation terminators, initiation sequences, and promoters useful for regulation of the expression of the desired nucleic acid sequence.

[0392] The polynucleotides encoding the receptors can be cloned into a number of types of vectors. For example, the polynucleotides can be cloned into a vector including, but not limited to a plasmid, a phagemid, a phage derivative, an animal virus, and a cosmid. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors, and sequencing vectors.

[0393] Further, the expression vector may be provided to cells, such as immune cells, in the form of a viral vector. Viral vector technology is well known in the art and is described, for example, in Sambrook et al. (2001, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York), and in other virology and molecular biology manuals. Viruses, which are useful as vectors include, but are not limited to, retroviruses, adenoviruses, adeno-associated viruses, herpes viruses, and lentiviruses. In general, a suitable vector contains an origin of replication functional in at least one organism, a promoter sequence, convenient restriction endonuclease sites, and one or more selectable markers, (e.g., WO 01/96584; WO 01/29058; and U.S. Pat. No. 6,326,193).

[0394] A number of viral based systems have been developed for gene transfer into mammalian cells. For example, retroviruses provide a convenient platform for gene delivery systems. A selected gene can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to cells of the subject either in vivo or ex vivo. A number of retroviral systems are known in the art. In some embodiments, adenovirus vectors are used. A number of adenovirus vectors are known in the art. In one embodiment, lentivirus vectors are used.

[0395] Additional promoter elements, e.g., enhancers, regulate the frequency of transcriptional initiation. Typically, these are located in the region 30-110 basepairs (bp) upstream of the start site, although a number of promoters have recently been shown to contain functional elements downstream of the start site as well. The spacing between promoter elements frequently is flexible, so that promoter function is preserved when elements are inverted or moved relative to one another. In the thymidine kinase (tk) promoter, the spacing between promoter elements can be increased to 50 bp apart before activity begins to decline. Depending on the promoter, it appears that individual elements can function either cooperatively or independently to activate transcription.

[0396] One example of a suitable promoter is the immediate early cytomegalovirus (CMV) promoter sequence. This promoter sequence is a strong constitutive promoter sequence capable of driving high levels of expression of any polynucleotide sequence operatively linked thereto. Another example of a suitable promoter is Elongation Growth Factor-1α (EF-1α). However, other constitutive promoter sequences may also be used, including, but not limited to the simian virus 40 (SV40) early promoter, mouse mammary tumor virus (MMTV), human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, MoMuLV promoter, an avian leukemia virus promoter, an Epstein-Barr virus immediate early promoter, a Rous sarcoma virus promoter, a U6 promoter, as well as human gene

promoters such as, but not limited to, the actin promoter, the myosin promoter, the hemoglobin promoter, and the creatine kinase promoter. Further, the disclosure should not be limited to the use of constitutive promoters. Inducible promoters are also contemplated as part of the disclosure. The use of an inducible promoter provides a molecular switch capable of turning on expression of the polynucleotide sequence which it is operatively linked when such expression is desired, or turning off the expression when expression is not desired. Examples of inducible promoters include, but are not limited to a metallothionine promoter, a glucocorticoid promoter, a progesterone promoter, and a tetracycline promoter.

[0397] In order to assess the expression of a receptor, the expression vector to be introduced into a cell can also contain either a selectable marker gene or a reporter gene or both to facilitate identification and selection of expressing cells from the population of cells sought to be transfected or infected through viral vectors. In other aspects, the selectable marker may be carried on a separate piece of DNA and used in a co-transfection procedure. Both selectable markers and reporter genes may be flanked with appropriate regulatory sequences to enable expression in the host cells. Useful selectable markers include, for example, antibiotic-resistance genes, such as neo and the like.

[0398] Reporter genes are used for identifying potentially transfected or transduced cells and for evaluating the functionality of regulatory sequences. In general, a reporter gene is a gene that is not present in or expressed by the recipient organism or tissue and that encodes a polypeptide whose expression is manifested by some easily detectable property, e.g., enzymatic activity. Expression of the reporter gene is assayed at a suitable time after the DNA has been introduced into the recipient cells. Suitable reporter genes may include genes encoding luciferase, beta-galactosidase, chloramphenicol acetyl transferase, secreted alkaline phosphatase, or the green fluorescent protein gene (e.g., Ui-Tei et al., 2000 FEBS Letters 479: 79-82). Suitable expression systems are well known and may be prepared using known techniques or obtained commercially. In general, the construct with the minimal 5′ flanking region showing the highest level of expression of reporter gene is identified as the promoter. Such promoter regions may be linked to a reporter gene and used to evaluate agents for the ability to modulate promoter-driven transcription.

[0399] Methods of introducing and expressing genes into a cell are known in the art. In the context of an expression vector, the vector can be readily introduced into a host cell, e.g., mammalian, bacterial, yeast, or insect cell by any method in the art. For example, the expression vector can be transferred into a host cell by physical, chemical, or biological means.

[0400] Physical methods for introducing a polynucleotide into a host cell include calcium phosphate precipitation, lipofection, particle bombardment, microinjection, electroporation, and the like. Methods for producing cells comprising vectors and/or exogenous nucleic acids are well-known in the art. See, for example, Sambrook et al. (2001, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York). One method for the introduction of a polynucleotide into a host cell is calcium phosphate transfection.

[0401] Biological methods for introducing a polynucleotide of interest into a host cell include the use of DNA and RNA vectors. Viral vectors, and especially retroviral vectors, have become the most widely used method for inserting genes into mammalian, e.g., human cells. Other viral vectors can be derived from lentivirus, poxviruses, herpes simplex virus I, adenoviruses and adeno-associated viruses, and the like. See, for example, U.S. Pat. Nos. 5,350,674 and 5,585,362.

[0402] Chemical means for introducing a polynucleotide into a host cell include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. An exemplary colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (e.g., an artificial membrane vesicle).

[0403] Regardless of the method used to introduce exogenous nucleic acids into a host cell or otherwise expose a cell to the inhibitor of the present disclosure, in order to confirm the presence of the recombinant DNA sequence in the host cell, a variety of assays may be performed. Such assays include, for example, "molecular biological" assays well known to those of skill in the art, such as Southern and Northern blotting, RT-PCR and PCR; "biochemical" assays, such as detecting the presence or absence of a particular peptide, e.g., by immunological means (ELISAs and Western blots) or by assays described herein to identify agents falling within the scope of the disclosure.

Immune Cells

[0404] The disclosure provides immune cells comprising the receptors, vectors and polynucleotides described herein.

[0405] In some embodiments, the immune cells comprise: (a) first receptor, comprising a first extracellular ligand binding domain specific to a target antigen selected from: (i) a cancer cell-specific antigen, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); or (ii) MSLN, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and (b) a second receptor,

comprising a second extracellular ligand binding specific to a non-target antigen selected from intercellular adhesion molecule 1 (ICAM1), catechol-O-methyltransferase (COMT), C-X-C motif chemokine ligand 16 (CXCL16), leucine rich repeat neuronal 4 (LRRN4) and uroplakin 3B UPK3B, or an antigen peptide thereof in a complex with a major histocompatibility complex class I (MHC-I), or HLA-A*02. In some embodiments, the first receptor is a CAR or TCR. In some embodiments, the second receptor is an inhibitory receptor, such as an inhibitory chimeric antigen receptor or TCR.

[0406] The disclosure provides immune cells comprising a first receptor comprising a sequence of SEQ ID NO: 303, and second receptor comprising a sequence of SEQ ID NO: 348, or sequences having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. In some embodiments, the immune cells comprise an shRNA encoded by a sequence comprising SEQ ID NO: 349 or 350, or a sequence having at least 80%, at least 90%, or at least 95% identity thereto. In some embodiments, the immune cells comprise first receptor comprising a sequence of SEQ ID NO: 303, a second receptor comprising a sequence of SEQ ID NO: 348, and a sequence encoding an shRNA comprising a sequence of SEQ ID NO: 349 or 350. In some embodiments, the first receptor and second receptor are encoded by a single polynucleotide, and wherein the sequences encoding the first and second receptors are separated by a sequence encoding a self-cleaving polypeptide. In some embodiments, the self-cleaving polypeptide comprises a T2A self-cleaving polypeptide comprising a sequence of GSGEGRGSLLTCGDVEENPGP (SEQ ID NO: 351).

[0407] As used herein, the term "immune cell" refers to a cell involved in the innate or adaptive (acquired) immune systems. Exemplary innate immune cells include phagocytic cells such as neutrophils, monocytes and macrophages, Natural Killer (NK) cells, polymophonuclear leukocytes such as neutrophils eosinophils and basophils and mononuclear cells such as monocytes, macrophages and mast cells. Immune cells with roles in acquired immunity include lymphocytes such as T-cells and B-cells.

[0408] As used herein, a "T-cell" refers to a type of lymphocyte that originates from a bone marrow precursor that develops in the thymus gland. There are several distinct types of T-cells which develop upon migration to the thymus, which include, helper CD4+ T-cells, cytotoxic CD8+ T cells, memory T cells, regulatory CD4+ T-cells and stem memory T-cells. Different types of T-cells can be distinguished by the ordinarily skilled artisan based on their expression of markers. Methods of distinguishing between T-cell types will be readily apparent to the ordinarily skilled artisan.

[0409] In some embodiments, the first receptor and the second receptor together specifically activate the immune cell in the presence of the target cell.

[0410] In some embodiments, the immune cell is CD4+, CD8+, a gamma delta T cell, an invariant T cells, an iNK cell , a NK cell, a macrophages, or combinations thereof. In some embodiments, the immune cell is a gamma delta (γδ) T cell. In some embodiments, the immune cell is an invariant T cell. In some embodiments, the immune cell is an invariant natural killer T cell (iNKT cell). In some embodiments, the immune cell is a T cell. In some embodiments, the immune cell is a B cell. In some embodiments, the immune cell is a Natural Killer (NK) cell. In some embodiments, the immune cell is CD8-. In some embodiments, the immune cell is CD8+. In some embodiments, the immune cell is CD4+. In some embodiments, the immune cell is CD4-. In some embodiments, the immune cell is CD8-/CD4+. In some embodiments, the immune cell is a CD8+ CD4- T cell.

[0411] In some embodiments, the immune cell is non-natural. In some embodiments, the immune cell is isolated.

[0412] Methods transforming populations of immune cells, such as T cells, with the vectors of the instant disclosure will be readily apparent to the person of ordinary skill in the art. For example, CD3+ T cells can be isolated from PBMCs using a CD3+ T cell negative isolation kit (Miltenyi), according to manufacturer's instructions. T cells can be cultured at a density of 1 x 10^6 cells/mL in X-Vivo 15 media supplemented with 5% human A/B serum and 1% Pen/strep in the presence of CD3/28 Dynabeads (1:1 cell to bead ratio) and 300 Units/mL of IL-2 (Miltenyi). After 2 days, T cells can be transduced with viral vectors, such as lentiviral vectors using methods known in the art. In some embodiments, the viral vector is transduced at a multiplicity of infection (MOI) of 5. Cells can then be cultured in IL-2 or other cytokines such as combinations of IL-7/15/21 for an additional 5 days prior to enrichment. Methods of isolating and culturing other populations of immune cells, such as B cells, or other populations of T cells, will be readily apparent to the person of ordinary skill in the art. Although this method outlines a potential approach it should be noted that these methodologies are rapidly evolving. For example excellent viral transduction of peripheral blood mononuclear cells can be achieved after 5 days of growth to generate a >99% CD3+ highly transduced cell population.

[0413] Methods of activating and culturing populations of T cells comprising the TCRs, CARs, inhibitory receptors, receptors or vectors encoding same, will be readily apparent to the person of ordinary skill in the art.

[0414] Whether prior to or after genetic modification of T cells to express a TCR, the T cells can be activated and expanded generally using methods as described, for example, in U.S. Pat. Nos. 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, 10040846; and U.S. Pat. Appl. Pub. No. 2006/0121005.

[0415] In some embodiments, T cells of the instant disclosure are expanded and activated in vitro. Generally, the T cells of the instant disclosure are expanded in vitro by contact with a surface having attached thereto an agent that stimulates a CD3/TCR complex associated signal and a ligand that stimulates a co-stimulatory molecule on the surface of the T cells. In particular, T cell populations may be stimulated as described herein, such as by contact with an anti-CD3 antibody. 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. To stimulate proliferation of either CD4+ T cells or CD8+ T cells, an anti-CD3 antibody and an anti-CD28 antibody can be used. Examples of an anti-CD28 antibody include 9.3, B-T3, XR-CD28 (Diaclone, Besançon, France) can be used as can other methods commonly known in the art (Berg et al., Transplant Proc. 30(8):3975-3977, 1998; Haanen et al., J. Exp. Med. 190(9):13191328, 1999; Garland et al., J. Immunol Meth. 227(1-2):53-63, 1999).

[0416] In some embodiments, the primary stimulatory signal and the co-stimulatory signal for the T cell may be provided by different protocols. For example, the agents providing each signal may be in solution or coupled to a surface. When coupled to a surface, the agents may be coupled to the same surface (i.e., in "cis" formation) or to separate surfaces (i.e., in "trans" formation). Alternatively, one agent may be coupled to a surface and the other agent in solution. In some embodiments, the agent providing the co-stimulatory signal is bound to a cell surface and the agent providing the primary activation signal is in solution or coupled to a surface. In certain embodiments, both agents can be in solution. In another embodiment, the agents may be in soluble form, and then cross-linked to a surface, such as a cell expressing Fc receptors or an antibody or other binding agent which will bind to the agents. In this regard, see for example, U.S. Patent Application Publication Nos. 20040101519 and 20060034810 for artificial antigen presenting cells (aAPCs) that are contemplated for use in activating and expanding T cells in the present disclosure.

[0417] In some embodiments, the two agents are immobilized on beads, either on the same bead, i.e., "cis," or to separate beads, i.e., "trans." By way of example, the agent providing

the primary activation signal is an anti-CD3 antibody or an antigen-binding fragment thereof and the agent providing the co-stimulatory signal is an anti-CD28 antibody or antigen-binding fragment thereof; and both agents are co-immobilized to the same bead in equivalent molecular amounts. In one embodiment, a 1:1 ratio of each antibody bound to the beads for CD4+ T cell expansion and T cell growth is used. In some embodiments, the ratio of CD3:CD28 antibody bound to the beads ranges from 100:1 to 1:100 and all integer values there between. In one aspect of the present disclosure, more anti-CD28 antibody is bound to the particles than anti-CD3 antibody, i.e., the ratio of CD3:CD28 is less than one. In certain embodiments of the disclosure, the ratio of anti CD28 antibody to anti CD3 antibody bound to the beads is greater than 2:1.

[0418] Ratios of particles to cells from 1:500 to 500:1 and any integer values in between may be used to stimulate T cells or other target cells. As those of ordinary skill in the art can readily appreciate, the ratio of particles to cells may depend on particle size relative to the target cell. For example, small sized beads could only bind a few cells, while larger beads could bind many. In certain embodiments the ratio of cells to particles ranges from 1:100 to 100:1 and any integer values in-between and in further embodiments the ratio comprises 1:9 to 9:1 and any integer values in between, can also be used to stimulate T cells. In some embodiments, a ratio of 1:1 cells to beads is used. One of skill in the art will appreciate that a variety of other ratios may be suitable for use in the present disclosure. In particular, ratios will vary depending on particle size and on cell size and type.

[0419] In further embodiments of the present disclosure, the cells, such as T cells, are combined with agent-coated beads, the beads and the cells are subsequently separated, and then the cells are cultured. In an alternative embodiment, prior to culture, the agent-coated beads and cells are not separated but are cultured together. In a further embodiment, the beads and cells are first concentrated by application of a force, such as a magnetic force, resulting in increased ligation of cell surface markers, thereby inducing cell stimulation.

[0420] By way of example, cell surface proteins may be ligated by allowing paramagnetic beads to which anti-CD3 and anti-CD28 are attached to contact the T cells. In one embodiment the cells (for example, CD4+ T cells) and beads (for example, DYNABEADS CD3/CD28 T paramagnetic beads at a ratio of 1:1) are combined in a buffer. Again, those of ordinary skill in the art can readily appreciate any cell concentration may be used. In certain embodiments, it may be desirable to significantly decrease the volume in which particles and cells are mixed together (i.e., increase the concentration of cells), to ensure maximum contact of cells and particles. For example, in one embodiment, a concentration of about 2 billion

cells/ml is used. In another embodiment, greater than 100 million cells/ml is used. In a further embodiment, a concentration of cells of 10, 15, 20, 25, 30, 35, 40, 45, or 50 million cells/ml is used. In yet another embodiment, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further embodiments, concentrations of 125 or 150 million cells/ml can be used. In some embodiments, cells that are cultured at a density of $1x10^6$ cells/mL are used.

[0421] In some embodiments, the mixture may be cultured for several hours (about 3 hours) to about 14 days or any hourly integer value in between. In another embodiment, the beads and T cells are cultured together for 2-3 days. Conditions appropriate for T cell culture include an appropriate media (e.g., Minimal Essential Media or RPMI Media 1640 or, X-vivo 15, (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-12, IL-15, TGFβ, and TNF-α 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-mercaptoethanol. Media can include RPMI 1640, AIM-V, DMEM, MEM, α-MEM, F-12, X-Vivo 15, 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. In some embodiments, the media comprises X-VIVO-15 media supplemented with 5% human A/B serum, 1% penicillin/streptomycin (pen/strep) and 300 Units/ml of IL-2 (Miltenyi).

[0422] The T 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% CO2).

[0423] In some embodiments, the T cells comprising TCRs, CARs and inhibitory receptors of the disclosure are autologous. Prior to expansion and genetic modification, a source of T cells is obtained from a subject. Immune cells such as T cells can be obtained from a number of 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 certain embodiments of the present disclosure, any number of T cell lines available in the art, may be used. In certain embodiments of the present disclosure, T cells can be obtained from a unit of blood collected from a subject using any number of techniques known to the skilled artisan, such as Ficoll™ separation.

[0424] In some embodiments, cells from the circulating blood of an individual are obtained by apheresis. The apheresis product typically contains lymphocytes, including T cells, monocytes, granulocytes, B cells, other nucleated white blood cells, red blood cells, and platelets. In some embodiments, the cells collected by apheresis may be washed to remove the plasma fraction and to place the cells in an appropriate buffer or media for subsequent processing steps. In some embodiments, the cells are washed with phosphate buffered saline (PBS). In alternative embodiments, the wash solution lacks calcium and may lack magnesium or may lack many if not all divalent cations. As those of ordinary skill in the art would readily appreciate a washing step may be accomplished by methods known to those in the art, such as by using a semi-automated "flow-through" centrifuge (for example, the Cobe 2991 cell processor, the Baxter CytoMate, or the Haemonetics Cell Saver 5) according to the manufacturer's instructions. After washing, the cells may be resuspended in a variety of biocompatible buffers, such as, for example, Ca2+-free, Mg2+-free PBS, PlasmaLyte A, or other saline solution with or without buffer. Alternatively, the undesirable components of the apheresis sample may be removed and the cells directly resuspended in culture media.

[0425] In some embodiments, immune cells such as T cells are isolated from peripheral blood lymphocytes by lysing the red blood cells and depleting the monocytes, for example, by centrifugation through a PERCOLL™ gradient or by counterflow centrifugal elutriation. Specific subpopulations of immune cells, such as T cells, B cells, or CD4+ T cells can be further isolated by positive or negative selection techniques. For example, in one embodiment, T cells are isolated by incubation with anti-CD4 -conjugated beads, for a time period sufficient for positive selection of the desired T cells.

[0426] Enrichment of an immune cell population, such as a T cell population, by negative selection can be accomplished with a combination of antibodies directed to surface markers unique to the negatively selected cells. One method is cell sorting and/or selection via negative magnetic immune-adherence or flow cytometry that uses a cocktail of monoclonal antibodies directed to cell surface markers present on the cells negatively selected. For example, to enrich for CD4+ cells by negative selection, a monoclonal antibody cocktail typically includes antibodies to CD 14, CD20, CD 11b, CD 16, HLA-DR, and CD8.

[0427] For isolation of a desired population of immune cells by positive or negative selection, the concentration of cells and surface (e.g., particles such as beads) can be varied. In certain embodiments, it may be desirable to significantly decrease the volume in which beads and cells are mixed together (i.e., increase the concentration of cells), to ensure maximum contact of cells and beads.

[0428] In some embodiments, the cells may be incubated on a rotator for varying lengths of time at varying speeds at either 2-10° C or at room temperature.

[0429] T cells for stimulation, or PBMCs from which immune cells such as T cells are isolated, can also be frozen after a washing step. Wishing not to be bound by theory, the freeze and subsequent thaw step provides a more uniform product by removing granulocytes and to some extent monocytes in the cell population. After the washing step that removes plasma and platelets, the cells may be suspended in a freezing solution. While many freezing solutions and parameters are known in the art and will be useful in this context, one method involves using PBS containing 20% DMSO and 8% human serum albumin, or culture media containing 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin and 7.5% DMSO, or 31.25% Plasmalyte-A, 31.25% Dextrose 5%, 0.45% NaCl, 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin, and 7.5% DMSO or other suitable cell freezing media containing for example, Hespan and PlasmaLyte A, the cells then are frozen to −80° C at a rate of 1° per minute and stored in the vapor phase of a liquid nitrogen storage tank. Other methods of controlled freezing may be used as well as uncontrolled freezing immediately at −20° C or in liquid nitrogen.

[0430] The disclosure provides an immune cell expressing the activator and/or blocker receptors described herein, wherein the immune cell has reduced expression and/or function the major histocompatibility (MHC) class I complex.

[0431] In some embodiments, the immune cell is autologous. For example, the immune cells is isolated or derived from same subject who will receive the cell as part of a therapeutic regimen. It can be advantageous to modify autologous immune cells to have reduced expression and/or function of MHC class I with the blocker receptor is specific to an MHC class I antigen. Without wishing to be bound by theory, modification of autologous immune cells to have reduced expression and/or function of MHC class I reduces binding of the blocker receptor by MHC class I expressed by the immune cells, either in cis or in trans .

[0432] In some embodiments, the immune cell is all allogeneic. Allogeneic immune cells can be derived from a donor other than the subject to which the immune cells will be administered. Allogeneic immune cells have been commonly referred to in cell therapy as "off-the-shelf" or "universal" because of the possibility for allogeneic cells to be prepared and stored for use in subjects of a variety of genotypes.

[0433] Any suitable methods of reducing expression and/or function the MHC class I complex are envisaged as within the scope of the instant disclosure, and include, inter alia,

expression of interfering RNAs that knock down one or more RNAs encoding MHC class I components, or modifications of genes encoding MHC class I components.

[0434] The major histocompatibility complex (MHC) is a locus on the vertebrate genome that encodes a set of polypeptides required for the adaptive immune system. Among these are MHC class I polypeptides that include HLA-A, HLA-B, and HLA-C and alleles thereof. MHC class I alleles are highly polymorphic and expressed in all nucleated cells. MHC class I polypeptides encoded by HLA-A, HLA-B, and HLA-C and alleles thereof form heterodimers with β2 microglobulin (B2M) and present in complex with antigens on the surface of cells. As referred to herein, an MHC class I gene or polypeptide may refer to any polypeptide found in the MHC or the corresponding gene encoding said polypeptide. In some embodiments, the immune cells of the disclosure are inactivated by an inhibitor ligand comprising an MHC class I polypeptide, e.g. HLA-A, HLA-B, and HLA-C and alleles thereof. HLA-A alleles can be, for example and without limitation, HLA-A*02, HLA-A*02:01, HLA-A*02:01:01, HLA-A*02:01:01:01, and/or any gene that encodes protein identical or similar to HLA-A*02 protein. Thus, to prevent autocrine signaling/binding as described herein, it is desirable to eliminate or reduce expression of polypeptides encoded by HLA-A, HLA-B, and HLA-C and alleles thereof in the immune cells.

Immune Cells with Reduced MHC Class I Polypeptide Expression

[0435] In some embodiments, the immune cells described herein are modified to inactivate, or reduce or eliminate expression or function of an endogenous gene encoding an allele of an endogenous MHC class I polypeptide. In some embodiments, the gene encoding the MHC class I polypeptide is HLA-A, HLA-B, and/or HLA-C. HLA-A, HLA-B and HLA-C are encoded by the HLA-A, HLA-B and HLA-C loci. Each of HLA-A, HLA-B and HLA-C includes many variant alleles, all of which are envisaged as within the scope of the instant disclosure. In some embodiments, the gene encoding the MHC class I polypeptide is HLA-A. In some embodiments, the gene encoding the MHC class I polypeptide is HLA-A*02. In some embodiments, the gene encoding the MHC class I polypeptide is HLA-A*02:01. In some embodiments, the gene encoding the MHC class I polypeptide is HLA-A*02:01:01. In some embodiments, the gene encoding the MHC class I polypeptide is HLA-A*02:01:01:01.

[0436] In some embodiments, the genetically engineered immune cells described herein are modified to reduce or eliminate expression of the B2M gene product. The beta-2 microglobulin (B2M) gene encodes a protein that associates with the major histocompatibility complex (MHC) class I, i.e. MHC-I complex. The MHC-I complex is

required for presentation of antigens on the cell surface. The MHC -I complex is disrupted and non-functional when the B2M is deleted (Wang D et al. Stem Cells Transl Med. 4:1234-1245 (2015)). Furthermore, the B2M gene can be disrupted with high efficiency using gene editing techniques known in the art (Ren et al. Clin. Cancer Res. 23:2255-2266 (2017)). Reducing or eliminating B2M can reduce, or eliminate functional MHC I on the surface of the immune cell.

[0437] The disclosure provides gene editing systems for editing an endogenous target gene in an immune cell. The disclosure provides interfering RNAs specific to sequences of target genes. Gene editing systems such as CRISPR/Cas systems, TALENs and zinc fingers can be used to generate double strand breaks, which, through gene repair mechanisms such as homology directed repair or non-homologous end joining (NHEJ), can be used to introduce mutations. NHEJ after resection of the ends of the break, or improper end joining, can be used to introduce deletions. In some embodiments, the target gene comprises a gene encoding a subunit of the MHC-I complex.

[0438] Target gene sequences include, but are not limited to, promoters, enhancers, introns, exons, intron/exon junctions, transcription products (pre-mRNA, mRNA, and splice variants), and/or 3' and 5' untranslated regions (UTRs). Any gene element or combination of gene elements may be targeted for the purpose of genetic editing in the immune cells described herein. Modifications to the target genes can be accomplished using any method known in the art to edit the target gene that results in altered or disrupted expression or function the target gene or gene product.

[0439] In some embodiments, modifying the gene encoding the MHC class I polypeptide comprises deleting all or a portion of the gene. In some embodiments, modifying the gene encoding the MHC class I polypeptide comprises introducing a mutation in the gene. In some embodiments, the mutation comprises a deletion, insertion, substitution, or frameshift mutation. In some embodiments, modifying the gene comprises using a nucleic acid guided endonuclease.

[0440] Gene sequences for the target genes described herein are known in the art. The sequences can be found at public databases, such as NCBI GenBank or the NCBI nucleotide database. Sequences may be found using gene identifiers, for example, the HLA-A gene has NCBI Gene ID: 3105, the HLA-B gene has NCBI Gene ID: 3106, the HLA-C gene has NCBI Gene ID: 3107, and the *B2M* gene has NCBI Gene ID: 567 and NCBI Reference Sequence: NC_000015.10. Gene sequences may also be found by searching public databases using keywords. For example, HLA-A alleles may be found in the NCBI nucleotide database by

searching keywords, "HLA-A*02", "HLA-A*02:01", "HLA-A*02:01:01", or "HLA-A*02:01:01:01." These sequences can be used for targeting in various gene editing techniques known in the art. Table 10 provides non-limiting illustrative sequences of HLA-A allele and B2M gene sequences targeted for modification as described herein.

Table 10. Exemplary Target Gene Sequences

B2M mRNA	SEQ ID NO: 769
B2M Gene (GenBank: 567)	SEQ ID NO: 770
HLA-A*02:01:01:01 sequence encoding mRNA	SEQ ID NO: 771
HLA-A*02 (GenBank: LK021978.1)	SEQ ID NO: 772

[0441] The person of ordinary skill in the art will appreciate that T can be substituted for U to convert an RNA sequence to a DNA sequence and vice versa, and both are envisaged as target gene sequences of the disclosure.

[0442] In some embodiments, a target gene is edited in the immune cells described herein using a nucleic acid guided endonuclease. Exemplary nucleic acid guided endonucleases include Class II endonucleases, such as CRISPR/Cas9.

[0443] "CRISPR" or "CRISPR gene editing" as used herein refers to a set of clustered regularly interspaced short palindromic repeats, or a system comprising such a set of repeats. "Cas", as used herein, refers to a CRISPR-associated protein. A "CRISPR/Cas" system refers to a system derived from CRISPR and Cas which can be used to silence, knock out, or mutate a target gene. This system is a type of prokaryotic immune system that confers resistance to foreign genetic elements such as plasmids and phages and provides a form of acquired immunity. The CRISPR/Cas system has been modified for use in gene editing. This is accomplished by introducing into the eukaryotic cell a one or more specifically designed guide nucleic acids (gNAs), typically guide RNAs (gRNAs), and an appropriate Cas endonuclease which forms a ribonucleoprotein complex with the gNA. The gNA guides the gNA-endonuclease protein complex to a target genomic location, and the endonuclease introduces strand breakage at the target genomic location. This strand breakage can be repaired by cellular mechanisms such non-homologous end joining (leading to deletions) or homologous repair (which can generate insertions), thereby introducing genetic modifications into the host cell genome.

[0444] CRISPR/Cas systems are classified by class and by type. Class 2 systems currently represent a single interference protein that is categorized into three distinct types (types II, V and VI). Any class 2 CRISPR/Cas system suitable for gene editing, for example a type II, a type V or a type VI system, is envisaged as within the scope of the instant disclosure. Exemplary Class 2 type II CRISPR systems include Cas9, Csn2 and Cas4. Exemplary Class

2, type V CRISPR systems include, Cas12, Cas12a (Cpf1), Cas12b (C2c1), Cas12c (C2c3), Cas12d (CasY), Cas12e (CasX), Cas12f, Cas12g, Cas12h, Cas12i and Cas12k (C2c5). Exemplary Class 2 Type VI systems include Cas13, Cas13a (C2c2) Cas13b, Cas13c and Cas13d.

[0445] The CRISPR sequence, sometimes called a CRISPR locus, comprises alternating repeats and spacers. In a naturally-occurring CRISPR, the spacers usually comprise sequences foreign to the bacterium such as a plasmid or phage sequence. As described herein, spacer sequences may also be referred to as "targeting sequences." In CRISPR/Cas systems for a genetic engineering, the spacers are derived from the target gene sequence (the gNA).

[0446] An exemplary Class 2 type II CRISPR system relies on the protein Cas9, which is a nuclease with two active cutting sites, one for each strand of the double helix. Combining Cas9 and modified CRISPR locus RNA can be used in a system for gene editing. Pennisi (2013) Science 341: 833-836. In some embodiments, the Cas protein used to modify the immune cells is Cas9.

[0447] The CRISPR/Cas system can thus be used to edit a target gene, such as a gene targeted for editing in the immune cells described herein, by adding or deleting a base pair, or introducing a premature stop which thus decreases expression of the target. The CRISPR/Cas system can alternatively be used like RNA interference, turning off a target gene in a reversible fashion. In a mammalian cell, for example, the RNA can guide the Cas protein to a target gene promoter, sterically blocking RNA polymerases.

[0448] A Cas protein may be derived from any bacterial or archaeal Cas protein. Any suitable CRISPR/Cas system is envisaged as within the scope of the instant disclosure. In other aspects, Cas protein comprises one or more of Cas1, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas6, Cas7, Cas8, Cas9, Cas10, Cas12a (Cpf1), Cas13, Csy1, Csy2, Csy3, Cse1, Cse2, Csc1, Csc2, Csa5, Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, CasX, CasY, homologs thereof, or modified versions thereof. In some embodiments, the Cas protein is a Cas9 protein, a Cpf1 protein, a C2c1 protein, a C2c2 protein, a C2c3 protein, Cas3, Cas3-HD, Cas 5, Cas7, Cas8, Cas10, or combinations or complexes of these. In some embodiments, the Cas protein is a Cas9 protein.

[0449] Artificial CRISPR/Cas systems can be generated which inhibit a target gene, using technology known in the art, *e.g.*, that described in U.S. Publication No. 20140068797, and Cong (2013) Science 339: 819-823. Other artificial CRISPR/Cas systems that are known in the art may also be generated which inhibit a target gene, *e.g.*, that described in Tsai (2014)

Nature Biotechnol., 32:6 569-576, U.S. Pat. Nos. 8,871,445; 8,865,406; 8,795,965; 8,771,945; and 8,697,359. Methods of designing suitable gNAs for a particular Cas protein will be known by persons of ordinary skill in the art.

[0450] The present disclosure provides gene-targeting guide nucleic acids (gNAs) that can direct the activities of an associated polypeptide (e.g., nucleic acid guided endonuclease) to a specific target gene sequence within a target nucleic acid genome. The genome-targeting nucleic acid can be an RNA. A genome-targeting RNA is referred to as a "guide RNA" or "gRNA" herein. A guide RNA can comprise at least a targeting sequence that hybridizes to a target nucleic acid sequence of interest, and a CRISPR repeat sequence. In some Type II systems, the gRNA also comprises a second RNA called the tracrRNA sequence, also referred to herein as a "scaffold" sequence. In the Type II guide RNA (gRNA), the CRISPR repeat sequence and scaffold sequence hybridize to each other to form a duplex. In the Type V guide RNA (gRNA), the crRNA forms a duplex. In both systems, the duplex can bind a site-directed polypeptide, such that the guide RNA and site-directed polypeptide form a complex. The gene-targeting nucleic acid can provide target specificity to the complex by virtue of its association with the site-directed polypeptide. The gene-targeting nucleic acid thus can direct the activity of the site-directed polypeptide.

[0451] In some embodiments, the disclosure provides a guide RNA comprising a targeting sequence and a guide RNA scaffold sequence, wherein the targeting sequence is complementary to the sequence of a target gene.

[0452] Exemplary guide RNAs include targeting sequences of about 15-20 bases. As is understood by the person of ordinary skill in the art, each gRNA can be designed to include a targeting sequence complementary to its genomic target sequence. For example, each of the targeting sequences, e.g., the RNA version of the DNA sequences presented in Tables 11 and 14, minus the three 3' nucleotides which represent that PAM site, can be put into a single RNA chimera or a crRNA.

[0453] The gene targeting nucleic acid can be a double-molecule guide RNA. The gene targeting nucleic acid can be a single-molecule guide RNA. The gene targeting nucleic acid can be any known configuration of guide RNA known in the art, such as, for example, including paired gRNA, or multiple gRNAs used in a single step. Although it is clear from genomic sequences where the coding sequences and splice junctions are, other features required for gene expression may be idiosyncratic and unclear.

[0454] A double-molecule guide RNA can comprise two strands of RNA. The first strand comprises a sequence in the 5′ to 3′ direction, an optional spacer extension sequence, a

targeting sequence and a minimum CRISPR repeat sequence. The second strand can comprise a minimum tracrRNA sequence (complementary to the minimum CRISPR repeat sequence), a 3′ tracrRNA sequence and an optional tracrRNA extension sequence.

[0455] A single-molecule guide RNA (sgRNA) in a Type II system can comprise, in the 5′ to 3′ direction, an optional spacer extension sequence, a targeting sequence, a minimum CRISPR repeat sequence, a single-molecule guide linker, a minimum tracrRNA sequence, a 3′ tracrRNA sequence and an optional tracrRNA extension sequence. The optional tracrRNA extension can comprise elements that contribute additional functionality (e.g., stability) to the guide RNA. The single-molecule guide linker can link the minimum CRISPR repeat and the minimum tracrRNA sequence to form a hairpin structure. The optional tracrRNA extension can comprise one or more hairpins.

[0456] In some embodiments, guide RNA or single-molecule guide RNA (sgRNA) can comprise a targeting sequence and a scaffold sequence. In some embodiments, the scaffold sequence is a Cas9 gRNA sequence. In some embodiments, the scaffold sequence is encoded by a DNA sequence that comprises a sequence that shares at least 90%, at least 95%, at least 96%, at least
98%, or at least 99% identity to GTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCT AGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTT (SEQ ID NO: 773). In some embodiments, the scaffold sequence is encoded by a DNA sequence that compr ises GTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTT GAAAAAGTGGCACCGAGTCGGTGCTTTTTTT (SEQ ID NO: 773).

[0457] In some embodiments, for example those embodiments where the CRISPR/Cas system is a Cas9 system, the sgRNA can comprise a 20 nucleotide targeting sequence at the 5′ end of the sgRNA sequence. The sgRNA can comprise a less than a 20 nucleotide targeting sequence at the 5′ end of the sgRNA sequence. The sgRNA can comprise a more than 20 nucleotide targeting sequence at the 5′ end of the sgRNA sequence. The sgRNA can comprise a variable length targeting sequence with 17-30 nucleotides at the 5′ end of the sgRNA sequence.

[0458] Suitable scaffold sequences, and arrangement of scaffold targeting sequences, will depend on choice of endonuclease, and will be known to persons of skill in the art.

[0459] A single-molecule guide RNA (sgRNA) in a Type II system, *e.g.* Cas9, can comprise, in the 5′ to 3′ direction, a minimum CRISPR repeat sequence and a targeting sequence.

[0460] By way of illustration, guide RNAs used in the CRISPR/Cas9 or CRISPR/Cpf1 system, or other smaller RNAs can be readily synthesized by chemical means, as illustrated

below and described in the art. While chemical synthetic procedures are continually expanding, purifications of such RNAs by procedures such as high performance liquid chromatography (HPLC, which avoids the use of gels such as PAGE) tends to become more challenging as polynucleotide lengths increase significantly beyond a hundred or so nucleotides. One approach used for generating RNAs of greater length is to produce two or more molecules that are ligated together. Much longer RNAs, such as those encoding a Cas9 or Cpf1 endonuclease, are more readily generated enzymatically. Various types of RNA modifications can be introduced during or after chemical synthesis and/or enzymatic generation of RNAs, e.g., modifications that enhance stability, reduce the likelihood or degree of innate immune response, and/or enhance other attributes, as described in the art.

[0461] The targeting sequence of a gRNA hybridizes to a sequence in a target nucleic acid of interest. The targeting sequence of a genome-targeting nucleic acid can interact with a target nucleic acid in a sequence-specific manner via hybridization (i.e., base pairing). The nucleotide sequence of the targeting sequence can vary depending on the sequence of the target nucleic acid of interest.

[0462] In a Cas9 system described herein, the targeting sequence can be designed to hybridize to a target nucleic acid that is located 5′ of the reverse complement of a PAM of the Cas9 enzyme used in the system. The targeting sequence may perfectly match the target sequence or may have mismatches. Each CRISPR/Cas system protein may have a particular PAM sequence, in a particular orientation and position, that it recognizes in a target DNA. For example, S. pyogenes Cas9 recognizes in a target nucleic acid a PAM that comprises the sequence 5′-NRG-3′, where R comprises either A or G, where N is any nucleotide and N is immediately 3′ of the target nucleic acid sequence targeted by the targeting sequence. Selection of appropriate PAM sequences will be apparent to the person of ordinary skill in the art.

[0463] The target sequence is complementary to, and hybridizes with, the targeting sequence of the gRNA. The target nucleic acid sequence can comprise 20 nucleotides. The target nucleic acid can comprise less than 20 nucleotides. The target nucleic acid can comprise more than 20 nucleotides. The target nucleic acid can comprise at least: 5, 10, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30 or more nucleotides. In some embodiments, for example those embodiments where the CRISPR/Cas system is a Cas9 system, the target nucleic acid sequence can comprise 20 nucleotides immediately 5′ of the first nucleotide of the reverse complement of the PAM sequence. This target nucleic acid sequence is often referred to as the PAM strand or a target strand, and the complementary nucleic acid sequence is often

referred to the non-PAM strand or non-target strand. One of skill in the art would recognize that the targeting sequence hybridizes to the non-PAM strand of the target nucleic acid, see *e.g.*, US20190185849A1.

[0464] In some examples, the percent complementarity between the targeting sequence and the target nucleic acid is at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99%, or 100%. In some examples, the percent complementarity between the targeting sequence and the target nucleic acid is at most about 30%, at most about 40%, at most about 50%, at most about 60%, at most about 65%, at most about 70%, at most about 75%, at most about 80%, at most about 85%, at most about 90%, at most about 95%, at most about 97%, at most about 98%, at most about 99%, or 100%. In some examples, the percent complementarity between the targeting sequence and the target nucleic acid is 100% over the six contiguous 5′-most nucleotides of the target sequence of the complementary strand of the target nucleic acid. The percent complementarity between the targeting sequence and the target nucleic acid can be at least 60% over about 20 contiguous nucleotides. The length of the targeting sequence and the target nucleic acid can differ by 1 to 6 nucleotides, which may be thought of as a bulge or bulges.

[0465] The targeting sequence can be designed or chosen using computer programs known to persons of ordinary skill in the art. The computer program can use variables, such as predicted melting temperature, secondary structure formation, predicted annealing temperature, sequence identity, genomic context, chromatin accessibility, % GC, frequency of genomic occurrence (e.g., of sequences that are identical or are similar but vary in one or more spots as a result of mismatch, insertion or deletion), methylation status, presence of SNPs, and the like. Available computer programs can take as input NCBI gene IDs, official gene symbols, Ensembl Gene IDs, genomic coordinates, or DNA sequences, and create an output file containing sgRNAs targeting the appropriate genomic regions designated as input. The computer program may also provide a summary of statistics and scores indicating on- and off-target binding of the sgRNA for the target gene (Doench et al. *Nat Biotechnol.* 34:184-191 (2016)).The disclosure provides guide RNAs comprising a targeting sequence. In some embodiments, the guide RNA further comprises a guide RNA scaffold sequence. In some embodiments, the targeting sequence is complementary to the sequence of a target gene selected from the group consisting of HLA-A, HLA-B, HLA-C, B2M or an allele thereof. In some embodiments, the target gene is an HLA-A gene. In some embodiments, the target gene

is an HLA-B gene. In some embodiments, the target gene is an HLA-C gene. In some embodiments the target gene is HLA-A, HLA-B, HLA-C, or a combination thereof. In some embodiments, targeting sequence comprises a sequence that shares about 90%, about 95%, about 96%, about 97%, about 98%, about 99% identity to or is identical to a sequence disclosed in Tables 11 and14.

[0466] In some embodiments, the gNAs specifically target the sequence of an endogenous HLA-A locus. In some embodiments, the gNAs that specifically target the sequence of an HLA-A locus comprise a sequence that shares about 90%, about 95%, about 96%, about 97%, about 98%, or about 99% identity to a sequence selected from the sequences disclosed in Table 11. In some embodiments, the gNAs that specifically target the sequence of an HLA-A locus comprise a sequence selected from the sequences disclosed in Table 11.

[0467] In some embodiments, the gNAs specifically target a sequence of HLA-A*02 alleles. For example, the gRNAs specifically target, and hybridize to, a sequence shared by all HLA-A*02 alleles, but that is not shared by HLA-A*02 and HLA-A*03 alleles. In some embodiments, the gNAs specifically target a sequence of HLA-A*02:01 alleles. In some embodiments, the gNAs specifically target a sequence of HLA-A*02:01:01 alleles. In some embodiments, the gNAs specifically target a sequence of HLA-A*02:01:01:01 alleles. In some embodiments, the gNAs specifically target a sequence of HLA-A*02:01:01:01 alleles.

[0468] In some embodiments, the gNAs specifically target a coding DNA sequence of HLA-A*02.

[0469] In some embodiments, the gNAs specifically target a coding DNA sequence that is shared by more than 1000 HLA-A*02 alleles. In some embodiments, the gNAs that specifically target a coding DNA sequence in greater than 1000 HLA-A*02 alleles comprise a sequence that shares about 90%, about 95%, about 96%, about 97%, about 98%, about 99% identity or is identical to a sequence selected from the sequences set forth in Table 11.

[0470] The sequences in Tables 11-14 are presented as DNA sequences. The skilled artisan will understand that thymine (T) can be replaced with uracil (U) in any DNA sequence including those set forth in Tables 11-14, to arrive at the corresponding RNA sequence.

[0471] Table 11. Illustrative sequences targeting HLA-A and HLA-A alleles

SEQ ID NO	Guide Nucleic Acid Targeting Sequences
774	TGGACGACACGCAGTTCGTG
775	CAGATACCTGGAGAACGGGA
776	TCCCGTTCTCCAGGTATCTG
777	CCGCCGCGGTCCAAGAGCGC
778	CCTGCGCTCTTGGACCGCGG
779	GGACCTGCGCTCTTGGACCGC
780	AAGGAGACGCTGCAGCGCACGGG
781	GAAGGAGACGCTGCAGCGCACGG
782	GCGGGCGCCGTGGATAGAGCAGG
783	TGCTCTATCCACGGCGCCCGCGG
784	CGATGAAGCGGGGCTCCCCGCGG
785	CGTGTCCCGGCCCGGCCGCGGGG
786	CGGCTCCATCCTCTGGCTCGCGG
787	GATGTAATCCTTGCCGTCGTAGG
788	ACAGCGACGCCGCGAGCCAGAGG
789	GGATGGAGCCGCGGGCGCCGTGG
790	GGCGCCGTGGATAGAGCAGGAGG
791	GCGCCGTGGATAGAGCAGGAGGG
792	CGGCTACTACAACCAGAGCGAGG
793	CTGGTTGTAGTAGCCGCGCAGGG
794	TACTACAACCAGAGCGAGGCCGG
795	CTACCTGGAGGGCACGTGCGTGG
796	CACGCACGTGCCCTCCAGGTAGG
797	GCAGGGTCCCCAGGTCCACTCGG
798	GTGGACCTGGGGACCCTGCGCGG
799	TGGAGGGCACGTGCGTGGAGTGG
800	GTATGGCTGCGACGTGGGGTCGG
801	CTGAGCTGCCATGTCCGCCGCGG
802	GGATTACATCGCCCTGAAAGAGG
803	CAAGTGGGAGGCGGCCCATGTGG
804	GTGGGAGGCGGCCCATGTGGCGG
805	CAGTTGAGAGCCTACCTGGAGGG
806	GCAGTTGAGAGCCTACCTGGAGG
807	TACCACCAGTACGCCTACGACGG
808	TGCCGTCGTAGGCGTACTGGTGG
809	CCAGTACGCCTACGACGGCAAGG
810	GGATGTGAAGAAATACCTCATGG
811	ATTTCTTCACATCCGTGTCCCGG
812	AGGCGTACTGGTGGTACCCGCGG
813	CGTACTGGTGGTACCCGCGGAGG
814	GAGGATGTATGGCTGCGACGTGG
815	GGATGTATGGCTGCGACGTGGGG
816	CTCAGACCACCAAGCACAAGTGG

SEQ ID NO	Guide Nucleic Acid Targeting Sequences
817	TCAGACCACCAAGCACAAGTGGG
818	CACCAAGCACAAGTGGGAGGCGG
819	GACCACCAAGCACAAGTGGGAGG
820	GAGCCCCGCTTCATCGCAGTGGG
821	GTAGCCCACTGCGATGAAGCGGG
822	TAGCCCACTGCGATGAAGCGGGG
823	CGTAGCCCACTGCGATGAAGCGG
824	CTTCATCGCAGTGGGCTACGTGG
825	GGAGCCCCGCTTCATCGCAGTGG
826	CGGGGAGACACGGAAAGTGAAGG
827	AGTATTGGGACGGGGAGACACGG
828	AGGGTCCGGAGTATTGGGACGGG
829	GAGGGTCCGGAGTATTGGGACGG
830	GGACCCTCCTGCTCTATCCACGG
831	GTGGATAGAGCAGGAGGGTCCGG
832	AGACTCACCGAGTGGACCTGGGG
833	CACTCGGTGAGTCTGTGAGTGGG
834	CAGACTCACCGAGTGGACCTGGG
835	CCACTCACAGACTCACCGAGTGG
836	CCACTCGGTGAGTCTGTGAGTGG
837	TCGGACTGGCGCTTCCTCCGCGG
838	GCAGCCATACATCCTCTGGACGG
839	TCTCAACTGCTCCGCCACATGGG
840	ACCCTCATGCTGCACATGGCAGG
841	ACCTGCCATGTGCAGCATGAGGG
842	CACCTGCCATGTGCAGCATGAGG
843	GGAGGACCAGACCCAGGACACGG
844	GGATGGGGAGGACCAGACCCAGG
845	GACCTGGCAGCGGGATGGGGAGG
846	AGATCACACTGACCTGGCAGCGG
847	GATCACACTGACCTGGCAGCGGG
848	AGGTCAGTGTGATCTCCGCAGGG
849	AAGCCCCTCACCCTGAGATGGGG
850	CTGCGGAGATCACACTGACCTGG
851	CAGCAATGATGCCCACGATGGGG
852	CCAGCAATGATGCCCACGATGGG
853	GCCAGCAATGATGCCCACGATGG
854	GGATGGAACCTTCCAGAAGTGGG
855	GGGATGGAACCTTCCAGAAGTGG
856	ATGCCCACGATGGGGATGGTGGG
857	CAGCCCACCATCCCCATCGTGGG
858	CCAGCCCACCATCCCCATCGTGG
859	GATGCCCACGATGGGGATGGTGG

SEQ ID NO	Guide Nucleic Acid Targeting Sequences
860	CAGGGCCCAGCACCTCAGGGTGG
861	AATGATGCCCACGATGGGGATGG
862	GGCCCTGACCCAGACCTGGGCGG
863	GACCCAGGACACGGAGCTCGTGG
864	ACACGGAGCTCGTGGAGACCAGG
865	CGTGGAGACCAGGCCTGCAGGGG
866	TCGTGGAGACCAGGCCTGCAGGG
867	AGCTGTGATCACTGGAGCTGTGG
868	AAAAGGAGGGAGCTACTCTCAGG
869	ATGTGGAGGAGGAAGAGCTCAGG
870	GTGTCTCTCACAGCTTGTAAAGG
871	GAGAGACACATCAGAGCCCTGGG
872	CTCCGCAGGGTAGAAGCTCAGGG
873	GGCCCTGAGCTTCTACCCTGCGG
874	GCTCAGGGCCCAGCACCTCAGGG
875	TATCTCTGCTCCTGTCCAGAAGG
876	AGTAGCAGGACGAGGGTTCGGGG

SEQ ID NO	Guide Nucleic Acid Targeting Sequences
877	CCCCGAGAGTAGCAGGACGAGGG
878	CCCTCGTCCTGCTACTCTCGGGG
879	CCTCGTCCTGCTACTCTCGGGGG
880	CTGTGGTCGCTGCTGTGATGTGG
881	TCGCTGCTGTGATGTGGAGGAGG
882	TGGTCGCTGCTGTGATGTGGAGG
883	CACAGCCGCCCACTTCTGGAAGG
884	CCAGAAGTGGGCGGCTGTGGTGG
885	TGGAACCTTCCAGAAGTGGGCGG
886	TCACAGCTCCAAAGAGAACCAGG
887	CTGACCATGAAGCCACCCTGAGG
888	GCAAACCCTCATGCTGCACATGG
889	TGAAGCCACCCTGAGGTGCTGGG
890	GGTGAGTCATATGCGTTTTGGGG
891	GTGAGTCATATGCGTTTTGGGGG
892	CTTCATGGTCAGAGACAGCGTGG
893	TCTGGCCCTGACCCAGACCTGGG

[0472] The sequences disclosed in Table 11 include the corresponding genomic sequences, inclusive of the PAM sequence. The skilled artisan will understand that the targeting sequence of the gRNA does not include three 3' terminal nucleotides of the sequences in Table 11, which represent the corresponding PAM site for the gRNA.

[0473] The disclosure provides gNAs comprising a targeting sequence specific to the *B2M* gene. In some embodiments, the gNAs specifically target the coding sequence (CDS) sequence of the B2M gene. In some embodiments, the gNA comprises a sequence that targets the *B2M* gene promoter sequence.

[0474] In some embodiments the gNA comprise a targeting sequence and a gNA scaffold sequence. In some embodiments, the targeting sequence comprises a sequence set forth in Table 12, or a sequence shares about 90%, about 95%, about 96%, about 97%, about 98%, about 99% identity thereto.

[0475] In some embodiments, the targeting sequence is complementary to a sequence of the *B2M* gene. In some embodiments, the *B2M* gene comprises a sequence that shares about 90%, about 95%, about 96%, about 97%, about 98%, about 99% identity to the B2M sequence set forth in Table 10.

Table 12. Illustrative sequences targeting *B2M*

SEQ ID NO	Sequence
894	CGCGAGCACAGCTAAGGCCA
895	GAGTAGCGCGAGCACAGCTA
896	AGGGTAGGAGAGACTCACGC
897	CTGAATCTTTGGAGTACCTG
898	TCACGTCATCCAGCAGAGAA
899	TCCTGAATTGCTATGTGTCT
900	AAGTCAACTTCAATGTCGGA
901	GTCTTTTCCCGATATTCCTC
902	TGGAGTACCTGAGGAATATC
903	CAGCCCAAGATAGTTAAGTG
904	ACAAAGTCACATGGTTCACA
905	ACTCTCTCTTTCTGGCCTGG
906	TGGGCTGTGACAAAGTCACA
907	GGCCGAGATGTCTCGCTCCG
908	CAGTAAGTCAACTTCAATGT
909	ACTCACGCTGGATAGCCTCC
910	CATACTCATCTTTTTCAGTG
911	CACAGCCCAAGATAGTTAAG
912	TTCAGACTTGTCTTTCAGCA
913	AGTCACATGGTTCACACGGC
914	ATACTCATCTTTTTCAGTGG
915	GGCATACTCATCTTTTTCAG
916	ACAGCCCAAGATAGTTAAGT
917	GCTACTCTCTCTTTCTGGCC
918	TGGAGAGAGAATTGAAAAAG
919	ACTTGTCTTTCAGCAAGGAC
920	GAAGTTGACTTACTGAAGAA
921	GGCCACGGAGCGAGACATCT
922	GCATACTCATCTTTTTCAGT
923	CGTGAGTAAACCTGAATCTT
924	TTACCCCACTTAACTATCTT
925	TTGGAGTACCTGAGGAATAT
926	ACCCAGACACATAGCAATTC
927	TTTGACTTTCCATTCTCTGC
928	TTCCTGAATTGCTATGTGTC
929	CTCAGGTACTCCAAAGATTC
930	CTTACCCCACTTAACTATCT
931	CTCGCGCTACTCTCTCTTTC
932	TCGATCTATGAAAAAGACAG
933	GAGACATGTAAGCAGCATCA
934	ACATGTAAGCAGCATCATGG
935	GAAGTCCTAGAATGAGCGCC
936	GAGCGCCCGGTGTCCCAAGC
937	AGCGCCCGGTGTCCCAAGCT
938	GCGCCCGGTGTCCCAAGCTG
939	CTGGGGCGCGCACCCCAGAT

SEQ ID NO	Sequence
940	GGGCGCGCACCCCAGATCGG
941	GGCGCGCACCCCAGATCGGA
942	CATCACGAGACTCTAAGAAA
943	TAAGAAAAGGAAACTGAAAA
944	AAGAAAAGGAAACTGAAAAC
945	GAAAGTCCCTCTCTCTAACC
946	CTAACCTGGCACTGCGTCGC
947	CTGGCACTGCGTCGCTGGCT
948	TGCGTCGCTGGCTTGGAGAC
949	GCTGGCTTGGAGACAGGTGA
950	GAGACAGGTGACGGTCCCTG
951	AGACAGGTGACGGTCCCTGC
952	CCTGCGGGCCTTGTCCTGAT
953	CGGGCCTTGTCCTGATTGGC
954	GGGCCTTGTCCTGATTGGCT
955	GGGCACGCGTTTAATATAAG
956	CACGCGTTTAATATAAGTGG
957	TATAAGTGGAGGCGTCGCGC
958	AAGTGGAGGCGTCGCGCTGG
959	AGTGGAGGCGTCGCGCTGGC
960	TTCCTGAAGCTGACAGCATT
961	TCCTGAAGCTGACAGCATTC
962	GCCCGAATGCTGTCAGCTTC
963	AAACGCGTGCCCAGCCAATC
964	GTGCCCAGCCAATCAGGACA
965	CCAATCAGGACAAGGCCCGC
966	CAATCAGGACAAGGCCCGCA
967	CAAGCCAGCGACGCAGTGCC
968	CGCAGTGCCAGGTTAGAGAG
969	GCAGTGCCAGGTTAGAGAGA
970	GAGTCTCGTGATGTTTAAGA
971	TAAGAAGGCATGCACTAGAC
972	AAGAAGGCATGCACTAGACT
973	TGAGTTTGCTGTCTGTACAT
974	TACATCGGCGCCCTCCGATC
975	ACATCGGCGCCCTCCGATCT
976	CATCGGCGCCCTCCGATCTG
977	CTGGGGTGCGCGCCCCAGCT
978	TGGGGTGCGCGCCCCAGCTT
979	CGCGCCCCAGCTTGGGACAC
980	GCGCCCCAGCTTGGGACACC
981	CAAGTCACTTAGCATCTCTG
982	ACAGAAGTTCTCCTTCTGCT
983	ATTCAAAGATCTTAATCTTC
984	TTCAAAGATCTTAATCTTCT
985	TTTTCTCGAATGAAAAATGC

SEQ ID NO	Sequence
986	TGCAGGTCCGAGCAGTTAAC
987	GGTCCGAGCAGTTAACTGGC
988	GTCCGAGCAGTTAACTGGCT
989	TCCGAGCAGTTAACTGGCTG
990	AGCAAGTCACTTAGCATCTC
991	GCAAGTCACTTAGCATCTCT
992	TGGGGCCAGTCTGCAAAGCG
993	GGGGCCAGTCTGCAAAGCGA
994	GGGCCAGTCTGCAAAGCGAG
995	GGCCAGTCTGCAAAGCGAGG
996	GGACACCGGGCGCTCATTCT
997	GGCGCTCATTCTAGGACTTC
998	CTCATTCTAGGACTTCAGGC
999	ATTCTAGGACTTCAGGCTGG
1000	TTCAGGCTGGAGGCACATTA
1001	TGCCCCCTCGCTTTGCAGAC
1002	GATGCTAAGTGACTTGCTAA
1003	GCCCCAGCCAGTTAACTGCT
1004	GCATTTTTCATTCGAGAAAA
1005	TTTGAATGCTACCTAGCAGA
1006	TTCTGTTTATAACTACAGCT
1007	TCTGTTTATAACTACAGCTT

[0476] In some embodiments, the immune cells described herein are edited using TALEN gene editing.

[0477] "TALEN" or "TALEN gene editing" refers to a transcription activator-like effector nuclease, which is an artificial nuclease used to edit a target gene.

[0478] TALENs are produced artificially by fusing a TAL effector DNA binding domain to a DNA cleavage domain. Transcription activator-like effectors (TALEs) derived from Xanthomonas bacteria can be engineered to bind any desired DNA sequence, including a portion of target genes such as TCR subunits, MHC class I complex components, or CD52. By combining an engineered TALE with a DNA cleavage domain, a restriction enzyme can be produced which is specific to any desired DNA sequence, including a target gene sequence. These can then be introduced into a cell, wherein they can be used for genome editing.

[0479] To produce a TALEN, a TALE protein is fused to a nuclease (N), which is a wild-type or mutated Fold endonuclease. Several mutations to FokI have been made for its use in TALENs; these, for example, improve cleavage specificity or activity.

[0480] The FokI domain functions as a dimer, requiring two constructs with unique DNA binding domains for sites in the target genome with proper orientation and spacing. Both the number of amino acid residues between the TALE DNA binding domain and the FokI cleavage domain and the number of bases between the two individual TALEN binding sites appear to be important parameters for achieving high levels of activity.

[0481] TALENs specific to sequences in a target gene can be constructed using any method known in the art, including various schemes using modular components.

[0482] In some embodiments, a target gene is edited in the immune cells described herein using ZFN gene editing.

[0483] "ZFN" or "Zinc Finger Nuclease" or "ZFN gene editing" refer to a zinc finger nuclease, an artificial nuclease which can be used to edit a target gene.

[0484] Like a TALEN, a ZFN comprises a Fold nuclease domain (or derivative thereof) fused to a DNA-binding domain. In the case of a ZFN, the DNA-binding domain comprises one or more zinc fingers.

[0485] A zinc finger is a small protein structural motif stabilized by one or more zinc ions. A zinc finger can comprise, for example, Cys2His2, and can recognize an approximately 3-bp sequence. Various zinc fingers of known specificity can be combined to produce multi-finger polypeptides which recognize about 6, 9, 12, 15 or 18-bp sequences. Various selection and modular assembly techniques are available to generate zinc fingers (and combinations thereof)

recognizing specific sequences, including phage display, yeast one-hybrid systems, bacterial one-hybrid and two-hybrid systems, and mammalian cells.

[0486] Like a TALEN, a ZFN must dimerize to cleave DNA. Thus, a pair of ZFNs are required to target non-palindromic DNA sites. The two individual ZFNs must bind opposite strands of the DNA with their nucleases properly spaced apart.

[0487] Also like a TALEN, a ZFN can create a double-stranded break in the DNA, which can create a frame-shift mutation if improperly repaired, leading to a decrease in the expression and amount of a target gene or gene product in a cell. ZFNs can also be used with homologous recombination to mutate in a target gene.

[0488] ZFNs specific to sequences in a target gene can be constructed using any method known in the art.

[0489] In some embodiments, the expression and of function of one or more MCH-I components are reduced using RNA interference. "RNAi" or "RNA interference" refers to the process of sequence-specific post-transcriptional gene silencing, mediated by double-stranded RNA (dsRNA). Duplex RNAs such as siRNA (small interfering RNA), miRNA (micro RNA), shRNA (short hairpin RNA), ddRNA (DNA- directed RNA), piRNA (Piwi-interacting RNA), or rasiRNA (repeat associated siRNA) and modified forms thereof are all capable of mediating RNA interference. These dsRNA molecules may be commercially available or may be designed and prepared based on known sequence information. The anti-sense strand of these molecules can include RNA, DNA, PNA, or a combination thereof. DNA/RNA chimeric polynucleotides include, but are not limited to, a double-strand polynucleotide composed of DNA and RNA that inhibits the expression of a target gene. dsRNA molecules can also include one or more modified nucleotides, as described herein, which can be incorporated on either or both strands.

[0490] In RNAi gene silencing or knockdown, dsRNA comprising a first (anti-sense) strand that is complementary to a portion of a target gene and a second (sense) strand that is fully or partially complementary to the first anti-sense strand is introduced into an organism. After introduction into the organism, the target gene-specific dsRNA is processed into relatively small fragments (siRNAs) and can subsequently become distributed throughout the organism, decrease messenger RNA of target gene, leading to a phenotype that may come to closely resemble the phenotype arising from a complete or partial deletion of the target gene.

[0491] Certain dsRNAs in cells can undergo the action of Dicer enzyme, a ribonuclease III enzyme. Dicer can process the dsRNA into shorter pieces of dsRNA, i.e. siRNAs. RNAi also involves an endonuclease complex known as the RNA induced silencing complex (RISC). Following cleavage by Dicer, siRNAs enter the RISC complex and direct cleavage of a single

stranded RNA target having a sequence complementary to the anti-sense strand of the siRNA duplex. The other strand of the siRNA is the passenger strand. Cleavage of the target RNA takes place in the middle of the region complementary to the anti-sense strand of the siRNA duplex. siRNAs can thus down regulate or knock down gene expression by mediating RNA interference in a sequence-specific manner.

[0492] As used herein with respect to RNA interference, "target gene" or "target sequence" refers to a gene or gene sequence whose corresponding RNA is targeted for degradation through the RNAi pathway using dsRNAs or siRNAs as described herein. Exemplary target gene sequences are shown in Table 10. To target a gene, for example using an siRNA, the siRNA comprises an anti-sense region complementary to, or substantially complementary to, at least a portion of the target gene or sequence, and sense strand complementary to the anti-sense strand. Once introduced into a cell, the siRNA directs the RISC complex to cleave an RNA comprising a target sequence, thereby degrading the RNA. The disclosure provides interfering RNAs. The double stranded RNA molecule of the disclosure may be in the form of any type of RNA interference molecule known in the art. In some embodiments, the double stranded RNA molecule is a small interfering RNA (siRNA). In other embodiments, the double stranded RNA molecule is a short hairpin RNA (shRNA) molecule. In other embodiments, the double stranded RNA molecule is a Dicer substrate that is processed in a cell to produce an siRNA. In other embodiments the double stranded RNA molecule is part of a microRNA precursor molecule.

[0493] In some embodiments, the shRNA is a length to be suitable as a Dicer substrate, which can be processed to produce a RISC active siRNA molecule. See, e.g., Rossi et al., US2005/0244858.

[0494] A Dicer substrate double stranded RNA (*e.g.* a shRNA) can be of a length sufficient that it is processed by Dicer to produce an active siRNA, and may further include one or more of the following properties: (i) the Dicer substrate shRNA can be asymmetric, for example, having a 3' overhang on the anti-sense strand, (ii) the Dicer substrate shRNA can have a modified 3' end on the sense strand to direct orientation of Dicer binding and processing of the dsRNA to an active siRNA, for example the incorporation of one or more DNA nucleotides, and (iii) the first and second strands of the Dicer substrate ds RNA can be from 21-30 bp in length..

[0495] In some embodiments, the interfering RNAs comprise a sequence complementary to a sequence of a B2M mRNA. In some embodiments, the interfering RNA is capable of inducing RNAi-mediated degradation of the B2M mRNA. In some embodiments, the B2M mRNA sequence comprises a coding sequence. In some embodiments, the B2M mRNA sequence comprises an untranslated region.

[0496] In some embodiments, the interfering RNAs comprise a sequence complementary to a sequence of an HLA-A*02 mRNA. In some embodiments, the interfering RNA is capable of inducing RNAi-mediated degradation of the HLA-A*02 mRNA. In some embodiments, the HLA-A*02 mRNA sequence comprises a coding sequence. In some embodiments, the HLA-A*02 mRNA sequence comprises an untranslated region.

[0497] In some embodiments, the interfering RNA is a short hairpin RNA (shRNA). In some embodiments, the shRNA comprises a first sequence, having from 5' to 3' end a sequence complementary to the B2M mRNA; and a second sequence, having from 5' to 3' end a sequence complementary to the first sequence, wherein the first sequence and second sequence form the shRNA.

[0498] In some embodiments, the first sequence is 18, 19, 20, 21, or 22 nucleotides. In some embodiments, the first sequence is complementary to a sequence selected from the sequences set forth in Tables 13 and 14. In some embodiments, the first sequence has GC content greater than or equal to 25% and less than 60%. In some embodiments, the first sequence is complementary to a sequence selected from the sequences set forth in Tables 13 and 14. In some embodiments, the first sequence does not comprise four nucleotides of the same base or a run of seven C or G nucleotide bases. In some embodiments, the first sequence is 21 nucleotides.

[0499] Illustrative target B2M sequences complementary to the first sequence are shown in Table 13.

[0500] In some cases, the first sequence may have 100% identity, i.e. complete identity, homology, complementarity to the target nucleic acid sequence. In other cases, there may be one or more mismatches between the first sequence and the target nucleic acid sequence. For example, there may be 1, 2, 3, 4, 5, 6, or 7 mismatches between the sense region and the target nucleic acid sequence.

[0501] The sequences set forth in Table 13 are presented as DNA sequences. In all sequences set forth in Table 13, thymine (T) may be replaced by uracil (U) to arrive at the sequence of the target mRNA sequence.

Table 13. Illustrative target B2M sequences complementary to first sequence

SEQ ID NO	Sequence
1008	AGAGAATGGAAAGTCAAATTT
1009	ATGGACATGATCTTCTTTATA
1010	TGGACATGATCTTCTTTATAA
1011	GGACATGATCTTCTTTATAAT
1012	TGACAGGATTATTGGAAATTT
1013	TTGTGGTTAATCTGGTTTATT
1014	TGTGGTTAATCTGGTTTATTT

SEQ ID NO	Sequence
1015	GCAGAGAATGGAAAGTCAAAT
1016	CAGAGAATGGAAAGTCAAATT
1017	GAGAATGGAAAGTCAAATTTC
1018	GTCACAGCCCAAGATAGTTAA
1019	TGCTTATACACTTACACTTTA
1020	GCTTATACACTTACACTTTAT
1021	CTTATACACTTACACTTTATG

SEQ ID NO	Sequence
1022	ACATGGACATGATCTTCTTTA
1023	CATGGACATGATCTTCTTTAT
1024	ATCAACATCTTGGTCAGATTT
1025	CTTGCACTCAAAGCTTGTTAA
1026	AGTTAAGCGTGCATAAGTTAA
1027	GCATAAGTTAACTTCCAATTT
1028	TACATACTCTGCTTAGAATTT
1029	ACATACTCTGCTTAGAATTTG
1030	TTGACAGGATTATTGGAAATT
1031	GACAGGATTATTGGAAATTTG
1032	TAAGGCATGGTTGTGGTTAAT
1033	GTTGTGGTTAATCTGGTTTAT
1034	GTTCCACAAGTTAAATAAATC
1035	TCCAGCGTACTCCAAAGATTC
1036	TACTCCAAAGATTCAGGTTTA
1037	ACTCCAAAGATTCAGGTTTAC
1038	CACGTCATCCAGCAGAGAATG
1039	GGTTTCATCCATCCGACATTG
1040	CCGACATTGAAGTTGACTTAC
1041	TGAAGAATGGAGAGAGAATTG
1042	GAGCATTCAGACTTGTCTTTC
1043	TTCAGCAAGGACTGGTCTTTC
1044	GCAAGGACTGGTCTTTCTATC
1045	CGTGTGAACCATGTGACTTTG
1046	CTTTGTCACAGCCCAAGATAG
1047	TCACAGCCCAAGATAGTTAAG
1048	AGTGGGATCGAGACATGTAAG
1049	AGGTTTGAAGATGCCGCATTT
1050	GGTTTGAAGATGCCGCATTTG
1051	TTGATATGCTTATACACTTAC
1052	TGAGTGCTGTCTCCATGTTTG
1053	TGTCTCCATGTTTGATGTATC
1054	TCAACATCTTGGTCAGATTTG
1055	TCAGATTTGAACTCTTCAATC
1056	TTCAATCTCTTGCACTCAAAG
1057	TTGCACTCAAAGCTTGTTAAG
1058	ACTCAAAGCTTGTTAAGATAG
1059	AGATAGTTAAGCGTGCATAAG
1060	TGCATAAGTTAACTTCCAATT
1061	GTTAACTTCCAATTTACATAC
1062	ATTGACAGGATTATTGGAAAT
1063	GTAAGGCATGGTTGTGGTTAA
1064	GGTTGTGGTTAATCTGGTTTA
1065	TTCCTGAAGCTGACAGCATTC
1066	GCTATCCAGCGTACTCCAAAG
1067	CATCCAGCAGAGAATGGAAAG
1068	CAAATTTCCTGAATTGCTATG
1069	ATTGCTATGTGTCTGGGTTTC
1070	GAAGATGCCGCATTTGGATTG
1071	CAATTTACATACTCTGCTTAG
1072	TATCCAGCGTACTCCAAAGAT
1073	ATCCAGCGTACTCCAAAGATT
1074	CTCCAAAGATTCAGGTTTACT
1075	TGCTATGTGTCTGGGTTTCAT
1076	TTTCATCCATCCGACATTGAA
1077	GAAGTTGACTTACTGAAGAAT

SEQ ID NO	Sequence
1078	GAAGAATGGAGAGAGAATTGA
1079	AGAATGGAGAGAGAATTGAAA
1080	CAGCAAGGACTGGTCTTTCTA
1081	AGCAAGGACTGGTCTTTCTAT
1082	ACTTTGTCACAGCCCAAGATA
1083	TTGTCACAGCCCAAGATAGTT
1084	TGTCACAGCCCAAGATAGTTA
1085	CACAGCCCAAGATAGTTAAGT
1086	GCAGCATCATGGAGGTTTGAA
1087	CCGCATTTGGATTGGATGAAT
1088	TTGAGTGCTGTCTCCATGTTT
1089	AGTGCTGTCTCCATGTTTGAT
1090	CTGTCTCCATGTTTGATGTAT
1091	TCTAGGAGGGCTGGCAACTTA
1092	CAACATCTTGGTCAGATTTGA
1093	GTCAGATTTGAACTCTTCAAT
1094	TCTTGCACTCAAAGCTTGTTA
1095	TGCACTCAAAGCTTGTTAAGA
1096	GCACTCAAAGCTTGTTAAGAT
1097	CACTCAAAGCTTGTTAAGATA
1098	TCAAAGCTTGTTAAGATAGTT
1099	CAAAGCTTGTTAAGATAGTTA
1100	GATAGTTAAGCGTGCATAAGT
1101	ATAGTTAAGCGTGCATAAGTT
1102	TAGTTAAGCGTGCATAAGTTA
1103	TTAAGCGTGCATAAGTTAACT
1104	TAAGCGTGCATAAGTTAACTT
1105	ATTTACATACTCTGCTTAGAA
1106	TTTACATACTCTGCTTAGAAT
1107	ACAGGATTATTGGAAATTTGT
1108	CAGGATTATTGGAAATTTGTT
1109	AGGCATGGTTGTGGTTAATCT
1110	CAGCAGAGAATGGAAAGTCAA
1111	TCCGACATTGAAGTTGACTTA
1112	CTGGTCTTTCTATCTCTTGTA
1113	CCGTGTGAACCATGTGACTTT
1114	CCCAAGATAGTTAAGTGGGAT
1115	GGTTGCTCCACAGGTAGCTCT
1116	GCTCCACAGGTAGCTCTAGGA
1117	GGGAGCAGAGAATTCTCTTAT
1118	GGAGCAGAGAATTCTCTTATC
1119	GAGCAGAGAATTCTCTTATCC
1120	GAGAATTCTCTTATCCAACAT
1121	GAATTCTCTTATCCAACATCA
1122	AAGTGGAGCATTCAGACTTGT
1123	AAGGACTGGTCTTTCTATCTC
1124	AAGCTTGTTAAGATAGTTAAG
1125	AAGCGTGCATAAGTTAACTTC
1126	AAGATGCCGCATTTGGATTGG
1127	AAGAATGGAGAGAGAATTGAA
1128	AACATCAACATCTTGGTCAGA
1129	AAGGCATGGTTGTGGTTAATC
1130	AAGCAGCATCATGGAGGTTTG
1131	AAGATGAGTATGCCTGCCGTG
1132	AAGTTGACTTACTGAAGAATG
1133	AAGATAGTTAAGCGTGCATAA

SEQ ID NO	Sequence
1134	AACTTCCAATTTACATACTCT
1135	AACATCTTGGTCAGATTTGAA
1136	AACTCTTCAATCTCTTGCACT
1137	AATTTCCTGAATTGCTATGTG
1138	AATGGAAAGTCAAATTTCCTG
1139	AACCATGTGACTTTGTCACAG

SEQ ID NO	Sequence
1140	AATTGACAGGATTATTGGAAA
1141	AATTCTCTTATCCAACATCAA
1142	AAAGTGGAGCATTCAGACTTG
1143	AAAGTCAAATTTCCTGAATTG
1144	GTTGCTCCACAGGTAGCTCTA
1145	AATTTACATACTCTGCTTAGA

[0502] An exemplary sequence encoding a B2M shRNA comprises a sequence of GCACTCAAAGCTTGTTAAGATCGAAATCTTAACAAGCTTTGAGTGC (SEQ ID NO: 349), or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto. A further exemplary sequence encoding a B2M shRNA comprises a sequence of GTTAACTTCCAATTTACATACCGAAGTATGTAAATTGGAAGTTAAC (SEQ ID NO: 350), or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0503] In some embodiments, the interfering RNAs comprise a sequence complementary to a sequence of an HLA-A*02 mRNA. In some embodiments, the interfering RNA is capable of inducing RNAi-mediated degradation of the HLA-A*02 mRNA. In some embodiments, the HLA-A*02 mRNA sequence comprises a coding sequence. In some embodiments, the HLA-A*02 mRNA sequence comprises an untranslated region.

[0504] In some embodiments, the interfering RNA is a short hairpin RNA (shRNA). In some embodiments, the shRNA comprises a first sequence, having from 5' to 3' end a sequence complementary to the HLA-A*02 mRNA; and a second sequence, having from 5' to 3' end a sequence complementary to the first sequence, wherein the first sequence and second sequence form the shRNA

[0505] Illustrative target HLA sequences complementary to the first sequence are shown in Table 14.

Table 14. Illustrative target HLA sequences complementary to first sequence

SEQ ID NO	Sequence
1146	CTTCTTCCTTCCCTATTAAAA
1147	TCTCACTCCATGAGGTATTTC
1148	CTCTCACTCCATGAGGTATTT
1149	GAGGAGGAAGAGCTCAGATAG
1150	GCTCTCACTCCATGAGGTATT
1151	AGGATTACATCGCCCTGAAAG
1152	ACACCGTCCAGAGGATGTATG
1153	AGGGTCCTTCTTCCTGGATAC
1154	CCTACGACGGCAAGGATTACA
1155	TCACTCCATGAGGTATTTCTT
1156	CTACGACGGCAAGGATTACAT

SEQ ID NO	Sequence
1157	CTCACTCCATGAGGTATTTCT
1158	GGAGGAAGAGCTCAGATAGAA
1159	CACACCGTCCAGAGGATGTAT
1160	CACGCTGTCTCTGACCATGAA
1161	CTGGACAGGAGCAGAGATACA
1162	TGGAGGAGGAAGAGCTCAGAT
1163	GGCTCTCACTCCATGAGGTAT
1164	CATCTCTGTCTCAACTTCATG
1165	TACGACGGCAAGGATTACATC
1166	GGATTACATCGCCCTGAAAGA
1167	GATTACATCGCCCTGAAAGAG

SEQ ID NO	Sequence
1168	CTCAGACCACCAAGCACAAGT
1169	TCACACCGTCCAGAGGATGTA
1170	ACTCCATGAGGTATTTCTTCA
1171	CACTCCATGAGGTATTTCTTC
1172	CCATGAGGTATTTCTTCACAT
1173	ACTTCTTCCTTCCCTATTAAA
1174	GTGTCTCTCACAGCTTGTAAA
1175	CTGTGTTCGTGTAGGCATAAT
1176	TGTGTTCGTGTAGGCATAATG
1177	TAACTTCTTCCTTCCCTATTA
1178	TCTGGACAGGAGCAGAGATAC
1179	TTGCTGGCCTGGTTCTCTTTG
1180	TGTCTCTCACAGCTTGTAAAG
1181	ACTTGAAGAACCCTGACTTTG
1182	GAAGAACCCTGACTTTGTTTC
1183	TCTGTGTTCGTGTAGGCATAA
1184	CATGGTGCACTGAGCTGTAAC
1185	GTAACTTCTTCCTTCCCTATT
1186	CATGTGCAGCATGAGGGTTTG
1187	TTGTTCCTGCCCTTCCCTTTG
1188	ACCCAGTTCTCACTCCCATTG
1189	GGGTTTCCAGAGAAGCCAATC
1190	TTCTCCCTCTCCCAACCTATG
1191	GTCTCTCACAGCTTGTAAAGT
1192	TGTGTCTCTCACAGCTTGTAA
1193	GAGGAAGAGCTCAGATAGAAA
1194	TGAAGAACCCTGACTTTGTTT
1195	TTGAAGAACCCTGACTTTGTT
1196	GTGTTCGTGTAGGCATAATGT
1197	TGGTGCACTGAGCTGTAACTT
1198	CTCCCTCTCCCAACCTATGTA
1199	AGGAGGAAGAGCTCAGATAGA
1200	ACCTATGTAGGGTCCTTCTTC
1201	GGGTCCTTCTTCCTGGATACT
1202	GGTCCTTCTTCCTGGATACTC
1203	GTCCTTCTTCCTGGATACTCA
1204	AAGCCAATCAGTGTCGTCGCG
1205	AAGAGGACCTGCGCTCTTGGA
1206	AAGTGTGAGACAGCTGCCTTG
1207	AAGGCACCTGCATGTGTCTGT
1208	AATCATCTTTCCTGTTCCAGA
1209	AAAGGCACCTGCATGTGTCTG
1210	AAAGAGGACCTGCGCTCTTGG
1211	AAACGCATATGACTCACCACG
1212	GGAAGAGCTCAGATAGAAA
1213	GGGAGACACGGAAAGTGAA
1214	CACCTGCCATGTGCAGCATGA
1215	GGAGATCACACTGACCTGGCA
1216	GGATTACATCGCCCTGAAAG
1217	GCAGGAGGGTCCGGAGTATT
1218	GGACGGGGAGACACGGAAAG
1219	GAAAGTGAAGGCCCACTCA

SEQ ID NO	Sequence
1220	GATACCTGGAGAACGGGAAG
1221	GCTGTGGTGGTGCCTTCTGG
1222	GCTACTACAACCAGAGCGAG
1223	GTGGCTCCGCAGATACCTG
1224	GCCAATCAGTGTCGTCGCG
1225	GAGGACCTGCGCTCTTGGA
1226	GTGTGAGACAGCTGCCTTG
1227	GGCACCTGCATGTGTCTGT
1228	TCATCTTTCCTGTTCCAGA
1229	AGGCACCTGCATGTGTCTG
1230	AGAGGACCTGCGCTCTTGG
1231	ACGCATATGACTCACCACG

[0506] In some embodiments, the first sequence and second sequence are separated by a linker, sometimes referred to as a loop. In some embodiments, both the first sequence and the second sequence are encoded by one single-stranded RNA or DNA vector. In some embodiments, the loop is between the first and second sequences. In these embodiments, and the first sequence and the second sequence hybridize to form a duplex region. The first sequence and second sequence are joined by a linker sequence, forming a "hairpin" or "stem-loop" structure. The shRNA can have complementary first sequences and second sequences at opposing ends of a single stranded molecule, so that the molecule can form a duplex region with the complementary sequence portions, and the strands are linked at one end of the duplex region by a linker (*i.e.* loop sequence). The linker, or loop sequence, can be either a nucleotide or non-nucleotide linker. The linker can interact with the first sequence, and optionally, second sequence through covalent bonds or non-covalent interactions.

[0507] Any suitable nucleotide loop sequence is envisaged as within the scope of the disclosure. An shRNA of this disclosure may include a nucleotide, non-nucleotide, or mixed nucleotide/non-nucleotide linker that joins the first sequence of the shRNA to the second sequence of the shRNA. A nucleotide loop sequence can be ≥ 2 nucleotides in length, for example about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 nucleotides in length. Illustrative loop sequences are disclosed in Table 16.

[0508] In some embodiments, the shRNA further comprises a 5' flank sequence and a 3' flank sequence. In some embodiments, wherein the 5' flank sequence is joined to the 5' end of the first sequence, and wherein the 3' flank sequence is joined to the 3' end of the second sequence.

[0509] Without wishing to be bound by theory, it is thought that flanking shRNA stem loop sequence with 5' and 3' sequences similar to those found in microRNAs can target the shRNA for processing by the endogenous microRNA processing machinery, increasing the effectiveness of shRNA processing. Alternatively, or in addition, flanking sequences may increase shRNA compatibility with polymerase II or polymerase III promoters, leading to more effective regulation of shRNA expression.

[0510] In some embodiments, the 5' flank sequence is selected from the sequences set forth in Table 15. Illustrative flank sequence are shown in Table 15.

Table 15. Illustrative flank sequences

SEQ ID NO	**5' Flank Sequence**
1232	GG

1233	ACACCAUGUUGCCAGUCUCUAGG
1234	UGAUAGCAAUGUCAGCAGUGCCU
1235	UAUUGCUGUUGACAGUGAGCGAC
SEQ ID NO	**3' Flank Sequence**
1236	UGGCGUCUGGCCCAACCACAC
1237	GUAAGGUUGACCAUACUCUAC

[0511] In some embodiments, the first and second sequence are present on a single stranded polynucleotide, wherein the first sequence and second sequence are separated by 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 nucleotides, wherein the 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 nucleotides form a loop region in the shRNA. In some embodiments, the loop region comprises a sequence selected from the sequences set forth in Table 16.

Table 16. Illustrative loop region sequences

SEQ ID NO	**Loop Region Sequence**
1238	CGAA
1239	UUCAAGA
1240	AUAUUCA
1241	UGUGCUGUC
1242	CUCGAG
1243	CUUCCUGUCAGA
1244	CUUCCCUUUGUCAGA
1245	GUGUUAUUCUUG
1246	GUGUCUUAAUUG
1247	GUGUUAGUCUUG
1248	UCAAGAG
1249	GGACAUCCAGGG
1250	GUGAAGCCACAGAUG
1251	GAUUCUAAAA

[0512] shRNAs of the disclosure may be generated exogenously by chemical synthesis, by in vitro transcription, or by cleavage of longer double-stranded RNA with Dicer or another appropriate nuclease with similar activity. Chemically synthesized siRNAs, produced from protected ribonucleoside phosphoramidites using a conventional DNA/RNA synthesizer, may be obtained from commercial suppliers such as Millipore Sigma (Houston, Tex.), Ambion Inc. (Austin, Tex.). Invitrogen (Carlsbad, Calif.), or Dharmacon (Lafayette, Colo.). siRNAs can be purified by extraction with a solvent or resin, precipitation, electrophoresis, chromatography, or a combination thereof, for example. Alternatively, siRNAs may be used with little if any purification to avoid losses due to sample processing.

[0513] In some embodiments, shRNAs of the disclosure can be produced using an expression vector into which a nucleic acid encoding the double stranded RNA has been cloned, for example under control of a suitable promoter.

Pharmaceutical Compositions

[0514] The disclosure provides pharmaceutical compositions comprising immune cells comprising the first and second receptors of the disclosure and a pharmaceutically acceptable diluent, carrier or excipient.

[0515] Such compositions may comprise buffers such as neutral buffered saline, phosphate buffered saline and the like; carbohydrates such as glucose, mannose, sucrose or dextrans, mannitol; proteins; polypeptides or amino acids such as glycine; antioxidants; chelating agents such as EDTA or glutathione; and preservatives.

[0516] In some embodiments, the immune cell expresses both the first receptor and the second receptor. In some embodiments, at least about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, or about 95% of the immune cells express both the first receptor and the second receptor. In some embodiments, at least 90% of the immune cells express both the first receptor and the second receptor.

Treating Cancer

[0517] Provided herein are methods of killing a plurality of cancer cells, or treating cancer, in a subject, comprising administering to the subject a therapeutically effective amount of a composition comprising immune cells comprising the first and second receptors of the disclosure. The immune cells express both receptors in the same cell.

[0518] Cancer is a disease in which abnormal cells divide without control and spread to nearby tissue. In some embodiments, the cancer comprises a liquid tumor or a solid tumor. Exemplary liquid tumors include leukemias and lymphomas. Cancers can arise in virtually an organ in the body, including epithelial tissues. Any cancer wherein a plurality of the cancer cells express the first, activator, ligand and do not express the second, inhibitor ligand is envisaged as within the scope of the instant disclosure. For example, MSLN positive cancers that can be treated using the methods described herein include mesothelioma, ovarian cancer, cervical cancer, uterine cancer, gastric cancer, pancreatic cancer, lung cancers such as lung adenocarcinomas, colorectal cancer and cholangiocarcinoma.

[0519] In some embodiments, the plurality of cancer cells express the target antigen. In some embodiments, the plurality cancer cells of the subject express MSLN. MSNL positive cancers

include mesothelioma cancer, ovarian cancer, cervical cancer, colorectal cancer, esophageal cancer, head and neck cancer, kidney cancer, uterine cancer, gastric cancer, pancreatic cancer, lung cancer, lung adenocarcinomas, colorectal cancer, or cholangiocarcinoma, as well as other solid epithelial tumors. Further cancers that express MSLN include relapsed, refractory or metastatic gastric, esophageal, head and neck and kidney cancers. In some embodiments, the MSLN positive cancer comprises an epithelial tumor, for example a carcinoma.

[0520] Provided herein are methods of treating MSLN+ cancer in a subject having a MSLN+ tumor, the tumor having loss of heterozygosity at an MHC class I locus. In some embodiments, the methods comprise administering to the subject an effective amount of the immune cells or pharmaceutical compositions described herein. In some embodiments, the methods comprise (a) determining HLA-A, HLA-B, or HLA-C genotype or expression of normal cells and a plurality of cancer cells of the subject; (b) determining the expression of MSLN in a plurality of cancer cells of the subject; and (c) administering to the subject an effective amount of the immune cells or pharmaceutical compositions of the disclosure if the normal cells express an HLA-A, HLA-B or HLA-C non-target antigen and the plurality of cancer cells do not express the HLA-A, HLA-B or HLA-C non-target antigen, and the plurality of cancer cells are also MSLN-positive. In some embodiments, for example those embodiments where the cancer is known to be MSLN+, the methods comprise (a) determining HLA-A, HLA-B or HLA-C genotype or expression of normal cells and a plurality of cancer cells of the subject; and (b) administering to the subject an effective amount of the immune cells or pharmaceutical compositions of the disclosure if the normal cells express an HLA-A, HLA-B or HLA-C non-target antigen and the plurality of cancer cells do not express the non-target antigen. In some embodiments, the non-target antigen comprises HLA-A*02, HLA-A*01, HLA-A*03, HLA-A*11, HLA-B*07 or HLA-C*07.

[0521] In some embodiments, a plurality of cancer cells do not express a polymorphic allele of ICAM1, COMT or CXCL16. For example, the cancer cells have lost an allele of CAM1, COMT or CXCL16 through loss of heterozygosity at that locus.

[0522] In some embodiments, the plurality of cancer cells do not express, or have lower expression than normal cells, of LRRN4 or UPK3B.

[0523] The disclosure provides methods of treating a cancer in a subject comprising: (a) determining the genotype of normal cells and a plurality of cancer cells of the subject at a polymorphic locus selected from the group consisting of a polymorphic locus of ICAM1, a polymorphic locus of COMT and a polymorphic locus of CXCL16; (b) determining the

expression of MSLN in a plurality of cancer cells; and (c) administering a plurality of immune cells to the subject if the normal cells are heterozygous for the polymorphic locus and the plurality of cancer cells are hemizygous for the polymorphic locus, and the plurality of cancer cells are MSLN positive, wherein the plurality of immune cells comprise: (i) a first receptor, optionally a chimeric antigen receptor (CAR) or T cell receptor (TCR), comprising an extracellular ligand binding domain specific to MSLN, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and (ii) a second receptor, optionally an inhibitory chimeric antigen receptor, comprising an extracellular ligand binding specific to a non-target antigen selected from ICAM1, COMT, and CXCL16, or an antigen peptide thereof in a complex with an a major histocompatibility complex class I (MHC-I), wherein the non-target antigen comprises a polymorphism.

[0524] Methods of genotyping cancer cells and normal cells from a subject for the presence or absence of SNPs will be readily apparent to persons of ordinary skill in the art. SNP genotyping methods include, *inter alia*, PCR based methods such as dual-probe TaqMan assays, array based hybridization methods and sequencing.

[0525] Methods of measuring the expression of the target antigen in cancer or normal cells from a subject will be readily apparent to persons of ordinary skill in the art. These include, *inter alia*, methods of measuring RNA expression such as RNA sequencing and reverse transcription polymerase chain reaction (RT-PCR), as well as methods of measuring protein expression such as immunohistochemistry based methods. Methods of measuring loss of heterozygosity in a plurality of cancer cells, include, inter alia, high throughput sequencing of genomic DNA extracted from cancer cells using methods known in the art.

[0526] The disclosure provides methods of treating a cancer in a subject comprising measuring the expression level of the non-target antigen in a plurality of cancer cells, and treating the subject when the expression level of the non-target antigen in the plurality of cancer cells is less than the expression level of the non-target antigen in the plurality of cancer cells is less than the expression level of the non-target antigen a plurality of healthy cells. In some embodiments, the non-target antigen comprises LRRN4 or UPKB3, or a peptide antigen of LRRN4 or UPKB3. In some embodiments, the methods comprise determining the expression of MSLN in a plurality of cancer cells; and administering a plurality of immune cells to the subject if the plurality of cancer cells have low or no expression of the non-target antigen, and the plurality of cancer cells are MSLN positive. Methods of measuring the expression of the target antigen in cancer or cells from a subject will be readily apparent to persons of ordinary skill in the art. These include, *inter alia*,

methods of measuring RNA expression such as RNA sequencing and reverse transcription polymerase chain reaction (RT-PCR), as well as methods of measuring protein expression such as immunohistochemistry based methods.

[0527] In some embodiments, the immune cells are T cells.

[0528] In some embodiments, the immune cells are allogeneic or autologous.

[0529] In some embodiments, the second receptor increases the specificity of the immune cells for the MSLN positive cancer cells compared to immune cells that express the first receptor but do not express the second receptor. In some embodiments, the immune cells have reduced side effects compared to immune cells that express the first receptor but do not express the second receptor.

[0530] Administration of the immune cells or pharmaceutical compositions described herein can arrest the growth of a tumor in the subject. For example, the immune cells or pharmaceutical compositions can kill tumor cells, so that the tumor stops growing, or is reduced in size. In some cases, immune cells or pharmaceutical compositions can prevent formation of additional tumors, or reduce the total number of tumors in the subject.

[0531] Administration of the immune cells or pharmaceutical compositions described herein can result in selective killing of a cancer cell but not a wild-type cell in the subject. In some embodiments, about 60% of the cells killed are cancer cells, about 65% of the cells killed are cancer cells, about 70% of the cells killed are cancer cells, about 75% of the cells killed are cancer cells, about 80% of the cells killed are cancer cells, about 85% of the cells killed are cancer cells, about 90% of the cells killed are cancer cells, about 95% of the cells killed are cancer cells, or about 100% of the cells killed are cancer cells.

[0532] Administration of the immune cells or pharmaceutical compositions described herein can result in the killing of about 40%, about 50%, about 60%, about 70%, about 80%, about 90% or all of the cancer cells of the subject.

[0533] Administration of the immune cells or pharmaceutical compositions described herein can result in fewer side effects for the subject than administration of an otherwise equivalent immune cell comprising the first activator receptor but no second inhibitory receptor. For example, administering the immune cells or pharmaceutical compositions described herein can reduce dose limited toxicity relative to the MSLN CAR, or MSLN TCR administered without the second inhibitory receptor.

[0534] Treating cancer can result in a reduction in size of a tumor. A reduction in size of a tumor may also be referred to as “tumor regression”. Preferably, after treatment, tumor size is reduced by 5% or greater relative to its size prior to treatment; more preferably, tumor size is

reduced by 10% or greater; more preferably, reduced by 20% or greater; more preferably, reduced by 30% or greater; more preferably, reduced by 40% or greater; even more preferably, reduced by 50% or greater; and most preferably, reduced by greater than 75% or greater. Size of a tumor may be measured by any reproducible means of measurement. The size of a tumor may be measured as a diameter of the tumor.

[0535] Treating cancer can result in a reduction in tumor volume. Preferably, after treatment, tumor volume is reduced by 5% or greater relative to its size prior to treatment; more preferably, tumor volume is reduced by 10% or greater; more preferably, reduced by 20% or greater; more preferably, reduced by 30% or greater; more preferably, reduced by 40% or greater; even more preferably, reduced by 50% or greater; and most preferably, reduced by greater than 75% or greater. Tumor volume may be measured by any reproducible means of measurement.

[0536] Administration of the immune cells or pharmaceutical compositions described herein can reduce the size of a tumor in the subject. In some embodiments, the size of the tumor is reduced by about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%, relative to the size of the tumor before administration of the immune cells or pharmaceutical compositions. In some embodiments, the tumor is eliminated.

[0537] Treating cancer results in a decrease in number of tumors. Preferably, after treatment, tumor number is reduced by 5% or greater relative to number prior to treatment; more preferably, tumor number is reduced by 10% or greater; more preferably, reduced by 20% or greater; more preferably, reduced by 30% or greater; more preferably, reduced by 40% or greater; even more preferably, reduced by 50% or greater; and most preferably, reduced by greater than 75%. Number of tumors may be measured by any reproducible means of measurement. The number of tumors may be measured by counting tumors visible to the naked eye or at a specified magnification. Preferably, the specified magnification is 2x, 3x, 4x, 5x, 10x, or 50x.

[0538] Treating cancer can result in a decrease in number of metastatic lesions in other tissues or organs distant from the primary tumor site. Preferably, after treatment, the number of metastatic lesions is reduced by 5% or greater relative to number prior to treatment; more preferably, the number of metastatic lesions is reduced by 10% or greater; more preferably, reduced by 20% or greater; more preferably, reduced by 30% or greater; more preferably, reduced by 40% or greater; even more preferably, reduced by 50% or greater; and most

preferably, reduced by greater than 75%. The number of metastatic lesions may be measured by any reproducible means of measurement. The number of metastatic lesions may be measured by counting metastatic lesions visible to the naked eye or at a specified magnification. Preferably, the specified magnification is 2x, 3x, 4x, 5x, 10x, or 50x.

[0539] Treating cancer can result in an increase in average survival time of a population of treated subjects in comparison to a population receiving carrier alone. Preferably, the average survival time is increased by more than 30 days; more preferably, by more than 60 days; more preferably, by more than 90 days; and most preferably, by more than 120 days. An increase in average survival time of a population may be measured by any reproducible means. An increase in average survival time of a population may be measured, for example, by calculating for a population the average length of survival following initiation of treatment with an active compound. An increase in average survival time of a population may also be measured, for example, by calculating for a population the average length of survival following completion of a first round of treatment with an active compound.

[0540] Treating cancer can result in an increase in average survival time of a population of treated subjects in comparison to a population of untreated subjects. Preferably, the average survival time is increased by more than 30 days; more preferably, by more than 60 days; more preferably, by more than 90 days; and most preferably, by more than 120 days. An increase in average survival time of a population may be measured by any reproducible means. An increase in average survival time of a population may be measured, for example, by calculating for a population the average length of survival following initiation of treatment with an active compound. An increase in average survival time of a population may also be measured, for example, by calculating for a population the average length of survival following completion of a first round of treatment with an active compound.

[0541] Treating cancer can result in increase in average survival time of a population of treated subjects in comparison to a population receiving monotherapy with a drug that is not a compound of the present disclosure, or a pharmaceutically acceptable salt, prodrug, metabolite, analog or derivative thereof. Preferably, the average survival time is increased by more than 30 days; more preferably, by more than 60 days; more preferably, by more than 90 days; and most preferably, by more than 120 days. An increase in average survival time of a population may be measured by any reproducible means. An increase in average survival time of a population may be measured, for example, by calculating for a population the average length of survival following initiation of treatment with an active compound. An increase in average survival time of a population may also be measured, for example, by

calculating for a population the average length of survival following completion of a first round of treatment with an active compound.

[0542] Treating cancer can result in a decrease in the mortality rate of a population of treated subjects in comparison to a population receiving carrier alone. Treating cancer can result in a decrease in the mortality rate of a population of treated subjects in comparison to an untreated population. Treating cancer can result in a decrease in the mortality rate of a population of treated subjects in comparison to a population receiving monotherapy with a drug that is not a compound of the present disclosure, or a pharmaceutically acceptable salt, prodrug, metabolite, analog or derivative thereof. Preferably, the mortality rate is decreased by more than 2%; more preferably, by more than 5%; more preferably, by more than 10%; and most preferably, by more than 25%. A decrease in the mortality rate of a population of treated subjects may be measured by any reproducible means. A decrease in the mortality rate of a population may be measured, for example, by calculating for a population the average number of disease-related deaths per unit time following initiation of treatment with an active compound. A decrease in the mortality rate of a population may also be measured, for example, by calculating for a population the average number of disease-related deaths per unit time following completion of a first round of treatment with an active compound.

[0543] Treating cancer can result in a decrease in tumor growth rate. Preferably, after treatment, tumor growth rate is reduced by at least 5% relative to number prior to treatment; more preferably, tumor growth rate is reduced by at least 10%; more preferably, reduced by at least 20%; more preferably, reduced by at least 30%; more preferably, reduced by at least 40%; more preferably, reduced by at least 50%; even more preferably, reduced by at least 50%; and most preferably, reduced by at least 75%. Tumor growth rate may be measured by any reproducible means of measurement. Tumor growth rate can be measured according to a change in tumor diameter per unit time.

[0544] Treating cancer can result in a decrease in tumor regrowth. Preferably, after treatment, tumor regrowth is less than 5%; more preferably, tumor regrowth is less than 10%; more preferably, less than 20%; more preferably, less than 30%; more preferably, less than 40%; more preferably, less than 50%; even more preferably, less than 50%; and most preferably, less than 75%. Tumor regrowth may be measured by any reproducible means of measurement. Tumor regrowth is measured, for example, by measuring an increase in the diameter of a tumor after a prior tumor shrinkage that followed treatment. A decrease in tumor regrowth is indicated by failure of tumors to reoccur after treatment has stopped.

[0545] Treating or preventing a cancer can result in a reduction in the rate of cellular proliferation. Preferably, after treatment, the rate of cellular proliferation is reduced by at least 5%; more preferably, by at least 10%; more preferably, by at least 20%; more preferably, by at least 30%; more preferably, by at least 40%; more preferably, by at least 50%; even more preferably, by at least 50%; and most preferably, by at least 75%. The rate of cellular proliferation may be measured by any reproducible means of measurement. The rate of cellular proliferation is measured, for example, by measuring the number of dividing cells in a tissue sample per unit time.

[0546] Treating or preventing cancer can result in a reduction in the proportion of proliferating cells. Preferably, after treatment, the proportion of proliferating cells is reduced by at least 5%; more preferably, by at least 10%; more preferably, by at least 20%; more preferably, by at least 30%; more preferably, by at least 40%; more preferably, by at least 50%; even more preferably, by at least 50%; and most preferably, by at least 75%. The proportion of proliferating cells may be measured by any reproducible means of measurement. Preferably, the proportion of proliferating cells is measured, for example, by quantifying the number of dividing cells relative to the number of nondividing cells in a tissue sample. The proportion of proliferating cells can be equivalent to the mitotic index.

[0547] Treating or preventing cancer can result in a decrease in size of an area or zone of cellular proliferation. Preferably, after treatment, size of an area or zone of cellular proliferation is reduced by at least 5% relative to its size prior to treatment; more preferably, reduced by at least 10%; more preferably, reduced by at least 20%; more preferably, reduced by at least 30%; more preferably, reduced by at least 40%; more preferably, reduced by at least 50%; even more preferably, reduced by at least 50%; and most preferably, reduced by at least 75%. Size of an area or zone of cellular proliferation may be measured by any reproducible means of measurement. The size of an area or zone of cellular proliferation may be measured as a diameter or width of an area or zone of cellular proliferation.

[0548] Treating or preventing cancer can result in a decrease in the number or proportion of cells having an abnormal appearance or morphology. Preferably, after treatment, the number of cells having an abnormal morphology is reduced by at least 5% relative to its size prior to treatment; more preferably, reduced by at least 10%; more preferably, reduced by at least 20%; more preferably, reduced by at least 30%; more preferably, reduced by at least 40%; more preferably, reduced by at least 50%; even more preferably, reduced by at least 50%; and most preferably, reduced by at least 75%. An abnormal cellular appearance or morphology may be measured by any reproducible means of measurement. An abnormal cellular

morphology can be measured by microscopy, *e.g.*, using an inverted tissue culture microscope. An abnormal cellular morphology can take the form of nuclear pleiomorphism.

Dosage and Administration

[0549] The immune cells and of the present disclosure may be administered in a number of ways depending upon whether local or systemic treatment is desired.

[0550] In general, administration may be parenteral.

[0551] Methods for administration of cells for adoptive cell therapy are known and may be used in connection with the provided methods and compositions. For example, adoptive T cell therapy methods are described, e.g., in US Patent Application Publication No. 2003/0170238 to Gruenberg et al and U.S. Pat. No. 4,690,915 to Rosenberg.

[0552] The compositions of the disclosure are suitable for parenteral administration. As used herein, "parenteral administration" of a pharmaceutical composition includes any route of administration characterized by physical breaching of a tissue of a subject and administration of the pharmaceutical composition through the breach in the tissue, thus generally resulting in the direct administration into the blood stream, into muscle, or into an internal organ. Parenteral administration thus includes, but is not limited to, administration of a pharmaceutical composition by injection of the composition, by application of the composition through a surgical incision, by application of the composition through a tissue-penetrating non-surgical wound, and the like. In particular, parenteral administration is contemplated to include, but is not limited to, subcutaneous, intraperitoneal, intramuscular, intrasternal, intravenous, intraarterial, intrathecal, intraventricular, intraurethral, intracranial, intratumoral, intrasynovial injection or infusions; and kidney dialytic infusion techniques. In some embodiments, parenteral administration of the compositions of the present disclosure comprises intravenous or intraarterial administration.

[0553] The disclosure provides pharmaceutical compositions comprising a plurality of immune cells of the disclosure, and a pharmaceutically acceptable carrier, diluent or excipient.

[0554] Formulations of a pharmaceutical composition suitable for parenteral administration typically generally comprise of immune cells combined with a pharmaceutically acceptable carrier, such as sterile water or sterile isotonic saline. Such formulations may be prepared, packaged, or sold in a form suitable for bolus administration or for continuous administration. Injectable formulations may be prepared, packaged, or sold in unit dosage form, such as in ampoules or in multi-dose containers containing a preservative. Formulations for parenteral

administration include, but are not limited to, suspensions, solutions, emulsions in oily or aqueous vehicles, pastes, and the like. Such formulations may further comprise one or more additional ingredients including, but not limited to, suspending, stabilizing, or dispersing agents. Parenteral formulations also include aqueous solutions which may contain excipients such as salts, carbohydrates and buffering agents. Exemplary parenteral administration forms include solutions or suspensions in sterile aqueous solutions, for example, aqueous propylene glycol or dextrose solutions. Such dosage forms can be suitably buffered, if desired.. Formulations for parenteral administration may be formulated to be immediate and/or modified release. Modified release formulations include delayed-, sustained-, pulsed-, controlled-, targeted and programmed release.

[0555] In some embodiments, the formulated composition comprising the immune cells is suitable for administration via injection. In some embodiments, the formulated composition comprising the immune cells is suitable for administration via infusion.

[0556] The pharmaceutical compositions of the present disclosure, which may conveniently be presented in unit dosage form, may be prepared according to conventional techniques well known in the pharmaceutical industry. Such techniques include the step of bringing into association the immune cells with the pharmaceutical carrier(s) or excipient(s), such as liquid carriers.

[0557] Aqueous suspensions may further contain substances that increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol and/or dextran. The suspension may also contain stabilizers.

[0558] The compositions of the present disclosure may additionally contain other adjunct components conventionally found in pharmaceutical compositions. Thus, for example, the compositions may contain additional, compatible, pharmaceutically-active materials such as, for example, antipruritics, astringents, local anesthetics or anti-inflammatory agents, or may contain additional materials useful in physically formulating various dosage forms of the compositions of the present disclosure, such as dyes, preservatives, antioxidants, opacifiers, thickening agents and stabilizers. However, such materials, when added, should not unduly interfere with the biological activities of the immune cells of the compositions of the present disclosure.

[0559] The formulation or composition may also contain more than one active ingredient useful for the particular indication, disease, or condition being treated with the immune cells, where the respective activities do not adversely affect one another. Such active ingredients are suitably present in combination in amounts that are effective for the purpose intended.

Thus, in some embodiments, the pharmaceutical composition further includes other pharmaceutically active agents or drugs, such as chemotherapeutic agents.

[0560] The pharmaceutical composition in some aspects can employ time-released, delayed release, and sustained release delivery systems such that the delivery of the composition occurs prior to, and with sufficient time to cause, sensitization of the site to be treated. Many types of release delivery systems are available and known. Such systems can avoid repeated administrations of the composition, thereby increasing convenience to the subject and the physician.

[0561] Administration can be effected in one dose, continuously or intermittently throughout the course of treatment. Single or multiple administrations can be carried out with the dose level and pattern being selected by the treating physician.

[0562] The pharmaceutical composition in some embodiments contains the immune cells in amounts effective to treat or prevent a cancer, such as a therapeutically effective or prophylactically effective amount. Therapeutic or prophylactic efficacy in some embodiments is monitored by periodic assessment of treated subjects. For repeated administrations over days, weeks or months, depending on the condition, the treatment can be repeated until a desired suppression of cancer signs or symptoms occurs. However, other dosage regimens may be useful and can be determined. The desired dosage can be delivered by a single bolus administration or infusion of the composition or by multiple bolus administrations or infusions of the composition.

[0563] The cells or population of cells can be administrated in one or more doses. In some embodiments, an effective amount of cells can be administrated as a single dose. In some embodiments, an effective amount of cells can be administrated as more than one doses over a period time. Timing of administration is within the judgment of a managing physician and depends on the clinical condition of the patient.

[0564] The cells or population of cells may be obtained from any source, such as a blood bank or a donor, or the patient themselves.

[0565] An effective amount means an amount which provides a therapeutic or prophylactic benefit. The dosage administered 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.

[0001] For purposes of the disclosure, an assay, which comprises, for example, comparing the extent to which target cells are lysed or one or more cytokines are secreted by immune cells expressing the receptors, upon administration of a given dose of such immune cells to a mammal, among a set of mammals of which is each given a different dose of the immune cells, can be used to determine a starting dose to be administered to a mammal.

[0002] In some embodiments, the cells are administered as part of a combination treatment, such as simultaneously with or sequentially with, in any order, another therapeutic intervention, such as an antibody or engineered cell or receptor or agent, such as a cytotoxic or therapeutic agent. The immune cells of the disclosure are in some embodiments are co-administered with one or more additional therapeutic agents or in connection with another therapeutic intervention, either simultaneously or sequentially in any order. In some contexts, the immune cells are co-administered with another therapy sufficiently close in time such that the immune cell populations enhance the effect of one or more additional therapeutic agents, or vice versa. In some embodiments, the immune cells are administered prior to the one or more additional therapeutic agents. In some embodiments, the immune cells are administered after to the one or more additional therapeutic agents.

[0566] In embodiments, a lymphodepleting chemotherapy is administered to the subject prior to, concurrently with, or after administration (*e.g.*, infusion) of adoptive immune cells. In an example, the lymphodepleting chemotherapy is administered to the subject prior to administration of the immune cells. For example, the lymphodepleting chemotherapy ends 1-4 days (*e.g.*, 1, 2, 3, or 4 days) prior to adoptive cell infusion. In embodiments, multiple doses of adoptive cells are administered, *e.g.*, as described herein. In embodiments, a lymphodepleting chemotherapy is administered to the subject prior to, concurrently with, or after administration (*e.g.*, infusion) of the immune cells described herein. Examples of lymphodepletion include, but may not be limited to, nonmyeloablative lymphodepleting chemotherapy, myeloablative lymphodepleting chemotherapy, total body irradiation, etc. Examples of lymphodepleting agents include, but are not limited to, antithymocyte globulin, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD52 antibodies, anti-CD2 antibodies, TCRαβ blockers, anti-CD20 antibodies, anti-CD19 antibodies, Bortezomib, rituximab, anti-CD 154 antibodies, rapamycin, CD3 immunotoxin, fludarabine, cyclophosphamide, busulfan, melphalan, Mabthera, Tacrolimus, alefacept, alemtuzumab, OKT3, OKT4, OKT8, OKT11, fingolimod, anti-CD40 antibodies, anti-BR3 antibodies, Campath-1H, anti-CD25 antibodies, calcineurin inhibitors, mycophenolate, and steroids, which may be used alone or in combination. As a further example, a lymphodepletion

regimen can include, administration of alemtuzumab, cyclophosphamide, benduamustin, rituximab, pentostatin, and/or fludarabine. Lymphodepletion regimen can be administered in one or more cycles until the desired outcome of reduced circulating immune cells. In some embodiments, the lymphodepletion comprises administering an agent that specifically targets, and reduces or eliminates CD52+ cells in the subject, and the immune cells are modified to reduce or eliminate CD52 expression.

[0567] In some embodiments, an immune stimulating therapy is administered to the subject prior to, concurrently with, or after administration (*e.g.* infusion) of adoptive immune cells. In some embodiments, the immune stimulating therapy comprises homeostatic cytokines. In some embodiments, the immune stimulating therapy comprises immune-stimulatory molecules. In some embodiments, the immune stimulating therapy comprises IL-2, IL-7, IL-12, IL-15, IL-21, IL-9, or a functional fragment thereof. In some embodiments, the immune stimulating therapy comprises IL-2, IL-7, IL-12, IL-15, IL-21, IL-9, or combinations thereof. In some embodiments, the immune stimulating therapy comprises IL-2, or a functional fragment thereof.

[0568] Methods for adoptive cell therapy using autologous cells includes isolating immune cells from patient blood, performing a series of modifications on the isolated cells including transducing the cells with one or more vectors encoding the dual receptor system described herein, and administering the cells to a patient. Providing immune cells from a subject suffering from or at risk for cancer or a hematological malignancy requires isolation of immune cell from the patient's blood, and can be accomplished through methods known in the art, for example, by leukapheresis. During leukapheresis, blood from a subject is extracted and the peripheral blood mononuclear cells (PBMCs) are separated, and the remainder of the blood is returned to the subject's circulation. The PBMCs are stored either frozen or cryopreserved as a sample of immune cells and provided for further processing steps, such as, *e.g.* the modifications described herein.

[0569] In some embodiments, the method of treating a subject described herein comprises modifications to immune cells from the subject comprising a series of modifications comprising enrichment and/or depletion, activation, genetic modification, expansion, formulation, and cryopreservation.

[0570] The disclosure provides enrichment and/or depletion steps that can be, for example, washing and fractionating methods known in the art for preparation of subject PBMCs for downstream procedures, *e.g.* the modifications described herein. For example, without limitation, methods can include devices to remove gross red blood cells and platelet

contaminants, systems for size-based cell fractionation for the depletion of monocytes and the isolation of lymphocytes, and/or systems that allow the enrichment of specific subsets of T cells, such as, *e.g.* CD4+, CD8+, CD25+, or CD62L+ T cells. Following the enrichment steps, a target sub-population of immune cells will be isolated from the subject PMBCs for further processing. Those skilled in the art will appreciate that enrichment steps, as provided herein, may also encompass any newly discovered method, device, reagent or combination thereof.

[0571] The disclosure provides activation steps that can be any method known in the art to induce activation of immune cells, *e.g.* T cells, required for their ex vivo expansion. Immune cell activation can be achieved, for example, by culturing the subject immune cells in the presence of dendritic cells, culturing the subject immune cells in the presence of artificial antigen-presenting cells (AAPCs), or culturing the immune cells in the presence of irradiated K562-derived AAPCs. Other methods for activating subject immune cells can be, for example, culturing the immune cells in the presence of isolated activating factors and compositions, *e.g.* beads, surfaces, or particles functionalized with activating factors. Activating factors can include, for example, antibodies, *e.g.* anti-CD3 and/or anti-CD28 antibodies. Activating factors can also be, for example, cytokines, *e.g.* interleukin (IL)-2 or IL-21. Activating factors can also be costimulatory molecules, such as, for example, CD40, CD40L, CD70, CD80, CD83, CD86, CD137L, ICOSL, GITRL, and CD134L. Those skilled in the art will appreciate that activating factors, as provided herein, may also encompass any newly discovered activating factor, reagent, composition, or combination thereof that can activate immune cells.

[0572] The disclosure provides genetic modification steps for modifying the subject immune cells. In some embodiments, the genetic modification comprises transducing the immune cell with a vector comprising a shRNA described herein complementary to B2M or HLA-A. In some embodiments, the genetic modification comprises modifying the genome of the immune cells to induce mutations in B2M or HLA-A using CRISPR/Cas mediated genome engineering. In some embodiments, the method comprises transducing the immune cell with one or more vectors encoding the activator and inhibitory receptors, thereby producing immune cells expressing the activator and inhibitory receptors.

[0573] The disclosure provides expansion steps for the genetically modified subject immune cells. Genetically modified subject immune cells can be expanded in any immune cell expansion system known in the art to generate therapeutic doses of immune cells for administration. For example, bioreactor bags for use in a system comprising controller

pumps, and probes that allow for automatic feeding and waste removal can be used for immune cell expansion. Cell culture flasks with gas-permeable membranes at the base may be used for immune cell expansion. Any such system known in the art that enables expansion of immune cells for clinical use is encompassed by the expansion step provided herein. Immune cells are expanded in culture systems in media formulated specifically for expansion. Expansion can also be facilitated by culturing the immune cell of the disclosure in the presence of activation factors as described herein. Those skilled in the art will appreciate that expansion steps, as provided herein, may also encompass any newly discovered culture systems, media, or activating factors that can be used to expand immune cells.

[0574] The disclosure provides formulation and cryopreservation steps for the expanded genetically modified subject immune cells. Formulation steps provided include, for example, washing away excess components used in the preparation and expansion of immune cells of the methods of treatment described herein. Any pharmaceutically acceptable formulation medium or wash buffer compatible with immune cell known in the art may be used to wash, dilute/concentration immune cells, and prepare doses for administration. Formulation medium can be acceptable for administration of the immune cells, such as, for example crystalloid solutions for intravenous infusion. Cryopreservation can optionally be used to store immune cells long-term. Cryopreservation can be achieved using known methods in the art, including for example, storing cells in a cryopreservation medium containing cryopreservation components. Cryopreservation components can include, for example, dimethyl sulfoxide or glycerol. Immune cells stored in cryopreservation medium can be cryopreserved by reducing the storage temperature to -80°C to -196 °C.

[0575] In some embodiments, the method of treatment comprises determining the HLA germline type of the subject. In some embodiments, the HLA germline type is determined in bone marrow.

[0576] In some embodiments, the method of treatment comprises determining the level of expression of MSLN. In some embodiments, the level of expression of MSLN is determined in tumor tissue samples from the subject. In some embodiments, the expression level of MSLN is determined using next generation sequencing. In some embodiments, the expression level of MSLN is determined using RNA sequencing. In some embodiments, the level of MSLN is determined using immunohistochemistry.

[0577] In some embodiments, the method of treatment comprises administering a therapeutically effective dose of immune cells comprising an HLA-A*02 inhibitory receptor to a subject in need thereof, wherein the subject is determined to be HLA germline HLA-

A*02 heterozygous and have cancer cells with loss of HLA-A*02. In some embodiments, the method of treatment comprises administering a therapeutically effective dose of immune cells comprising an HLA-A*01 inhibitory receptor to a subject in need thereof, wherein the subject is determined to be HLA germline HLA-A*01 heterozygous and have cancer cells with loss of HLA-A*01. In some embodiments, the method of treatment comprises administering a therapeutically effective dose of immune cells comprising an HLA-A*03 to a subject in need thereof, wherein the subject is determined to be HLA germline HLA-A*03 heterozygous and have cancer cells with loss of HLA-A*03. In some embodiments, the method of treatment comprises administering a therapeutically effective dose of immune cells comprising an HLA-A*07 inhibitory receptor to a subject in need thereof, wherein the subject is determined to be HLA germline HLA-A*07 heterozygous and have cancer cells with loss of HLA-A*07. In some embodiments, the method of treatment comprises administering a therapeutically effective dose of immune cells comprising an HLA-C*07 inhibitory receptor to a subject in need thereof, wherein the subject is determined to be HLA germline HLA-C*07 heterozygous and have cancer cells with and loss of HLA-C*07. In some embodiments, the method of treatment comprises administering a therapeutically effective dose of immune cells comprising an HLA-B*07 inhibitory receptor in a subject in need thereof, wherein the subject is determined to be HLA germline HLA-B*07 heterozygous and have cancer cells with loss of HLA-B*07.

[0578] In various embodiments, the disclosure provides method of treatment of heterozygous HLA-A*02 patients with malignancies that express MSLN and have lost HLA-A*02 expression; and/or of treatment of heterozygous HLA-A*02 adult patients with recurrent unresectable or metastatic solid tumors that express MSLN and have lost HLA-A*02 expression.

[0579] In some embodiments, a therapeutically effective dose of the immune cells described herein are administered. In some embodiments, the immune cells of the disclosure are administered by intravenous injection. In some embodiments, the immune cells of the disclosure are administered by intraperitoneal injection. In some embodiments, a therapeutically effective dose comprises about 0.5×10^6 cells, about 1×10^6 cells, about 2×10^6 cells, about 3×10^6 cells, 4×10^6 cells, about 5×10^6 cells, about 6×10^6 cells, about 7×10^6 cells, about 8×10^6 cells, about 9×10^6 cells, about 1×10^7, about 2×10^7, about 3×10^7, about 4×10^7, about 5×10^7, about 6×10^7, about 7×10^7, about 8×10^7, about 9×10^7, about 1×10^8 cells, about 2×10^8 cells, about 3×10^8 cells, about 4×10^8 cells, about 5×10^8 cells, about 6×10^8 cells, about

7×10^8 cells, about 8×10^8 cells, about 9×10^8 cells, about 1×10^9 cells, about 2×10^9 cells, about 3×10^9 cells, about 3×10^9 cells, about 4×10^9 cells, about 5×10^9 cells, about 5×10^9 cells, about 6×10^9 cells, about 7×10^9 cells, about 8×10^9 cells, about 9×10^9 cells, about 1×10^{10} cells, about 2×10^{10} cells, about 3×10^{10} cells, about 4×10^{10} cells, about 5×10^{10} cells, about 6×10^{10} cells, about 7×10^{10} cells, about 8×10^{10} cells, or about 9×10^{10} cells.

[0580] In some embodiments, a therapeutically effective dose comprises about 0.5×10^6 cells to about 9×10^{10} cells, about 1×10^6 cells to about 5×10^{10} cells, about 2×10^6 cells to about 5×10^9 cells, about 3×10^6 cells to about 5×10^9 cells, about 4×10^6 cells to about 3×10^9 cells, about 5×10^6 cells to about 2×10^9 cells, about 6×10^6 cells to about 1×10^9 cells, 0.5×10^6 cells to about 6×10^9 cells, about 1×10^6 cells to about 5×10^9 cells, about 2×10^6 cells to about 5×10^9 cells, about 3×10^6 cells to about 4×10^9 cells, about 4×10^6 cells to about 3×10^9 cells, about 5×10^6 cells to about 2×10^9 cells, about 6×10^6 cells to about 1×10^9 cells, 0.5×10^6 cells to about 6×10^8 cells, about 1×10^6 cells to about 5×10^8 cells, about 2×10^6 cells to about 5×10^8 cells, about 3×10^6 cells to about 4×10^8 cells, about 4×10^6 cells to about 3×10^8 cells, about 5×10^6 cells to about 2×10^8 cells, about 6×10^6 cells to about 1×10^8 cells, about 7×10^6 cells to about 9×10^8 cells, about 8×10^6 cells to about 8×10^8 cells, about 9×10^6 cells to about 7×10^8 cells, about 1×10^7 cells to about 6×10^8 cells, about 2×10^7 cells to about 5×10^8 cells, about 7×10^6 cells to about 9×10^7 cells, about 8×10^6 cells to about 8×10^7 cells, about 9×10^6 cells to about 7×10^7 cells, about 1×10^7 cells to about 6×10^7 cells, or about 2×10^7 cells to about 5×10^7 cells.

[0581] In some embodiments, a therapeutically effective dose comprises about 0.5×10^5 cells to about 9×10^{10} cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^6 cells to about 1×10^{10} cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^6 cells to about 5×10^9 cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^6 cells to about 1×10^9 cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^6 cells to about 6×10^8 cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^6 cells to about 9×10^{10} cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^7 cells to about 1×10^{10} cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^7 cells to about 5×10^9 cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^7 cells to about 1×10^9 cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^7 cells to about 6×10^8 cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^8 cells to about 9×10^{10} cells. In some

embodiments, a therapeutically effective dose comprises about 0.5×10^8 cells to about 1×10^{10} cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^8 cells to about 5×10^9 cells. In some embodiments, a therapeutically effective dose comprises about 0.5×10^8 cells to about 1×10^9 cells. The term "about" as referred to in a therapeutically dose, can be, for example, $\pm 0.5\times10^6$ cells, $\pm 0.5\times10^7$ cells, or $\pm 0.5\times10^8$ cells.

Kits and Articles of Manufacture

[0582] The disclosure provides kits and articles of manufacture comprising the polynucleotides and vectors encoding the receptors described herein, and immune cells comprising the receptors described herein. In some embodiments, the kit comprises articles such as vials, syringes and instructions for use.

[0583] In some embodiments, the kit comprises a polynucleotide or vector comprising a sequence encoding one or more receptors of the disclosure.

[0584] In some embodiments, the kit comprises a plurality of immune cells comprising the first and second receptors as described herein. In some embodiments, the plurality of immune cells comprises a plurality of T cells.

[0585] In some embodiments, the kit further comprises instructions for use.

ENUMERATED EMBODIMENTS

[0586] The disclosure can be understood with reference to the following illustrative, enumerated embodiments:

[0587] 1. An immune cell responsive to loss of heterozygosity in a cancer cell, comprising:

a. a first receptor, optionally a chimeric antigen receptor (CAR) or T cell receptor (TCR), comprising an extracellular ligand binding domain specific to a target antigen selected from:

i. a cancer cell-specific antigen, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); or

ii. Mesothelin (MSLN), or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and

b. a second receptor, optionally an inhibitory chimeric antigen receptor, comprising an extracellular ligand binding domain specific to a non-target antigen selected from ICAM1, COMT, and CXCL16, or a peptide antigen thereof in a complex with a major

histocompatibility complex class I (MHC-I) , wherein the non-target antigen comprises a polymorphism.

[0588] 2. The immune cell of embodiment 1, wherein the non-target antigen is lost from the cancer cell through loss of heterozygosity (LOH).

[0589] 3. The immune cell of embodiment 1 or 2, wherein the non-target antigen is an ICAM1 antigen that shares at least 95% identity to SEQ ID NO: 27 and the polymorphism comprises a K or E at position 469 of SEQ ID NO: 27.

[0590] 4. The immune cell of embodiment 1 or 2, wherein the non-target antigen is a COMT antigen that shares at least 95% identity to SEQ ID NO: 28 and the polymorphism comprises a V or M at position 158 of SEQ ID NO: 28.

[0591] 5. The immune cell of embodiment 1 or 2, wherein the non-target antigen is a CXCL16 antigen that shares at least 95% identity to SEQ ID NO: 29 and the polymorphism is selected from the group consisting of:

a. an I or T at position 142 of SEQ ID NO: 29; and

b. an A or V at position 200 of SEQ ID NO: 29.

[0592] 6. The immune cell of any one of embodiments 1-5, wherein the non-target antigen is expressed in a non-target cell.

[0593] 7. The immune cell of any one of embodiments 1-6, wherein the non-target cell expresses both target antigen and the non-target antigen.

[0594] 8. An immune cell responsive to low or no expression of a protein in a cancer cell, comprising:

a. a first receptor, optionally a chimeric antigen receptor (CAR) or T cell receptor (TCR), comprising an extracellular ligand binding domain specific to a target antigen selected from:

i. a cancer cell-specific antigen, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); or

ii. MSLN, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and

b. a second receptor, optionally an inhibitory chimeric antigen receptor, comprising an extracellular ligand binding domain specific to a non-target antigen selected from LRRN4 and UPK3B, or peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I), wherein the non-target antigen is expressed at a lower level by the cancer cell than by a non-target cell.

[0595] 9. The immune cell of embodiment 8, wherein the non-target antigen is not expressed by the cancer cell.

[0596] 10. The immune cell of embodiment 9, wherein the non-target cell expresses both the target antigen and the non-target antigen.

[0597] 11. The immune cell of any one of embodiments 1-10, wherein the target antigen is a cancer cell-specific antigen.

[0598] 12. The immune cell of embodiment 11, wherein the target antigen is a peptide antigen of a cancer cell-specific antigen in a complex with a major histocompatibility complex class I (MHC-I).

[0599] 13. The immune cell of any one of embodiments 1-12, wherein the cancer cell is a mesothelioma cancer cell, an ovarian cancer cell, a cervical cancer cell, a colorectal cancer cell, an esophageal cancer cell, a head and neck cancer cell, a kidney cancer cell, an uterine cancer cell, a gastric cancer cell, a pancreatic cancer cell, a lung cancer cell, a colorectal cancer cell or a cholangiocarcinoma cell.

[0600] 14. The immune cell of any one of embodiments 1-13, wherein the cancer cell expresses MSLN.

[0601] 15. The immune cell of any one of embodiments 1-14, wherein the first receptor and the second receptor together specifically activate the immune cell in the presence of the cancer cell.

[0602] 16. The immune cell of embodiment 15, wherein the immune cell is a T cell.

[0603] 17. The immune cell of embodiment 16, wherein the T cell is a CD8+ CD4- T cell.

[0604] 18. The immune cell of any one of embodiments 1-17, wherein the MSLN comprises a sequence that shares at least 95% identity to SEQ ID NO: 1 or SEQ ID NO: 2.

[0605] 19. The immune cell of any one of embodiments 1-18, wherein the first receptor is a T cell receptor (TCR).

[0606] 20. The immune cell of any one of embodiments 1-18, wherein the first receptor is a chimeric antigen receptor (CAR).

[0607] 21. The immune cell of embodiment 19 or 20, wherein the extracellular ligand binding domain of the first receptor comprises an antibody fragment, a single chain Fv antibody fragment (scFv), a β chain variable domain (Vβ), or a TCR α chain variable domain and a TCR β chain variable domain.

[0608] 22. The immune cell of embodiment 19 or 20, wherein the extracellular ligand binding domain comprises an scFv.

[0609] 23. The immune cell of embodiment 22, wherein the scFv comprises a sequence selected from the group consisting of SEQ ID NOs: 3-6, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0610] 24. The immune cell of embodiment 22, wherein the scFv comprises or consists essentially of a sequence selected from the group consisting of SEQ ID NOs: 3-6.

[0611] 25. An immune cell responsive to loss of heterozygosity in a cancer cell, comprising:

a. a first receptor, optionally a chimeric antigen receptor (CAR) or T cell receptor (TCR), comprising an extracellular ligand binding domain specific to Mesothelin (MSLN), or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and

b. a second receptor, optionally an inhibitory chimeric antigen receptor, comprising an extracellular ligand binding domain specific to a non-target antigen, wherein the non-target antigen comprises HLA-A*02.

[0612] 26. The immune cell of embodiment 25, wherein the extracellular ligand binding domain of the first receptor comprises an antibody fragment, a single chain Fv antibody fragment (scFv), a β chain variable domain (Vβ), or a TCR α chain variable domain and a TCR β chain variable domain.

[0613] 27. The immune cell of embodiment 25, wherein the extracellular ligand binding domain of the first receptor comprises an scFv.

[0614] 28. The immune cell of embodiment 27, wherein the scFv comprises a sequence selected from the group consisting of SEQ ID NOs: 3-6, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

[0615] 28. The immune cell of embodiment 27, wherein the scFv comprises or consists essentially of a sequence selected from the group consisting of SEQ ID NOs: 3-6.

[0616] 29. The immune cell of any one of embodiments 25-28, wherein the extracellular ligand binding domain of the second receptor comprises an antibody fragment, a single chain Fv antibody fragment (scFv), a β chain variable domain (Vβ), or a TCR α chain variable domain and a TCR β chain variable domain.

[0617] 30. The immune cell of any one of embodiments 25-28, wherein the extracellular ligand binding domain of the second receptor comprises an scFv.

[0618] 31. The immune cell of embodiment 30, wherein the scFv comprises a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity to any one of SEQ ID NOs: 30-41.

[0619] 32. The immune cell of embodiment 30, wherein the scFv comprises or consists essentially of a sequence of any one of SEQ ID NOs: 30-41.

[0620] 33. The immune cell of any one of embodiments 25-32, wherein the extracellular ligand binding domain of the second receptor comprises CDRs selected from the group consisting of SEQ ID NOs: 42-53.

[0621] 34. The immune cell of any one of embodiments 25-33, wherein the second receptor comprises a LILRB1 intracellular domain or a functional variant thereof.

[0622] 35. The immune cell of embodiment 34, wherein the LILRB1 intracellular domain comprises a sequence at least 95% identical to SEQ ID NO: 65.

[0623] 36. The immune cell of any one of embodiments 25-35, wherein the second receptor comprises a LILRB1 transmembrane domain or a functional variant thereof.

[0624] 37. The immune cell of embodiment 36, wherein the LILRB1 transmembrane domain or a functional variant thereof comprises a sequence at least 95% identical to SEQ ID NO: 74.

[0625] 38. The immune cell of any one of embodiments 25-37, wherein the second receptor comprises a LILRB1 hinge domain or functional fragment or variant thereof.

[0626] 39. The immune cell of embodiment 38, wherein the LILRB1 hinge domain comprises a sequence at least 95% identical to SEQ ID NO: 73, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NOS: 81-84, or SEQ ID NOS: 90-91.

[0627] 40. The immune cell of any one of embodiments 25-39, wherein the second receptor comprises a LILRB1 intracellular domain and a LILRB1 transmembrane domain, or a functional variant thereof.

[0628] 41. The immune cell of embodiment 40, wherein the LILRB1 intracellular domain and LILRB1 transmembrane domain comprises SEQ ID NO: 69 or a sequence at least 95% identical to SEQ ID NO: 69.

[0629] 42. The immune cell of any one of embodiments 25-41, wherein the cancer cell is a mesothelioma cancer cell, an ovarian cancer cell, a cervical cancer cell, a colorectal cancer cell, an esophageal cancer cell, a head and neck cancer cell, a kidney cancer cell, an uterine cancer cell, a gastric cancer cell, a pancreatic cancer cell, a lung cancer cell, a colorectal cancer cell or a cholangiocarcinoma cell.

[0630] 43. wherein the cancer cell is a colorectal cancer cell.

[0631] 44. The immune cell of any one of embodiments 25-43, wherein the cancer expresses MSLN.

[0632] 45. The immune cell of any one of embodiments 25-44, wherein the cancer cell does not express HLA-A*02.

[0633] 46. The immune cell of any one of embodiments 25-45, wherein non-target cells express MSLN and HLA-A*02.

[0634] 47. The immune cell of any one of embodiments 25-46, wherein the first receptor and the second receptor together specifically activate the immune cell in the presence of the target cell.

[0635] 48. The immune cell of embodiment 47, wherein the immune cell is a T cell.

[0636] 49. The immune cell of embodiment 48, wherein the T cell is a CD8+ CD4- T cell.

[0637] 50. The immune cell of any one of embodiments 25-49, wherein the MSLN comprises a sequence that shares at least 95% identity to SEQ ID NO: 1.

[0638] 51. The immune cell of any one of embodiments 25-50, wherein the first receptor is a chimeric antigen receptor (CAR) or a TCR.

[0639] 52. A pharmaceutical composition, comprising a therapeutically effective amount of the immune cells of any one of embodiments 1-51.

[0640] 53. The pharmaceutical composition of embodiment 52, further comprising a pharmaceutically acceptable carrier, diluent or excipient.

[0641] 54. The pharmaceutical composition of embodiment 52 or 53, for use as a medicament in the treatment of cancer.

[0642] 55. A polynucleotide system, comprising one or more polynucleotides comprising polynucleotide sequences encoding:

a. a first receptor, optionally a chimeric antigen receptor (CAR) or T cell receptor (TCR), comprising an extracellular ligand binding domain specific to a target antigen selected from:

i. a cancer cell-specific antigen, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); or

ii. MSLN, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and

b. a second receptor, optionally an inhibitory chimeric antigen receptor, comprising an extracellular ligand binding domain specific to a non-target antigen selected from ICAM1, COMT and CXCL16, or an antigen peptide thereof in a complex with a major histocompatibility complex class I (MHC-I), wherein the non-target antigen comprises a polymorphism.

[0643] 56. A polynucleotide system, comprising one or more polynucleotides comprising polynucleotide sequences encoding:

a. a first receptor, optionally a chimeric antigen receptor (CAR) or T cell receptor (TCR), comprising an extracellular ligand binding domain specific to a target antigen selected from:

i. a cancer cell-specific antigen, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); or

ii. MSLN, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and

b. a second receptor, optionally an inhibitory chimeric antigen receptor, comprising an extracellular ligand binding domain specific to a non-target antigen selected from LRRN4 and UPK3B, or peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I), wherein the non-target antigen is expressed at a lower level by the cancer cell than by a non-target cell.

[0644] 57. A polynucleotide system, comprising one or more polynucleotides comprising polynucleotide sequences encoding:

a. a first receptor, optionally a chimeric antigen receptor (CAR) or T cell receptor (TCR), comprising an extracellular ligand binding domain specific to MSLN, or a peptide antigen thereof in a complex with a major histocompatibility complex class I (MHC-I); and

b. a second receptor, optionally an inhibitory chimeric antigen receptor, comprising an extracellular ligand binding domain specific to a non-target antigen, wherein the non-target antigen comprises HLA-A*02.

[0645] 58. A vector, comprising the one or more polynucleotides of any one of embodiments 55-57.

[0646] 59. A method of killing a plurality of cancer cell and/or treating cancer in a subject, comprising administering to the subject an effective amount of the immune cell of any one of embodiments 1-51 or the pharmaceutical composition of any one of embodiments 52-54.

[0647] 60. The method of embodiment 59, wherein a plurality of cancer cells express the target antigen.

[0648] 61. The method of embodiment 59 or 60, wherein a plurality of cancer cells do not express the non-target antigen.

[0649] 62. A method of making a plurality of immune cells, comprising:

a. providing a plurality of immune cells, and

b. transforming the plurality of immune cells with the polynucleotide system of any one of embodiments 55-57, or the vector of embodiment 58.

[0650] 63. A kit comprising the immune cell of any one of embodiments 1-51 or the pharmaceutical composition of any one of embodiments 52-54.

[0651] 62. The kit of embodiment 63, further comprising instructions for use.

EXAMPLES

[0652] The following Examples are intended for illustration only and do not limit the scope of the invention. Throughout the examples, the term "blocker antigen" is used to describe embodiments of a non-target antigen.

Example 1: Identification of Differentially Expressed Blockers

[0653] Candidate blocker targets were identified using a bioinformatics pipeline. In brief, publicly available expression databases, as described below, were searched for genes with loss of expression in tumor versus normal colon tissue. These genes were filtered for membrane proteins, and for expression in the TCGA-MESO dataset (mesothelioma). A diagram of this process is shown in FIG. 14. Candidate blocker targets are expressed in the mesothelium in healthy tissues, but are not expressed in Mesothelin (MSLN) positive cancers, which include ovarian cancers and pancreatic cancers, and approximately three-quarters of lung and colorectal cancers.

[0654] In brief, the total set of human proteins was filtered to identify predicted cell surface proteins. These proteins were examined for expression using The Cancer Genome Atlas (TCGA) database. Expression of candidate genes was examined in mesotheliomas, and genes whose expression was greater than 2 transcripts per kilobase million (TPM), or greater than 5 TPM in greater than 50% of the samples in the were included for further analysis. Expression of candidate genes in colorectal, ovarian, pancreatic and lung adenocarcinoma tumors was also evaluated, and genes whose expression in these tumor types was less than 2 TPM were included for further analysis. A summary of these genes is shown in FIG. 1. FIG. 2 shows RNA expression of MSLN in normal tissues (data from the Genotype-Tissue Expression, GTEx project, gtexportal.org/home). Mesothelin is expressed in normal adipose, fallopian tube, lung and salivary gland tissues. Thus, candidate blockers that can prevent MSLN CAR

or TCR T cells from targeting these tissues should also be expressed in health tissues that express MSLN.

[0655] MSLN expression in tumor versus normal tissues was examined (FIG. 3, TCGA database). MSLN expression in a variety of cell lines was also examined (FIG. 4, Cancer Cell Line Encyclopedia, or CCLE). The cell line rank order of expression shown in FIG. 4 correlated roughly with MSLN tumor rank expression seen in FIG. 3.

[0656] LRRN4 and UPK3B were identified as a candidate blocker target. FIG. 5 shows LRRN expression in normal tissues from the GTex portal (www.gtexportal.org/home/), while FIGS. 6 and 7 show LRRN4 expression in TCGA samples, and FIG. 8 shows LRRN4 expression in CCLE cell lines. As can be seen in FIGS. 5-7, LRRN4, like MSLN, is highly expressed in adipose and lung tissues. Moreover, LRRN4 has a large extracellular domain that contains multiple leucine rich repeat (LRR) and fibronectin type-III domains (FIG. 9).

Example 2: Identification of Candidate Blocker Targets Lost in Cancer Cells Due to Loss of Heterozygosity

[0657] Candidate blocker targets that are lost in MSLN positive cancers due to loss of heterozygosity were identified using a bioinformatics pipeline.

[0658] The following databases were used to identify candidate blocker targets: dbSNP, a database of single nucleotide polymorphisms that includes human single nucleotide variations and small-scale insertions and deletions along with publication, population frequency, molecular consequence, and genomic mapping information. Common variations were defined as having a minor allele frequency (MAF) of greater than or equal to 0.01 in at least one major population and with at least two unrelated individuals having the minor allele in NCBI. MAF of greater than or equal to 0.1 was used as the criterion for common variations. Uniprot (The Universal Protein Resource) was used as a resource for protein sequence and annotation data hosted by EMBL-EBI, SIB and PIR. GTEx (The Genotype-Tissue Expression) was used as a public resource for tissue-specific gene expression and regulation. It contains samples from 54 non-diseased tissue sites across nearly 1000 individuals. TCGA (The Cancer Genome Atlas) was used as resource for over 20,000 primary cancer and matched normal samples spanning 33 cancer types. CCLE (Cancer cell line Encyclopedia) contains information on 57 Colorectal Cancer (CRC) cell lines. Xena UCSC has renormalized TCGA and GTEx expression data (FPKM). The Broad GDAC Firehose Legacy data was used for copy number analysis.

[0659] The NCBI dbSNP database was downloaded and searched for common variants. Only variants in chromosomes identified based on a search in the Tumor Copy number portal with high loss of heterozygosity (greater than or equal to 0.5) were included, variants with a minor allele frequency of less than 0.1 were removed. VEP (Variant Effect Predictor) was used to filter for missense variants that are in protein coding regions. Genes without transmembrane domains were removed, as were genes that are not highly expressed in mesothelioma (TCGA-MESO expression level <5 TPM). Genes with an LOH frequency of less than or equal to 0.5 were removed. Genes expressed Golgi, ER, Nucleus, Cytoplasm, Mitochondrion, helical, Lysosome, and as propeptides were removed. LOH frequency was checked in the TCGA Copy Number Portal.

[0660] Genes that passed the filters were checked for other variants in Ensembl Genome Browser or VEP analysis output, as well as the locations of the variations in the gene. 11 genes passed all filters. A summary of this process is shown in FIG. 13.

[0661] Candidate blocker targets ICAM1, COMT and CXCL16 were identified. As summary of the frequency of LOH in various cancers for ICAM1, COMT and CXCL16 is shown in Table 17 below.

Table 17: Frequency of LOH

			LOH Freq	
		ICAM1	**COMT**	**CXCL16**
Ovarian (all)		0.33	0.64	0.74
Pancreatic (all)		0.15	0.25	0.48
Mesothelioma (all)		0.09	0.7	0.21
Lung (3/4)		0.46	0.3	0.58
Colorectal (3/4)		0.12	0.33	0.58
Blood cancers				0.1
AML				0.07
variant		K/E	V/M	I/T
MAF		0.36	0.37	0.46

Table 18: Summary of ICAM1, COMT and CXCL16 variants

Gene Name	Variant	Protein Position	Change	MAF
CXCL16	rs2277680, rs1050998	1. 200, 2. 142	1. A/V, 2. I/T	1. 0.4615, 2. 0.4633
COMT	rs4680	158	V/M	0.369
ICAM1	rs5498	469	K/E	0.359

Example 3: Identification of Blocker Ligand Binding Domains

[0662] Publicly available antibodies to candidate blocker antigens are sequenced, if CDR sequences are unknown. If no antibodies to candidate blocker targets are available, these antibodies are generated by immunization of mice, rats, or rabbits with purified protein (*e.g.*, ICAM1, CXCL16, and COMT1). Sera from immunized animals is used to screen for mAbs for binding to blocker targets. Antibodies to blocker targets are also generated using the huTARG™ system. Antibodies with the desired specificity are then isolated and sequenced to determine CDR sequences.

[0663] CDR sequence from antibodies to blocker targets are used to generate scFv using standard molecular biology techniques. Candidate scFv are fused to inhibitor receptor hinge or transmembrane domains to generate inhibitory receptors using standard molecular biology techniques. Candidate scFv are also fused to activator receptor hinge or transmembrane domains (e.g., CAR) to generate full length activator receptors to use as a positive control for scFv binding to target antigens. The ability of candidate scFv to work in the context of an inhibitory receptor is assayed in Jurkat cells using the NFAT-luciferase reporter assay.

Example 4: HLA-A*02 Blocker can Block MSLN Activator Mediated Activation of Jurkat Cells

[0664] Cell culture

[0665] Jurkat cells encoding an NFAT Luciferase reporter were obtained from BPS Bioscience. In culture, Jurkat cells were maintained in RPMI media supplemented with 10% FBS, 1% Pen/Strep and 0.4mg/mL G418/Geneticin. All other cell lines used in this study were obtained from ATCC, and maintained as suggested by ATCC.

[0666] Jurkat cell transfection

[0667] Jurkat cells were transiently transfected via 100uL format Neon electroporation system (Thermo Fisher Scientific) according to manufacturer's protocol using the following settings: 3 pulses, 1500V, 10 msec. Cotransfection was performed with 1-3ug of activator CAR or TCR construct and 1-3ug of blocker constructs or empty vector per 1e6 cells and recovered in RPMI media supplemented with 20% heat-inactivated FBS and 0.1% Pen/Strep.

[0668] Jurkat-NFAT-luciferase activation studies

[0669] Jurkat cells were resuspended in 15uL of RPMI supplemented with 10% heat-inactivated FBS and 0.1% Pen/Strep, added to the peptide-loaded beads and co-cultured for 6 hours. ONE-Step Luciferase Assay System (BPS Bioscience) was used to evaluate Jurkat luminescence. Assays were performed in technical duplicates.

[0670] Primary T cell transduction, expansion, and enrichment

[0671] Frozen PBMCs were thawed in 37°C water bath and cultured at 1e6 cells/mL in LymphoONE (Takara) with 1% human serum and activated using 1:100 of T cell TransAct (Miltenyi) supplemented with IL-15 (10ng/mL) and IL-21 (10ng/mL). After 24 hours, lentivirus was added to PBMCs at a MOI of 5. PBMCs were cultured for 2-3 additional days to allow cells to expand under TransAct stimulation. Post expansion, activator and blocker transduced primary T cells were enriched using anti-PE microbeads (Miltenyi) according to manufacturer's instructions. Briefly, primary T cells were incubated with CD19-Fc (R&D Systems) at 1:100 dilution for 30 minutes at 4°C in MACS buffer (0.5% BSA + 2mM EDTA in PBS). Cells were washed 3 times in MACS buffer and incubated in secondary antibody (1:200) for 30 minutes at 4°C in MACS buffer. Cells were then incubated in anti-PE microbeads and passed through the LS column (Miltenyi).

[0672] Primary T cell in *vitro* cytotoxicity studies

[0673] For cytotoxicity studies with pMHC targets, enriched primary T cells were incubated with SiHa or HeLa cells expressing renilla luciferase (Biosettia), and GFP or RFP. Live luciferase-expressing SiHa or HeLa cells were quantified using a Renilla Luciferase Reporter Assay System (Promega). Enriched primary T cells were incubated with SiHa or HeLa ("tumor" cells) or HLA-A*02 transduced SiHa or HeLa cells ("normal" cells). WT "tumor" SiHa or HeLa cells stably expressing GFP or RFP and renilla luciferase (Biosettia) or HLA-A*02 "normal" SiHa or HeLa cells stably expressing RFP and luciferase (Biosettia) were imaged together with unlabeled primary T cells using an IncuCyte live cell imager.

[0674] Activation of Jurkat effector cells expressing an MSLN CAR activator and a pMHC HLA-A*02 scFv LIR-1 based inhibitory receptor was assayed using the NFAT Luciferase assay.

[0675] Jurkat cells were transfected with activator:blocker DNA at a ratio of 1:4, and activation was assayed in a cell-free bead based assay (FIG. 10A). Beads were loaded with either activator antigen, or activator and blocker antigens, and the ratio of beads to Jurkat cells was varied. In the cell-free bead based assay, the pMHC HLA-A*02 scFv LIR-1 based inhibitory receptor was able to block activation of the Jurkat cells when cells were contacted with beads carrying the pMHC HLA-A*02 blocker and MSLN activator in *cis*. Presence of

the pMHC HLA-A*02 blocker on the beads was able to shift E_{MAX} of MSLN CAR by greater than or equal to 12X (FIG. 10A).

[0676] Activation Jurkat cells transfected with the same activator and blocker at a 1:4 DNA ratio were assayed for activation using the chronic myelogenous leukemia cell line K562. K562 expresses MSLN, the activator antigen. The response of Jurkat effector cells to K562 cells transduced with HLA-A*02 to express both activator and blocker antigens (MSLN+ HLA-A*02+) and untransduced K562 (MSLN+ HLA-A*02-) that expressed the activator but not the blocker antigen was assayed. As can be seen in FIG. 10B, expression of HLA-A*02+ by the K562 cells was able to shift the MSLN CAR E_{MAX} by greater than 5X.

[0677] The ability of the pMHC HLA-A*02 inhibitory receptor to block activation via the MSNL scFv CAR was also assayed using effector primary T cells and SiHa or HeLa target cells. SiHa and HeLa cells endogenously express MSLN, and were transduced to express the HLA-A*02 inhibitory receptor target. Activation of primary effector T cells was assayed by looking at fold induction of IFNγ. As shown in FIG. 11, the pMHC HLA-A*02 LIR-1 inhibitory receptor was able to block activation of primary T cells when the primary T cells were presented with SiHa or HeLa target cells expressing HLA-A*02 (greater than 10X and 5X inhibition, respectively).

[0678] The pMHC HLA-A*02 inhibitory receptor was also able to inhibit killing by T cells expressing both the MSLN scFv CAR and the pMHC HLA-A*02 LIR-1 inhibitory receptor, when the T cells were presented with SiHa cells that expressed MSLN but not HLA-A*02 (FIG. 12).

Example 5: HLA-A*02 Blocker Inhibits MSLN CAR Activators Directed at MSLN Using K562 and HeLa Target Cells

[0679] *Cell culture*

[0680] MSLN CAR activator and HLA-A02 LIR-1 inhibitory receptor were examined, using Jurkat effector cells and K562 target cells (FIG. 15A). The ability of MSLN CAR T cells expressing MSLN CAR (with two different MSLN ligand binding domains) to kill HeLa cells expressing the blocker target, HLA-A*02, was also assayed (FIGS. 15B-15C). The MSLN ligand represents surface antigens that can extend into the realm of 100,000 epitopes/cell. The ratio of A to B module expression was varied using different DNA concentrations in transient transfection assays. The activator and inhibitory receptor system is

flexible enough to accommodate low and high target densities, in principle allowing optimization for pMHC targets as well as non-pMHC surface antigens.

[0681] Jurkat cells encoding an NFAT luciferase reporter were obtained from BPS Bioscience. All other cell lines used in this study were obtained from ATCC. In culture, Jurkat cells were maintained in RPMI media supplemented with 10% FBS, 1% Pen/Strep and 0.4mg/mL G418/Geneticin. K562 and HeLa cells were maintained as suggested by ATCC.

[0682] *MSLN antigen binding domains*

[0683] MSLN-activating CAR scFv were derived from human M5 (LBD1) as described Beatty, et al. WO2015/090230A1 and humanized SS1 (LBD2) as described in BioLuminate, 2019 (BioLuminate, version 3.6, version 3.6 ed. Schrödinger, LLC, New York, NY) and US 6,809,184 B1.

[0684] *Jurkat cell transfection and activation*

[0685] Jurkat cells were transiently transfected via 100uL format Neon electroporation system (Thermo Fisher Scientific) according to manufacturer's protocol using the following settings: 3 pulses, 1500V, 10 msec. Co-transfection was performed with 1-3ug of activator construct and 1-3 ug of blocker constructs or empty vector per 1e6 cells and recovered in RPMI media supplemented with 20% heat-inactivated FBS and 0.1% Pen/Strep. To confirm blocker surface expression, Jurkat cells were stained 18-24 hours post-transfection with 10ug/mL streptavidin-PE-HLA-A*02-pMHC tetramer for 60 minutes at 4°C in PBS with 1% BSA and characterized by flow cytometry (BD FACS Canto II). Jurkat cell activation was evaluated using the NFAT-luciferase assay system as described in Example 4.

[0686] *Primary T cell transduction, expansion, and enrichment*

[0687] Leukopaks were purchased from AllCells®. Collection protocols and donor informed consent were approved by an Institutional Review Board (IRB), with strict oversight. HIPAA compliance and approved protocols were also followed. Frozen PBMCs were thawed and cultured as described in Example 4. Cells were simultaneously co-transduced at a MOI = 5 for each lentivirus, i.e. lentiviral vectors including activator or blocker receptor. PBMCs were cultured for 2-3 additional days to allow cells to expand under TransAct stimulation. Post expansion, activator and blocker transduced primary T cells were enriched for blocker-positive T cells by positive selection using anti-PE microbeads (Miltenyi) according to manufacturer's instructions. Briefly, primary T cells were incubated with 10ug/mL streptavidin-PE-HLA-A*02-pMHC tetramer for 60 minutes at 4°C in MACS buffer (0.5% BSA + 2mM EDTA in PBS). Cells were washed 3 times in MACS buffer and passed through

the LS column (Miltenyi) to separate blocker-positive cells (a mix of blocker-only and activator + blocker cells) from untransduced and activator-only cells.

[0688] *Primary T cell in vitro cytotoxicity studies*

[0689] For cytotoxicity studies with pMHC targets, enriched primary T cells were incubated with K562 or HeLa target cells expressing renilla luciferase (Biosettia). Target cells that were HLA-A*02 positive also expressed GFP and firefly luciferase (Biosettia), and target cells that were HLA-A*02 negative expressed RFP and firefly luciferase. Target cells were imaged together with unlabeled primary T cells using an IncuCyte live cell imager. Fluorescence intensity of live target cells over time was quantified using IncuCyte imaging software.

Example 6: Mouse SS1 MSLN Antigen Binding Domain Activator in 2nd and 3rd Generation CAR Architectures and HLA-A*02 Blocker

[0690] Originally, humanized M5 and SS1 scFv targeting MSLN were used with a third generation CAR architecture (CD28, 4-1BB and CD3 zeta). The effect of using a murine SS1 scFv antigen binding domain, and second generation CAR architecture (4-1BB and CD3zeta intracellular domains) was assayed.

[0691] HLA-A*02- donor T cells were transduced with MSLN third generation CAR activator (a CAR with CD28, 4-1BB and CD3 zeta intracellular domains) and an HLA-A*02 scFv LIR-1 blocker using a PA2.1 antigen binding domain. MSLN CAR activators with humanized M5, humanized SS1 and murine SS1 scFv were assayed (Table 1). HLA-A*02 blocker sequences are described in Table 5. T cells were transduced with activator and/or blocker constructs, cultured, and enriched as described in Examples 4 and 5. T cells were used on day 14 following transduction, and were cultured with MSLN + HeLa target cells at an effector: target ratio of 1:1. Cytotoxicity was assayed as described in Examples 4 and 5. FIG. 16 shows that inhibitor receptors were able to effectively block killing of HeLa cells by T cells expressing the MSLN third generation CAR when the HeLa cells also expressed HLA-A*02. Further, FIG. 16 shows that the murine SS1 generation 3 CAR (upper right plot, boxed) provides a better window than the humanized M5 and humanized SS1 CARs. Note, in FIG. 16, C-0883 is an HLA-A*02 CAR used as a positive control, additional sequences are described in Table 19.

[0692] The ability of T cells expressing the MSLN activator and HLA-A*02 LIR1 blocker to selectively kill MSLN+ HLA-A*02- Capan cells was also assayed (FIG. 17). T cells were transduced with activator and/or blocker receptor constructs, cultured, and enriched as

described in Examples 4 and 5. T cells were used on day 14 following transduction, and were cultured with Capan target cells at an effector: target ratio of 1:1. Cytotoxicity was assayed as described in Examples 4 and 5. FIG. 17 shows that inhibitor receptors were able to effectively block killing of Capan cells by T cells expressing the MSLN third generation CAR when the Capan cells also expressed HLA-A*02.

[0693] The murine SS1 MSLN1 scFv was also assayed in a generation 2 CAR (a CAR with a 4-1BB and CD3 zeta intracellular domain). FIG. 18 shows that killing of MSLN+ HLA-A*02+_HeLa cells, and HCT116 wild type cells (which natively express both MSLN and HLA-A*02) by T cells expressing the mSS1 2nd generation CAR was effectively blocked by HLA-A*02 scFv LIR-1 inhibitory receptor. As can be seen from FIG. 18, the 2nd generation mSS1 CAR was more effectively blocked by inhibitory receptors with a PA2.1 scFv antigen binding domain than by inhibitory receptors with a BB7.2 scFv antigen binding domain. The effect of short and long LIR-1 hinge sequences in the inhibitory receptor, and the arrangement of the VH and VL domains in the HLA-A*02 scFv, was also assayed.

[0694] Expression of the 2nd generation CAR with the murine SS1 scFv was also confirmed via FACS, and the results are shown in FIG. 19. The SS1 antigen binding domain was stained using a recombinant soluble MSLN ligand.

Table 19: Sequences of constructs

Name	Amino Acid Sequence	Nucleotide Sequence
PA2.1.14 (VL:VH) scFv LIR1 sHTICD	TEFTLTISSLQPDDFATYYCFQGSHVPRTFGQGTKV EVKGGGGSGGGGSGGGGSGGQVQLVQSGAEVKKPGS SVKVSCKASGYTFTSYHIHWVRQAPGQGLEWIGWIY PGNVNTEYNEKFKGKATITADESTNTAYMELSSLRS EDTAVYYCAREEITYAMDYWGQGTLVTVSSVVSGPS GGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHL GVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEEN LYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKH SRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEA AASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPA VPSIYATLAIH (SEQ ID NO: 85)	(SEQ ID NO: 1252)
PA2.1.14 (VL:VH) scFv LIR1 HTICD	DIQMTQSPSTLSASVGDRVTITCRSSQSIVHSNGNT YLEWYQQKPGKAPKLLIYKVSNRFSGVPARFSGSGS GTEFTLTISSLQPDDFATYYCFQGSHVPRTFGQGTK VEVKGGGGSGGGGSGGGGSGGQVQLVQSGAEVKKPG SSVKVSCKASGYTFTSYHIHWVRQAPGQGLEWIGWI YPGNVNTEYNEKFKGKATITADESTNTAYMELSSLR SEDTAVYYCAREEITYAMDYWGQGTLVTVSSYGSQS SKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSG PEDQPLTPTGSDPQSGLGRHLGVVIGILVAVILLLL LLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGP EPTDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVE MDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLS GEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLH	(SEQ ID NO: 1253)

	SLTLRREATEPPPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 86)	
MSLN_SsI CD8_HT 41BB CD3z	QVQLQQSGPELEKPGASVKISCKASGYSFTGYTMNW VKQSHGKSLEWIGLITPYNGASSYNQKFRGKATLTV DKSSSTAYMDLLSLTSEDSAVYFCARGGYDGRGFDY WGQGTTVTVSSGGGGSGGGGSGGGGSDIELTQSPAI MSASPGEKVTMTCSASSSVSYMHWYQQKSGTSPKRW IYDTSKLASGVPGRFSGSGSGNSYSLTISSVEAEDD ATYYCQQWSGYPLTFGAGTKLEITTTPAPRPPTPAP TIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIW APLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFM RPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMG GKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRR GKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 87)	(SEQ ID NO: 1254)
PA2.1.14 scFv LIR1 sHTICD	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYHIHW VRQAPGQGLEWIGWIYPGNVNTEYNEKFKGKATITA DESTNTAYMELSSLRSEDTAVYYCAREEITYAMDYW GQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPS TLSASVGDRVTITCRSSQSIVHSNGNTYLEWYQQKP GKAPKLLIYKVSNRFSGVPARFSGSGSGTEFTLTIS SLQPDDFATYYCFQGSHVPRTFGQGTKVEVKVVSGP SGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRH LGVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTS TQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVK HSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTE AAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSP AVPSIYATLAIH (SEQ ID NO: 88)	(SEQ ID NO: 1255)
PA2.1.14 scFv LIR1 HTICD	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYHIHW VRQAPGQGLEWIGWIYPGNVNTEYNEKFKGKATITA DESTNTAYMELSSLRSEDTAVYYCAREEITYAMDYW GQGTLVTVSSGGGGSGGGGSGGGGSGGDIQMTQSPS TLSASVGDRVTITCRSSQSIVHSNGNTYLEWYQQKP GKAPKLLIYKVSNRFSGVPARFSGSGSGTEFTLTIS SLQPDDFATYYCFQGSHVPRTFGQGTKVEVKYGSQS SKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSG PEDQPLTPTGSDPQSGLGRHLGVVIGILVAVILLLL LLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGP EPTDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVE MDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLS GEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLH SLTLRREATEPPPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 89)	(SEQ ID NO: 258)

Example 7: Assaying the Effect of the LIR-1 Hinge on Blocking Activity

[0695] The effects of different LIR-1 hinges on the ability of HLA-A*02 scFv LIR-1 inhibitory receptors to block killing by Jurkat cells expressing a KRAS TCR activator was assayed using the Jurkat NFat Luciferase assays described *supra*. A humanized PA2.1 scFv LIR-1 receptor and humanized BB7.2 scFv LIR-1 with a shorter LIR-1 hinge were assayed in Jurkat cells as previously described, and the results are shown in FIGS. 20A-20B. Jurkat cells

were transfected with a KRAS TCR activator receptor and/or HLA-A*02 scFv LIR-1 inhibitory receptor (humanized PA2.1 or humanized BB7.2) with a variety of LIR-1 derived hinges, methods as described *supra*, and co-cultured with T2 target cells that were either HLA-A11 positive, or HA-A11 and HLA-A*02 positive. Inhibitory receptors with both the shorter and longer hinge behaved similarly (FIG. 20A-B). An inhibitory receptor with a mouse PA2.1 scFv and slightly longer hinges was also assayed functioned similarly to shorter LIR-1 hinges in the T2-Jurkat assay (FIG. 21A-B). Hinge sequences are shown in black in FIG. 20B and FIG. 21B, with the gray SS representing a linker between the antigen binding domain and the hinge, and the gray VIGIL the start of the LIR-1 transmembrane domain. Hinge, transmembrane domain and intracellular domain of the inhibitory receptors were all derived from LIR-1. FIGS. 20A-20B and 21A-21B show that LIR-1 hinge length can be varied without negatively effecting the LIR-1 inhibitory receptor. Shorter hinges can provide an advantage when packaging nucleic acid sequences encoding LIR-1 inhibitory receptors in lentiviral vectors for delivery.

Example 8: Identification of new anti-MSLN Antibodies

[0696] Mesothelin (MSLN) is a classic tumor-associated antigen that is expressed in lung cancer and many other solid tumors. However, MSLN is also expressed in normal mesothelium that surrounds and lubricates the surfaces of key internal organs. This normal expression creates significant risk of serious inflammation for MSLN-directed therapeutics. This example describes a dual-receptor (Tmod) system which exploits common LOH at the HLA locus in cancer cells, allowing T cells to recognize the difference between tumor and normal tissue. T cells engineered with the MSLN CAR Tmod construct described in this example contain: (i) a MSLN-activated CAR; and, (ii) an inhibitory receptor gated by HLA-A*02. Without wishing to be bound by theory, the Tmod system robustly protects "normal" cells even in mixed-cell populations in vitro and in a xenograft model. The MSLN CAR can also be paired with other HLA class I blockers, supporting extension of the approach to patients beyond HLA-A*02 heterozygotes. The Tmod mechanism exemplified by the MSLN CAR Tmod construct may provide an alternative route to leverage solid-tumor antigens such as MSLN in safer, more effective ways than previously possible. Mesothelin (MSLN) was proposed as a cancer target in 1992 [1], yet there is still no viable therapy that utilizes MSLN. Not only is it expressed on most mesotheliomas but also large subsets of ovarian, cervical, uterine, gastric, pancreatic and lung adenocarcinomas [2]. In normal adults, MSLN is present only in mesothelium, a tissue that itself may be nonessential [2,3]. However, immunotherapy

targeting MSLN carries the risk of inflammatory attack on MSLN(+) mesothelial cells that surround important internal organs [4]. Several investigational therapeutics directed at MSLN have been tested; for example, immunotoxin-conjugates [5, 6], antibody-drug conjugates [7], bispecific antibodies [8], CAR-Ts [9], and a hybrid TCR-scFv [10]. All active systemically administered therapeutics so far have been toxic. Recently, an approach to deliver MSLN CAR-Ts via intrapleural infusion has been reported [11].

[0697] This example describes an exemplary method to treat MSLN(+) cancers that does not depend on local administration of therapeutics, but instead exploits LOH. This approach seeks to avoid systemic toxicity to normal tissues by pairing a MSLN-targeted CAR with a LIR-1-based inhibitory receptor that blocks effector function against normal cells that express the HLA-A*02 allele (**FIG. 22A-22B**). This dual-receptor construct is intended to treat genetically defined cancer patients who have LOH of the HLA-A*02 allele in their MSLN(+) tumor. The difference in HLA-A*02 expression in tumor vs. normal tissues caused by LOH creates an all-or-nothing input to the effector cells that is believed to confer high selectivity for tumor killing.

RESULTS

Isolation and characterization of potent, selective MSLN CARs

[0698] To identify potent, selective MSLN-directed ligand-binding domains (LBDs) that function in CARs, mammalian surface display libraries encoding either IgG antibodies (mAbs) or scFvs were screened (**FIGS. 23A-23B**). Soluble biotinylated MSLN labeled with fluorochrome were used as probe to enrich for cells in the library that stained for MSLN via FACS. As negative probe, a mixture of soluble CEA and EGFR was used to deplete cells encoding mAbs or scFvs with non-specific binding properties. After two rounds of enrichment for MSLN-binding, 62 individual LBDs were selected, converted to scFv CARs, confirmed for surface expression in Jurkat cells, and assessed for functional activity in solid-state Jurkat cell assays (**FIGS. 23C-23D**). This step allowed for the selection of a subset of the most sensitive, selective binders for further functional characterization.

[0699] While most of the 62 binders resulted in a functional response to cell surface displayed MSLN, six were selected for further characterization; sequences binder CDRs (heavy chain (HC) CDRs and light chain (LC) CDRs) and are provided in Table 2, Table 3 (heavy chain; VH) and Table 4 (light chain; VL). In each case, the HC-CDRs or VH may be paired with any of the LC-CDRs or VL, as the heavy chains and light chains share similarity, with routine testing to confirm desired expression and binding activity.

[0700] Single chain variable fragments (scFvs) may be generated by inserting a linker (e.g., GGGGSGGGGSGGGGSGG (SEQ ID NO: 152) or another suitable linker) between the VH and VL segments to form a VH-VL scFv; or VL-VH scFvs may alternatively be constructed. The light chains have high sequence similarity; pairing of VL and VH to generate full antibodies have been determined without undue experimentation. Illustrative scFvs are provided in Table 1, illustrative heavy and light chains are provided in Tables 3 and 4, and illustrative CDR sequences are provided in Table 2. Sequences of illustrative chimeric antigen receptors using the MSLN scFv are provided as Table 20, below.

Table 20: Sequences of Receptors comprising single chain variable fragments (scFv)

#	**SEQ ID NO**	**Receptor Sequence**
1	286	EVQLVESGGGLVKPGGSLRLSCAASGFTFSNAWMSWVRQAP GKGLEWVGRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYL QMNSLKTEDTAVYYCTTDLPKLRNFHIWGQGTLVTVSSGGG GSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSI SSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
2	287	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMHWVRQAP GKGLEYVSAISSNGGSTYYANSVKGRFTISRDNSKNTLYLQM GSLRAEDMAVYYCASLEYHGFRQYGLRYWHWGQGTLVTVS SGGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCR ASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGS GTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFW VLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTP RRPGPTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRP VQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQN QLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLY NELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDT YDALHMQALPPR
3	288	QLQLQESGSGLVKPSQTLSLTCAVSGGSISSGGYSWSWIRQPP GKGLEWIGYIYHSGSTYYNPSLKSRVTISVDRSKNQFSLKLSS VTAADTAVYYCASIKFWFAGINYFFPWGQGTLVTVSSGGGGS GGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISS YLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR

#	SEQ ID NO	Receptor Sequence
		KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
4	289	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMHWVRQAP GKGLVWVSRINSDGSSTSYADSVKGRFTISRDNAKNTLYLQM NSLRAEDTAVYYCASGFLGMGSNFIWGQGTLVTVSSGGGGS GGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISS YLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
5	290	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHP GKGLEWIGYIYYSGSTYYNPSLKSLVTISVDTSKNQFSLKLSSV TAADTAVYYCASGDRARYFDLWGRGTLVTVSSGGGGSGGG GSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
6	291	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMHWVRQAP GKGLVWVSRINSDGSSTSYADSVKGRFTISRDNAKNTLYLQM NSLRAEDTAVYYCARYPRGYHQMVDAFDIWGQGTMVTVSS GGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRA SQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSG TDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPA PRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWV LVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPR RPGPTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPV QTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQ LYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYN ELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR
7	292	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPG KGLEWIGSIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVT AADTAVYYCARVRFLAARTTIPEANFLWGQGTLVTVSSGGG

#	SEQ ID NO	Receptor Sequence
		GSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSI SSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
8	293	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPG KGLEWVSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARVLSRARFDYWGQGTLVTVSSGGGGSGGG GSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
9	294	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPG KGLEWVSSISSSSSYIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARLRGRVFDPWGQGTLVTVSSGGGGSGGGG SGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNW YQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVLA CYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHY QPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR
10	295	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPG KGLEWIGSIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVT AADTAVYYCARIKFTSFLYVHGFLWGQGTLVTVSSGGGGSG GGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYL NWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM

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		AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
11	296	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYAMHWVRQA PGQRLEWMGWINAGNGNTKYSQKFQGRVTITRDTSASTAYM ELSSLRSEDTAVYYCARGQRWLYLGGIRRHWGQGTLVTVSS GGGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRA SQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSG TDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPA PRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWV LVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPR RPGPTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPV QTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQ LYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYN ELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR
12	297	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGK GLEWIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTA ADTAVYYCAREWIPSRPYYFDYWGQGTLVTVSSGGGGSGGG GSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
13	298	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPP GKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSV TAADTAVYYCARESTGTGAFDIWGQGTMVTVSSGGGGSGGG GSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
14	299	EVQLVESGGGVVRPGGSLRLSCAASGFTFDDYGMSWVRQAP GKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKNSLYLQ MNSLRAEDTALYHCARERYRRVLHWYFDLWGRGTLVTVSSG GGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRAS QSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAP

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		RPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVL VVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRR PGPTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQ TTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQL YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNE LQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYD ALHMQALPPR
15	300	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQAT GQGLEWMGWMNPNSGNTGYAQKFQGRVTMTRNTSISTAYM ELSSLRSEDTAVYYCAREPDAFDIWGQGTMVTVSSGGGGSGG GGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
16	301	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPP GKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSV TAADTAVYYCAREHMGTIPYYFDYWGQGTLVTVSSGGGGSG GGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYL NWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
17	302	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQPP GKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSV TAADTAVYYCAREEFGYGDVLYWGQGTLVTVSSGGGGSGG GGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR

#	SEQ ID NO	Receptor Sequence
18	303	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGDYYWSWIRQPP GKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSV TAADTAVYYCAREDVVKGAFDIWGQGTMVTVSSGGGGSGG GGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
19	304	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPG KGLEWVSYISSSSSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCAREDFSHKLGYFQHWGQGTLVTVSSGGGGS GGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISS YLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
20	305	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARDYDYVWGQGTLVTVSSGGGGSGGGGSG GGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQ QKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTIASQ PLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVLACY SLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHYQPY APPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF PEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYS EIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
21	306	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGDYYWSWIRQPP GKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSV TAADTAVYYCARDRRDWDWFDPWGQGTLVTVSSGGGGSGG GGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG

#	SEQ ID NO	Receptor Sequence
		CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
22	307	QVQLQESGPGLVKPSGTLSLTCAVSGGSISSSNWWSWVRQPP GKGLEWIGEIYHSGSTNYNPSLKSRVTISVDKSKNQFSLKLSSV TAADTAVYYCARDQQALKYRVDWGQGTLVTVSSGGGGSGG GGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
23	308	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAP GQGLEWMGWISAYNGNTNYAQKLQGRVTMTTDTSTSTAYM ELRSLRSDDTAVYYCARDLTLGCFDYWGQGTLVTVSSGGGG SGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISS YLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
24	309	EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNYMSWVRQAP GKGLEWVSVIYSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCARDGSNSWYFDLWGRGTLVTVSSGGGGSG GGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYL NWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
25	310	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARAFLFLSFSVWGQGTLVTVSSGGGGS GGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISS

#	SEQ ID NO	Receptor Sequence
		YLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
26	311	EVQLVESGGVVVQPGGSLRLSCAASGFTFDDYTMHWVRQAP GKGLEWVSLISWDGGSTYYADSVKGRFTISRDNSKNSLYLQM NSLRTEDTALYYCAKGIFYSSKEDFDYWGQGTLVTVSSGGGG SGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISS YLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
27	312	EVQLVESGGVVVQPGGSLRLSCAASGFTFDDYTMHWVRQAP GKGLEWVSLISWDGGSTYYADSVKGRFTISRDNSKNSLYLQM NSLRTEDTALYYCAKDIWIFYSSNPKPTVYWGQGTLVTVSSG GGGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRAS QSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAP RPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVL VVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRR PGPTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQ TTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQL YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNE LQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYD ALHMQALPPR
28	313	QVQLVQSGSELKKPGASVKVSCKASGYTFTSYAMNWVRQAP GQGLEWMGWINTNTGNPTYAQGFTGRFVFSFDTSVSTAYLQI CSLKAEDTAVYYCARKDQTLTYGNWFDPWGQGTLVTVSSGG GGSGGGGSGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQS ISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPP TPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVV VGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPG PTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTT QEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYN ELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ

#	SEQ ID NO	Receptor Sequence
		KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDAL HMQALPPR
29	314	QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGSYYWSWIRQPP GKGLEWIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSV TAADTAVYYCARDHYERGLYWGQGTLVTVSSGGGGSGGGG SGGGGSGGDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNW YQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQQSYSTPLTFGGGTKVEIKTTTPAPRPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVLA CYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHY QPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR
30	315	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARYMYNWYFDLWGRGTLVTVSSGGGGSGG GGSGGGGSGGDIQMTQSPSSVSASVGDRVTITCRASQGISSWL AWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQANSFPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
31	316	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARDRRPAFDIWGQGTMVTVSSGGGGSGGGG SGGGGSGGDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAW YQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQQANSFPLTFGGGTKVEIKTTTPAPRPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVLA CYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHY QPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR
32	317	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCAVHLKRRPYFDYWGQGTLVTVSSGGGGSGG GGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI

#	SEQ ID NO	Receptor Sequence
		ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
33	318	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASVHKKPIFDYWGQGTLVTVSSGGGGSGGG GSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
34	319	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASTSRRCTFQHWGQGTLVTVSSGGGGSGGG GSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
35	320	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASTSPRPLFQHWGQGTLVTVSSGGGGSGGG GSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR

#	SEQ ID NO	Receptor Sequence
36	321	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASPYQVRGVYFDYWGQGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
37	322	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASPYKKRRTVFDYWGQGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
38	323	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASLQRGLALFQHWGQGTLVTVSSGGGGSGG GGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
39	324	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASILSVPYFDLWGRGTLVTVSSGGGGSGGGG SGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALAW YQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVLA CYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHY

#	SEQ ID NO	Receptor Sequence
		QPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR
40	325	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCASGWIRVPLRLPLFQHWGQGTLVTVSSGGG GSGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGIS SALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
41	326	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARVTIFAIFDIWGQGTMVTVSSGGGGSGGGG SGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALAW YQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVLA CYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHY QPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR
42	327	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARVGRGFVHFDLWGRGTLVTVSSGGGGSGG GGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
43	328	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARTSRGLCVLFDYWGQGTLVTVSSGGGGSG

#	SEQ ID NO	Receptor Sequence
		GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
44	329	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARSGPSSYWYFDLWGRGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
45	330	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARNIYMGGIWFDPWGQGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
46	331	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARLTVRTGAFDIWGQGTMVTVSSGGGGSGG GGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM

#	SEQ ID NO	Receptor Sequence
		AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
47	332	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARLRTAHLDFDLWGRGTLVTVSSGGGGSGG GGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
48	333	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARDLIFPVVFDYWGQGTLVTVSSGGGGSGG GGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
49	334	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARDGYRKYGYVFFDIWGQGTMVTVSSGGG GSGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGIS SALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
50	335	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARDGRYRRFWHAFDIWGQGTMVTVSSGGG GSGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGIS SALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPT

#	SEQ ID NO	Receptor Sequence
		PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
51	336	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPG KGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARAHIRGYFDLWGRGTLVTVSSGGGGSGGG GSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSALA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIKTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGVL ACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
52	337	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCATWMGGGGRWYFDLWGRGTLVTVSSGGG GSGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGIS SALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
53	338	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCARTSRTTWYFDLWGRGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPTPAP TIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGV LACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR

#	SEQ ID NO	Receptor Sequence
54	339	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKWMGGGGRLYFDLWGRGTLVTVSSGGG GSGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGIS SALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
55	340	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKWGGRLYWYFDLWGRGTLVTVSSGGGG SGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISS ALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
56	341	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKVIRQLWYFDLWGRGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPTPAP TIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGV LACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
57	342	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKVFANSWYFDLWGRGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPTPAP TIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGV LACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH

#	SEQ ID NO	Receptor Sequence
		YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
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59	344	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKRWGKDGPYWYFDLWGRGTLVTVSSGG GGSGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQG ISSALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPP TPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVV VGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPG PTRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTT QEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYN ELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDAL HMQALPPR
60	345	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKRRDSYGPYWYFDLWGRGTLVTVSSGGG GSGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGIS SALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVV GGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP TRKHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
61	346	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKNRPPPGYWYFDLWGRGTLVTVSSGGGG

#	SEQ ID NO	Receptor Sequence
		SGGGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISS ALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPTP APTIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVG GVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTR KHYQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR
62	347	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPG KGLEWVSAISGSGGGSTYYADSVKGRFTISRDNSKNTLYLQMN SLRAEDTAVYYCAKGRRFSWYFDLWGRGTLVTVSSGGGGSG GGGSGGGGSGGAIQLTQSPSSLSASVGDRVTITCRASQGISSAL AWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQFNNYPLTFGGGTKVEIKTTTPAPRPPTPAP TIASQPLSLRPEACRPAAGGAVHTRGLDFACDFWVLVVVGGV LACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKH YQPYAPPRDFAAYRSKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR

[0701] Six binders were expressed as third-generation (Gen3) chimeric antigen receptors (CAR1-CAR6) [corresponding to #16, 17, 18, 29, 55, and 59, respectively, in Tables 1-4 and 20], which were compared to anti-MSLN scFvs from the literature (SS1, M5 and m912) in Jurkat functional assays. The CARs displayed a range of sensitivities (EC_{50}) and maximal responses (E_{max}) (**FIG. 24A**). All constructs were Gen3 except SS1 (Gen2). Jurkat cell dose-response (RLU) was measured to assess the sensitivity in a 6 hour co-culture assay: **(1)** Titrated MSLN-encoding mRNA was used to transfect HEK293 cells; **(2)** QIFIKIT (quantitative analysis kit, Agilent®) was used to convert flow-cytometry based surface expression to MSLN molecules/cell; and, **(3)** The molecule/cell sensitivities (EC50) of 6 novel and three benchmark CARs were calculated from fitting the dose-response curves. For those CARs with sensitivities below the limit of detection of the assay, EC50 was reported as <3000 MSLN molecules/cell. Maximum signal (E_{max}) for each construct was also noted. Experiments were repeated 1-4 times.

[0702] Table 21 shows the selectivity window and killing efficiency of HeLa cells by transduced primary T cells. Quantification of the selectivity window between killing of

MSLN+ A2- and MSLN+ A2+ HeLa cells with activator and blocker+ primary T cells. Killing efficiency describes difference in killing of MSLN+ A2- HeLa cells by activator and blocker+ T cells compared to activator+ (only) T cells. Both measures are calculated up to the time corresponding to 80% maximum observed killing.

Table 21

Activator	**E:T (HeLa target)**	**Time (hours) to 80% max killing**	**Selectivity window**	**Killing efficiency**
hM5 CAR	4:1	28	6.9	1.2
mSS1 CAR	4:1	44	6.2	1.1
CAR 18	4:1	24	21.4	1.1
CAR 29	4:1	20	7.0	1.0
hM5 CAR	2:1	64	5.5	0.8
mSS1 CAR	2:1	72+	n/d	0.7
CAR 18	2:1	56	20.3	0.8
CAR 29	2:1	44	7.6	0.9

[0703] n/d = not determined due to poor overall killing

[0704] Six binders (CAR1-6) were compared to benchmark MSLN scFvs from the literature (SS1, M5 and m912) in Jurkat functional assays [12-14]. All were expressed as Gen3 CARs, with the exception of Gen2 SS1. For MSLN(+) target cells, HEK293 cells transfected with synthetic MSLN mRNA were used. The CARs displayed a range of sensitivities (EC_{50}) and maximal responses (E_{max}) (**FIG. 24A**). Of the six binders, all but CAR 16 exhibit higher sensitivity than hM5 and sSS1.

[0705] In short, an extensive campaign to identify anti-MSLN binders yielded hundreds of sequences identified in an NGS screen, and 62 candidate constructs were produced, all of which bind MSLN. Six of these shown superior activity. CAR 18 and CAR 29 demonstrated superior sensitivity to comparator CAR constructs.

[0706] Previous work suggested that E_{max} is related to surface expression of the receptor and EC_{50} to its binding and signal transduction properties, especially the LBD [15,16]. The EC_{50} was converted from relative response measured by luminescence in Jurkat cells to absolute molecules/cell using standard curves and QIFIKIT methodology necessary [27]. One of the benchmark CARs (m912) displayed low functional sensitivity, with an EC_{50} estimated at ~80K molecules/cell. The EC_{50}s for the other benchmarks and novel CARs ranged

downwards of ~6K molecules/cell. Several novel LBDs assayed as CARs in Jurkat cells had EC50s below the limit of detection (<3K molecules/cell). As an indicator of selectivity, CAR3 and the benchmark M5 were tested for responsiveness to a panel of MSLN(+) and (-) cell lines. Both CARs displayed MSLN-specific activation and were inactive against MSLN(-) lines (**FIG. 24B and 25A**).

MSLN Tmod constructs are blocked efficiently by HLA-A*02 antigen in Jurkat and primary T cells

[0707] CAR1-6 and the benchmark CARs were tested as components of Tmod constructs where the CARs were paired with an A*02-directed inhibitory receptor or "blocker" previously shown to inhibit functional response in Jurkat and primary T cells [18]. This blocker comprised an A*02-binding scFv fused to the hinge, transmembrane and intracellular domains of the ITIM-containing LIR-1 protein (**FIG. 22B**). As target cells we used cell lines characterized for MSLN surface expression (**FIGs. 25A and 25B, FIGs. 26A and 26B**). All the CARs were blocked in a ligand-dependent manner by the A*02-directed LIR-1 blocker (**FIG. 27A**). Because of the combination of high sensitivity, selectivity and effective functional pairing with the A*02 blocker, CAR3 was selected for further study as the MSLN Tmod lead activator construct.

[0708] The MSLN CAR3 Tmod construct was examined in detail in a series of quantitative mRNA titration experiments for activation and blocking sensitivity in Jurkat cells (**FIG. 27B and 27C**). For target cells, the cervical carcinoma HeLa cell line that, like most other cancer lines, expresses endogenous MSLN was used. This line is HLA-A*02(-). To control MSLN levels, a variant with MSLN inactivated by CRISPR was generated. mRNA titration experiments enabled estimation of EC_{50} and IC_{50} for the MSLN CAR3 Tmod construct and these parameters were viewed in the context of the expression levels of antigens on normal and tumor tissues derived from high-quality public databases (**FIG. 28A**).

[0709] To make these comparisons, a correlation between MSLN mRNA and surface protein levels was established as a first step (**FIG. 25B**). The same was done for HLA-A and the information used to plot the HLA-A and MSLN levels of different tissues relative to the EC_{50} and IC_{50} of the MSLN Tmod construct. The large majority of normal tissues expressed levels of MSLN well below the EC_{50} of MSLN Tmod. In contrast, certain tissues including lung expressed MSLN at a level well above the EC_{50} of the Tmod construct and, therefore, were considered high risk absent an effective blocker. However, these at-risk tissues also express HLA-A levels above the Tmod IC_{50}, suggesting they will be protected against

cytotoxicity by the A*02-targeted LIR-1 blocker component of Tmod. The cell lines (including transgenic HLA-A*02 HeLa and MS751) used to model normal and tumor tissues in functional assays are also shown on the graph.

[0710] The behavior of the MSLN CAR3 Tmod construct was then tested in primary T cells. Cytotoxicity was the principal readout, with IFN-γ secretion as a secondary measure. Target cells were HeLa cells and variants: (i) native MSLN(+)A*02(-) HeLa cells modeled tumor cells without blocker antigen; and, (ii) transgenic A*02(+) variant HeLa cells modeled normal mesothelial cells. Combinations of different constructs and target cells demonstrated that all MSLN CAR Tmod constructs kill tumor cells potently and block killing in an A*02-ligand-dependent fashion (**FIG. 28B**). Two other MSLN CARs from the literature (SS1 and M5) were used for comparison (**FIG. 29A**). Cytotoxicity was mirrored by IFN-γ release (**FIG. 29B**). Thus, the Tmod constructs composed of an HLA-A*02-directed blocker and different MSLN CAR activators displayed high potency and specificity for MSLN(+)A*02(-) target cells in both Jurkat and primary T cell assays.

The MSLN CAR3 Tmod construct mediates selective, reversible cytotoxicity in mixed-cell and serial cultures

[0711] A variety of other properties of the MSLN CAR3 Tmod construct important in the context of cancer cell therapy were tested. The construct mediated antigen-selective cytotoxicity in mixed cultures of tumor and normal target cells: Native MSLN(+)HLA-A*02(-) HeLa cells labeled with RFP were mixed at different ratios with MSLN(+)A*02(+) cells labeled with GFP. These cocultures were exposed to T cells engineered with different receptor constructs and imaged. Whereas CAR-only constructs killed indiscriminately, the Tmod constructs killed the native HeLa tumor cells only, leaving the A*02(+) cells unharmed (**FIG. 30A**). Selectivity was detectable even at normal:tumor cell ratios of 9:1 (**FIG. 30B**, **FIGs. 31A and 31B**).

[0712] The capacity of Tmod cells to switch between ON (active killing) and OFF (blocked) states was examined using cytotoxicity assays as readout. In these experiments the transduced T cells were transferred from one batch of target cells to another (**FIG. 32A, FIG. 33A**,). The Tmod cells displayed the capacity to activate and kill after being exposed for 2 days to normal cells where they were quiescent. The reverse was also true. Tmod cells engaged in killing tumor cells were able to quickly switch to the OFF state and refrain from

killing the normal cells after transfer and without a rest period. The ability to switch states was maintained through two cycles, over a total of four days.

[0713] It was investigated whether soluble MSLN (sMSLN), which is present in the blood of some cancer patients at high levels (median ~200ng/ml; range 20-2,000 ng/ml [19]), interfered with MSLN CAR3 Tmod cells. sMSLN added to the cultures at 500ng/ml had no effect on function of either the CAR or Tmod T cells **FIGs. 33B and 33C**). Together, these results suggested that MSLN CAR3 Tmod mediates selective, reversible cytotoxicity in mixed cultures of tumor and normal cells and is unaffected by sMSLN at levels observed in some cancer patients' blood. All of these features are consistent with a cell therapy that has the potential to be safe and efficacious in selected cancer patients.

MSLN CAR3 Tmod cells display no detectable off-target activity

[0714] To systematically explore off-target reactivity of MSLN CAR3 Tmod cells, Jurkat cell activation was tested by a panel of target cell lines chosen to encompass the large majority of adult gene expression (Wang et al., *in preparation*; see Methods). Positive controls were used to confirm that effector cells could be activated by MSLN(+) cell lines, and negative controls were used to set a baseline for response (**FIG. 26B**; **FIG. 32B**). No detectable responses were triggered in CAR3 Tmod Jurkat cells, despite high sensitivity of the assay, estimated at ~1,000 molecules/cell.

The MSLN CAR3 Tmod construct mediates selective killing of tumor cells in a xenograft model

[0715] To examine behavior of MSLN CAR3 Tmod cells in vivo, a mouse xenograft model was used. HeLa cells did not grow well in the immunocompromised (NSG) mice, so another cervical cancer cell line, MS751, was developed as grafted target cells. The native MSLN was used as the activator antigen and the blocker antigen HLA-A*02 was engineered by gene transfer to better approximate normal tissue levels. MSLN(+)A*02(-) MS751 cells, generated by CRISPR knockout of HLA-A*02, modeled tumor while the MSLN(+)A*02(+) transgenic variant modeled normal cells in these in vivo experiments.

[0716] The cell lines were engineered with luciferase to enable bioluminescence as an independent readout of tumor survival and growth. Mice (10/cohort) were implanted with tumor cells on their left flank and normal cells on their right flank in half of the mice in each cohort, and vice versa in the other half to control for flank growth variation (**FIG. 34A**). After xenografts reached ~100-150 mm^3 in volume, mice were infused via tail vein with 2E7

total T cells/mouse. After a short delay, both the CARs and the Tmod constructs killed the MSLN(+)A*02(-) tumor cells equally well measured by caliper and bioluminescence intensity (**FIGs. 34B and 34C**, **FIGs. 35B and 35C**). Whereas the CAR-only T cells killed both tumor and normal with equal effectiveness, Tmod cells killed only the tumor grafts, mirroring in vitro cytotoxicity (**FIG. 14A**). In the presence of Tmod cells, the normal cell grafts grew comparably to those in the control groups treated with untransduced T cells or saline. These results dramatically demonstrated selectivity of the MSLN Tmod system in a mammalian body, consistent with other activator-blocker pairs which have been observed (Sandberg et al., *submitted*; [18]).

Extension of the MSLN CAR Tmod platform

[0717] Use of an HLA-A*02-targeted blocker raises the possibility that the blocker may be bound *in cis* by endogenous HLA-A*02 molecules produced in autologous T cells. Indeed, decreased blocker binding was observed with HLA-A*02 tetramer in transfected transgenic A*02(+) Jurkat cells compared to native Jurkat A*02(-) cells (**FIG. 36**). A similar decrease was observed in primary T cells from HLA-A*02(+) donors transduced with MSLN CAR3 Tmod or SS1 Tmod constructs compared to A*02(-) donor T cells (**FIG. 36, FIG. 37A**). More importantly, this decreased binding translated to poor blocker function in both A*02(+) Jurkat and primary T cells relative to their A*02(-) counterparts (**FIG. 36, FIGs. 37B and 37C**). These observations illustrated how cis-binding may pose a problem for an autologous MSLN CAR3 Tmod product that utilizes an A*02-directed blocker.

[0718] To address this problem, we developed a solution based on CRISPR inactivation of endogenous β2 microglobulin (B2M). Because B2M is required for all HLA class I expression, this approach was expected to mitigate the cis-binding effect of HLA-A*02. As predicted, knockout of B2M in primary T cells restored blocker binding and function to levels comparable to A*02(-) donor T cells (**FIGs. 37A-37C**). Thus, CRISPR-mediated abrogation of cis-binding produced MSLN Tmod cells with functional properties in HLA-A*02(+) donors that were indistinguishable from function in HLA-A*02(-) donors. These results suggest that the MSLN CAR3 Tmod construct may be suitable for allogeneic cell therapy and autologous products, provided that a method is employed to reduce expression of A*02 in the patient's T cells.

The MSLN CAR3 can be paired with an HLA-A*11-directed blocker

[0719] The impressive performance of the MSLN CAR3 Tmod construct that utilizes an A*02-directed blocker suggested the possibility that CAR3 might be paired with blockers gated by other HLA class I alleles. If true, this would potentially allow the Tmod platform to be used to treat patients who are not heterozygous for HLA-A*02—a number estimated at >60% of the population [20]. For proof of concept of the modularity of the MSLN Tmod system, HLA-A*11, the most common class I allele in Asian populations was studied [20]. A screen for A*11-selective scFvs was carried out using the same method described for isolation of MSLN scFvs (see Methods, *infra*). A series of enrichment steps using the mammalian scFv-display library generated several A*11-specific scFvs (**FIGs. 38A**).

[0720] One high-performing scFv (A*11-LBD4) was fused to LIR-1 and paired with the MSLN CAR3 activator in Jurkat cells. This A*11 blocker demonstrated good function with an IC_{50} estimated at ~37,000 molecules/cell from mRNA titration experiments (**FIG. 38B**). Finally, the MSLN CAR3 paired with the A*11 blocker was confirmed to function well in Jurkat cell and primary T cells with potency and blockade comparable to the MSLN CAR3 Tmod construct that utilizes HLA-A*02 as blocker antigen (**FIGs. 39A-39C**). Encouraged by these results we converted two other anti-HLA-I monoclonal antibodies, targeting A*03 and B*07, to scFvs and tested them as MSLN Tmod blockers (**FIG. 39A**). These findings suggest that the Tmod system is sufficiently modular to accommodate pairings of one activator with multiple blockers, thereby extending the accessibility of the cell therapy platform to a larger number of patients.

DISCUSSION

[0721] Given the distribution of MSLN in the adult body [1, 2, 4], it is vital that the blocker functions well with a MSLN-targeted activator. The properties of the A*02 blocker described here suggest it will inhibit activation signals that arise from the CAR across a broad range of MSLN antigen levels. It is also likely that the blocker will inhibit other sources of T cell activation triggered by the CAR, including off-target. Because the HLA blocker antigen is ubiquitously expressed in nucleated cells, it should provide an inhibitory signal under all circumstances except when the blocker antigen is absent as in tumors selected for LOH. The blocker may also prevent cytokine-release syndrome, a continuing source of toxicity observed for T cell therapies [14, 33], if the stimulus involves normal cells or cell fragments.

[0722] The MSLN therapeutic candidate described here requires selection of patients who are germline heterozygous for the blocker-antigen allele and whose tumors have lost this allele via LOH. Fortunately, such diagnostic tests have been developed recently which utilize

the enormous power of DNA sequencing technology [27-29]. DNA-sequence-based LOH detection has sufficient sensitivity to distinguish most cases of clonal vs. subclonal LOH in the tumor, thereby enriching for patients most likely to benefit from the therapy. Because this diagnostic method utilizes genome sequence from the tumor, it detects any allelic variation and is not restricted to HLA-A*02. The lead MSLN Tmod construct described here is applicable to a subset of HLA-A*02(+) patients. With the goal of extending the Tmod platform to other patients, we have shown that the MSLN CAR3 activator can be paired with blockers directed at 3 other HLA-I allelic products including HLA-A*11. A*11 is the most frequent HLA-I allele in most Asian populations and represents a significant opportunity for benefit in parts of the world beyond the US. Indeed, with a collection of blockers directed at 6-8 of the most common HLA-I alleles in the world, it should be possible to cover the large majority of solid tumors that harbor LOH at the HLA locus—estimated to be >15% of solid-tumor mortality at present [22, 30]. In addition we have shown in a parallel line of work that the HLA-A*02 blocker can be paired effectively with other activators including a CAR directed at another well-known tumor-associated antigen, CEA (Sandberg et al., in preparation; 31).

[0723] The modular Tmod system leverages the capacity of cells—unique among therapeutic modalities—to integrate multiple signals into a coordinated response and thus offers a means to address the fundamental obstacles of solid-tumor therapy [18, 21, 22]. Therapeutics must access the tumor and overcome barriers that do not exist for blood cancers where cell therapies have proven effective [23]. T cells have an advantage over most other modalities, including antibodies, in that they possess a natural mechanism for active extravasation and biodistribution (see for review Mastrogiovanni et al. [24]). Furthermore, the Tmod approach described here that exploits LOH mitigates the key constraint on solid-tumor therapeutics posed by normal tissue expression of most targets. Though notoriously non-homogeneous, a large proportion of genetic alterations arise in the founding cell of the neoplasm and are present in all its descendants [25]. Such homogeneous mutations include LOH and, if such clonal LOH can be distinguished via a diagnostic test from later alterations present in tumors, LOH heterogeneity at the HLA locus should not constitute a source of resistance [26]. Unlike single nucleotide substitutions that generate most neoantigens, LOH is an irreversible event and should be stable even after strong selective pressure is applied via therapy. Finally, as use of checkpoint inhibitors becomes more prevalent, rates of HLA-I loss will likely increase, further expanding the pool of patients who may benefit from MSLN Tmod therapeutics [34].

MATERIALS AND METHODS

Cell line culture

[0724] Cell lines were purchased from ATCC (American Type Culture Collection) and handled according to manufacturer's instructions: T2, Shp77, Raji, MS751, A-375, A-498, SW982, SW480, HeLa, NIH-OVCAR-3, HepG2, NCI-H508, LNCaP clone FGC, K562, U2OS, BB7.1 and GAP A3 hybridomas. Jurkat cells encoding an NFAT luciferase reporter gene were obtained from BPS Bioscience and maintained in RPMI supplemented with 10% heat-inactivated (HIA) FBS (inactivated at 56 °C for 1 h), 1% penicillin and streptomycin (pen/strep), and 0.4 mg/ml Geneticin. Human peripheral blood mononuclear cells (PBMCs) were obtained from Stem Cell Technologies and thawed in X-VIVO 15 (Lonza) supplemented with 5% HIA human AB serum and activated with T Cell TransAct (Miltenyi Biotec) as recommended by manufacturer. Lentiviral transductions of CAR or CAR Tmod single vector constructs (see Fig. 1b, unless otherwise noted) were done at 24 h post-activation and cultures were maintained in LymphoONE T cell Expansion Medium (Takara Bio) supplemented with 1% HIA human AB serum and 300 IU/mL IL-2.

Molecular cloning and mRNA in vitro transcription

[0725] Activating and blocking CAR constructs were designed and constructed as previously described[9]. Briefly, activating CARs were created by fusing the anti-MSLN scFv LBDs to the CD8α hinge, CD28 transmembrane (TM), and CD28, 4-1BB and CD3ζ intracellular domains (ICD). Blocking CARs were generated by fusing the anti-HLA-A*02, A*03 or B*07 scFv LBDs derived from monoclonal antibodies PA2.1 [32], GAP A3 [36] or BB7.1 [37], respectively, to the hinge, TM and ICD domains of LIR-1. Gene segments were combined using Golden Gate cloning and inserted downstream of a human EF1α promoter in a lentiviral expression vector.

[0726] For messenger RNA (mRNA) preparation, PCR was used to generate the DNA template used for in vitro synthesis mRNA. Briefly, T7 promoter was introduced via N-terminal primer and common overhang regions were used for both N- and C-terminal primers. The PCR product was used as a template for in vitro transcription (IVT) using the T7 ARCA mRNA kit (New England Biolabs, E2060S). The IVT reaction comprised 1x ARCA/NTP mix, 1.25 mM Ψ-UTP (TriLink), 25 ug PCR product template, and 1x T7 RNA polymerase. The IVT reaction was incubated at 37 °C for 2 h, then 2 uL of DNase I (New

England Biolabs, M0303S) was added to each reaction and incubated at 37 ºC for 15 min. To the IVT reaction, 65 uL water, 10 uL 10x poly-adenylation reaction buffer (NEB M0276S) and 5 uL of poly-adenylation enzyme (NEB M0276S) was added to a total volume of ~100 uL. The reaction was incubated at 37 °C for 30 min. The resulting product was cleaned using the Monarch RNA cleanup kit (T2040L) according to the manufacturer's protocol.

MSLN and HLA-A*11 binder generation using mammalian display

[0727] Binder generation using the HuTARG mammalian display technology has been previously described (Patent No: US 8,012,714 B2; Wang et al., *in press*). For the MSLN binder generation, soluble MSLN (catalog #MSN-H82E9) and irrelevant, off-target proteins, EGFR and CEA, were purchased from Acro Biosystems. The HuTARG library was subjected to serial rounds of on-target enrichment and off-target depletion using fluorescence-activated cell sorting (FACS). The HLA-A*11 binder generation campaign was similarly conducted. The HuTARG library was subjected to on-target enrichment using HLA-A*11:01 tetramer and off-target depletion using a pool of 4 unrelated HLA class I tetramers. In the final round of both campaigns, on- and off-target binding cells were collected, and RNA was reverse transcribed into cDNA. Fragments containing the complementarity determining regions (CDRs) were amplified using polymerase chain reaction (PCR) and sequenced by next-generation sequencing (NGS). Binders of interest were selected by comparing the input and output NGS counts.

MSLN surface quantification

[0728] To quantify surface mesothelin molecules, adherent cells were first washed once with DPBS then once with Versene. Cells were coated with Versene and incubated at 37 ºC for ~15 min. After incubation, flasks were tapped vigorously to promote complete detachment. The cells were then diluted with DBPS at 1:2 ratio (Versene:DPBS) and counted. 300,000 cells were centrifuged at 500 xg for 5 min. Cells were resuspended in 300 uL 1x FACS buffer (DPBS + 1% BSA). 100 uL of aliquot was divided into 2 v-bottom wells. Cells were washed one more time with 100 uL FACS buffer, then stained with 100 uL of anti-MSLN antibody at 10 ug/mL (R&D Systems, clone 618923) on ice for 30 min. After the primary stain, 50 uL of calibration beads from the QIFIKIT (Agilent) were added for washing. The mixture was washed with 100 uL FACS buffer twice, then stained with 100 uL of anti-mouse F(ab')2-Goat Alexa Fluor 647 (Invitrogen) antibody diluted 2000x in FACS buffer for 45 min on ice. The stained cells and beads were washed 2x with 100 uL FACS

buffer, then resuspended in 100 uL FACS buffer to measure fluorescence. The calibration curve plotting median fluorescence intensity of each bead population vs. number of molecules was plotted according to manufacturer's protocol provided by the QIFIKIT (Agilent). The number of endogenous MSLN molecules was determined by fitting the cell's median fluorescence intensity onto the calibration curve generated with the QIFIKIT beads.

MSLN activator and various blocker sensitivity determination

[0729] To determine activator or blocker sensitivities, antigen was titrated into antigen(-) cell lines at various concentrations. Flow cytometry and QIFIKIT methodology [17] using standard curves could then be used to calculate absolute molecules/cell. The EC_{50} or IC_{50} value of activators or blockers, respectively, expressed in Jurkat cells was then measured by luminescence. Specifically, HEK293T or HeLa cell transfection with antigen mRNA was performed using the 4D nucleofection kit (Lonza). For single-antigen titrations (i.e., MSLN, HLA-A*02, HLA-A*11, HLA-A*03, HLA-B*07), mRNA was diluted to 1000 ng/uL in SE or SF buffer supplemented with Supplement solution (complete buffer) for HEK293T or HeLa cells respectively. The diluted mRNA was serially diluted 2x by adding stock mRNA to equal volumes of complete buffer 13 times, with the 15^{th} well lacking any added mRNA. Target cells were detached from the flask using TrypLE Express (Gibco). Appropriate number of cells were harvested then resuspended in complete buffer at 11.1e6 viable cells/mL. 22.5 uL of resuspended cells were added to 2.5 uL of serially-diluted mRNA to a final volume of 25 uL cell and mRNA mix. 20 uL of this sample was zapped using the 4D nucleofector using the CM-130 program for HEK293T cells or CN-114 program for HeLa cells. The cells were transferred into 280 uL of MEM + 10% FBS + 0.1% P/S. 15 uL of the diluted cells were transferred into 384-well plate and incubated 18-24 h at 37 °C, 5% CO_2. The remaining diluted cells were transferred to a 96-well plate and kept for next day analysis of surface antigen expression using the QIFIKIT as described above. In parallel, Jurkat-NFAT luciferase effector cells were transfected with appropriate CAR DNA at 1 ug per 1e6 cells or CAR Tmod DNA (single vector construct, unless otherwise noted) at 4 ug per 1e6 cells using the Neon electroporation system using the following parameters: 1500 V, 10 ms, 3 pulses. Transfected cells were immediately transferred to pre-warmed RPMI supplemented with 20% heat-inactivated (HIA) FBS and 0.1% pen/strep and incubated for 18-24 h at 37 °C, 5% CO_2. Next, Jurkat cells were counted and resuspended in RPMI + 10% HIA FBS and 0.1% pen/strep at 0.67e6 cells per mL. 1e4 resuspended Jurkat cells in 15 uL

were then co-cultured with transfected cells in the 384-well plate for 6 h. Luciferase activity was measured using ONE-Step Luciferase Assay System (BPS Bioscience).

[0730] For target cell co-transfections including MSLN and HLA-A*02 the protocol above was used except for minor adjustments to the mRNA dilutions step. mRNA encoding HLA-A*02 and MSLN were prepared by Aldevron and TriLink respectively. Briefly, to generate EC_{50} curves, a 14-point 2x serial dilution was performed with MSLN mRNA. This serial dilution was combined with each of four dilutions of various constant amounts of A*02 mRNA so that the top concentration of MSLN mRNA was 500 ng/ul and the A*02 mRNA concentrations were as follows: 500 ng/uL, 25 ng/ul, 1.25 ng/uL, and 0 ng/uL. To generate IC_{50} curves, a 14-point 2x serial dilution was performed with A*02 mRNA. This serial dilution was combined with each of four dilutions of various constant amounts of MSLN mRNA so that the top concentration of A*02 mRNA was 500 ng/uL and the MSLN mRNA concentrations were as follows: 125 ng/uL, 25 ng/ul, 5 ng/uL, and 1 ng/uL.

Primary T cell in vitro cytotoxicity assays

[0731] Killing of MSLN(+)A*02(-)RFP(+) tumor or MSLN(+)A*02(+)GFP(+) normal target cells by primary T cells transduced with Gen2 M5 CAR, MSLN CAR3 or CAR3 Tmod single vector constructs was assessed as previously described[9]. Briefly, 2,000 target cells were plated in 25 uL complete LymphoOne media (containing 1% HIA human AB serum) per well in a black, clear-bottom 384-well plate and allowed to adhere overnight at 37 °C with 5% CO_2. For mixed culture assays, target cells were pre-mixed at the desired ratios prior to seeding. ~16-18 h after target cell plating, T cells were counted, spun down at 300 xg for 10 min and resuspended at 2,000 CAR(+) or Tmod(+) T cells in 25 uL complete LymphoOne media (in the absence of additional cytokines) for an effective effector:target (E:T) = 1:1 (or more or less concentrated depending on the desired E:T) and gently plated on top of the target cells. For experiments including sMSLN, T cells were resuspended in LymphoOne media containing 1000 ng/mL (2x) soluble, monomeric MSLN (Acro Biosystems) for a final concentration of 500 ng/mL upon plating with target cells. Each sample was tested in triplicate wells. Within 30 min of co-culture, the plate was imaged for GFP(+) or RFP(+) target cell expression using an Incucyte imager and serial images were obtained every 2-4 h thereafter for up to 48 h. Quantification of target cell area (i.e., GFP(+) or RFP(+) total area per image) was done using Incucyte imaging software. Plating variability was accounted for by normalizing to area at time = 0 per well. Killing was then quantified as the difference in area between CAR or Tmod T cell wells to corresponding untransduced T cell wells,

normalized to the untrasduced T cell well (% Killing = ($A_{untransduced} - A_{CAR\ or\ Tmod}$)/$A_{untransduced}$).

[0732] For HLA-A*11 blocker evaluation in primary T cells, cytotoxicity assays were performed as described above, using HeLa target cells that express native levels of MSLN and transgenic HLA-A*11 antigen.

[0733] To further assess cytokine secretion and relative T cell activation post-48 h co-culture, the T cell containing media in each well was mixed and transferred to a v-bottom plate and spun down at 400 xg for 5 min. Supernatants were collected and frozen until further analysis for secreted IFN-γ using a BD Human IFN-γ flex kit as per manufacturer's instructions. Remaining T cells were then stained for human CD3, washed, and characterized for forward and side scatter by flow cytometry [35].

Repeat antigen-challenge assay (RACA) and reversibility assays

[0734] The RACA and reversibility assays were performed as previously described (Wang et al., *in press* [18]) with some modifications. Briefly, CAR or Tmod transduced primary T cells were co-cultured with MSLN(+)A*02(-) RFP(+) tumor or MSLN(+)A*02(+) GFP(+) normal target cells similarly as described above with effective E:T = 1.2:1. Round 1 images were taken over the course of 48 h in a 384-well plate format. Parallel 6-well plates with 250,000 target cells and 300,000 CAR3(+) or CAR3 Tmod(+) T cells were also set up to allow for bulk T cell isolation and transfer between rounds. After 48 h, T cell containing media was gently mixed and transferred to conical tubes. Remaining T cells engaged with live target cells were further dissociated by a single 1-min rinse with 10mM EDTA + 0.5% BSA in PBS and combined with the bulk T cell fraction. These cells (along with target cell debris and lifted target cells) were then spun down, washed, and stained with a cocktail of anti-MSLN, anti-EGFR, and anti-N-cadherin PE-conjugated antibodies to stain undesirable target cells. These target cells were then conjugated to anti-PE MACS beads followed by depletion through LS columns, resulting in clean T cell fractions. T cells were then counted and re-seeded for round 2 (similarly to round 1) onto fresh tumor or normal target cells. Imaging and quantification then proceeded exactly as was done in round 1.

MSLN knockout cell line generation

[0735] To develop MSLN(-) cell line controls for endogenous MSLN(+) cell lines, a CRISPR strategy to target full-length MSLN was utilized. Two Alt-R CRISPR-Cas9 sgRNAs targeting different exons of mesothelin were obtained from Integrated DNA Technologies

(IDT), with sgRNA_1 targeting exon 2, and sgRNA_2 targeting exon 16. The sgRNAs were rehydrated in nuclease-free water and combined with Alt-R® S.p. HiFi Cas9 Nuclease V3 (IDT) to yield a 9:1 sgRNA:Cas9 mole ratio. Both RNP solutions were incubated at room temperature for 10-20 min separately to allow each of the guides to complex with Cas9 independently. The RNP complexes of both guides were subsequently combined, added to the desired cells as per the manufacturer's instructions, and electroporated. After CRISPR, cells were scaled up and sorted on the MSLN(-) population (R&D, anti-MSLN pAb or clone #618923). Bulk-sorted MSLN(-) cells were then screened against MSLN binders in Jurkat cell-based assays.

Selectivity screening using Jurkat cells

[0736] To explore off-target reactivity of MSLN CAR3 Tmod cells, Jurkat cell activation was tested against a diverse panel of target cell lines chosen to encompass the large majority of adult gene expression similarly as described elsewhere (Wang et al., *in preparation*). Positive controls were used to confirm that effector cells could be activated by MSLN(+) cell lines, and negative controls to set a baseline for response (see FIGs. 26B and 28A for cell line characterization). Briefly, Jurkat-NFAT-Luciferase cells were transiently transfected to express either CARs or CAR3 Tmod exactly as described above. In parallel, endogenous MSLN(+) target cells, along with their respective MSLN(-) control target cells generated using CRISPR as described above, were plated at 1e4 target cells in 15 uL complete RPMI (containing 10% FBS and 1% P/S) per well in a 384-well plate format. Approximately 18 h post-transfection, 1e4 Jurkat cells were co-cultured with each target cell and activity compared to Gen2 M5 CAR was assessed via luminescence after 6 h. Luciferase activity was measured using ONE-Step Luciferase Assay System (BPS Bioscience).

Mouse xenograft study

[0737] Blinded in vivo experiments were conducted by Explora BioLabs under Institutional Animal Care and Use Committee (IACUC)-approved protocols. 5–6 week old female NOD.Cg-Prkdcscid Il2rgtm1Wjl Tg(HLA-A/H2-D/B2M)1Dvs/SzJ (NSG-HLA-A2/HHD) mice were purchased from The Jackson Labs. Animals were acclimated to the housing environment prior to the initiation of the study. Animals (10/cohort) were implanted subcutaneously with 5e6 MS751 firefly luciferase(+) HLA-A KO tumor or renilla luciferase(+) A*02 transgenic normal cells mixed 1:1 with Matrigel in 100 uL on their right and left flanks, respectively, in half of the mice in each cohort, and vice versa in the other

half to control for flank growth variation. When tumors reached an average of 100-150 mm^3 each (V=L x W x W/2), animals were randomized into 5 groups (n = 10) and 2e7 T cells, or saline control, were administered via the tail vein. Prior to injection, T cells were ~60% CAR(+) or Tmod(+). Post T cell injection, graft measurements by calipers were performed 3x times per week and BLI 1x time per week for the duration of the study. At each BLI session, RediJect Coelenterazine h substrate (PerkinElmer) was first injected to visualize renilla luciferase(+) normal cells, followed by injection of XenoLight D-Luciferin Potassium Salt (PerkinElmer) 6 h later to visualize firefly luciferase(+) tumor cells on the reverse flank.

CRISPR knockout of B2M in primary T cells

[0738] Frozen PBMCs were thawed and activated as described above. Transductions were performed 24 h post-activation using lentivirus (Alstem) at MOI 10. 24 h post-transduction, primary T cells were transfected with CRISPR-Cas9:sgRNA complexes. Briefly, cells were collected and washed with PBS before resuspending in supplemented P3 nucleofection buffer (Lonza). 20 pmol of Cas9 (Synthego) was combined with 130 pmol B2M-targeting sgRNA (Synthego) and incubated in P3 nucleofection buffer before addition to cells. 20 uL of the cell and ribonucleoprotein (RNP) mixture was transferred to a 16-well Nucleocuvette Strip and electroporated with the 4D nucleofector using the stimulated T cell program (EO-115). The cells were recovered in 100 uL of prewarmed media, X-VIVO 15 (Lonza) supplemented with 5% HIA human AB serum and 300 IU/mL IL-2. PBMCs were cultured and expanded in LymphoONE Tcell Expansion Medium (Takara Bio) supplemented with 1% HIA human AB serum and 300 IU/mL IL-2 for 6 days. Post expansion, positively transduced primary T cells were enriched using anti-PE microbeads (Miltenyi) according to manufacturer's instructions against Protein L-biotin:streptavidin-PE using LS column. Cytotoxicity of B2M KO primary T cells was then assessed exactly as described above.

Statistical analysis

[0739] Statistical analyses were performed using GraphPad Prism software. All Jurkat cell-based in vitro studies (including mRNA titration experiments) are shown as mean ± standard deviation (SD) of technical replicates, while primary T cell-based in vitro studies are shown as mean ± SD of technical triplicates. Where applicable, technical replicates are shown as individual data points, with bars denoting means. All data is representative of a minimum of n=2 experimental repeats, unless otherwise noted. Data for in vivo studies are shown as mean ± standard error of the mean (SEM). For mRNA titration studies, curves were

fit using a four-parameter non-linear regression analysis. EC_{50} and IC_{50} values were calculated directly from the curves. Direct comparisons were analyzed using unpaired, parametric t tests, unless otherwise noted.

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CLAIMS

What is claimed is:

1. An immune cell comprising:
    a. a first receptor, comprising an extracellular ligand binding domain specific to Mesothelin (MSLN); and
    b. a second receptor, comprising an extracellular ligand binding domain specific to a non-target antigen lost in a MSLN + cancer cell,

wherein the first receptor is an activator receptor responsive to MSLN; and wherein the second receptor is an inhibitory receptor responsive to the non-target antigen.

2. The immune cell of claim 1, wherein the non-target antigen is lost in the MSLN+ cancer cell through loss of heterozygosity.

3. The immune cell of claim 1 or 2, wherein the extracellular ligand binding domain of the second receptor specifically binds an allelic variant of a major histocompatibility complex (MHC) protein.

4. The immune cell of any one of claims 1-3, wherein the extracellular ligand binding domain of the second receptor specifically binds an allelic variant of an HLA-A, HLA-B, or HLA-C protein.

5. The immune cell of any one of claims 1-4, wherein the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*01, HLA-A*02, HLA-A*03, HLA-A*11, HLA-B*07, or HLA-C*07.

6. The immune cell of claim 5, wherein the extracellular ligand binding domain of the second receptor specifically binds to HLA-A*02.

7. The immune cell of any one of claims 1-6, wherein the extracellular ligand binding domain of the second receptor comprises complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 6; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of Table 6 or Table 7.

8. The immune cell of any one of claims 1-6, wherein the extracellular ligand binding domain of the second receptor comprises complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 of SEQ ID NOS: 42-47 or of SEQ ID NOS: 48-53; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertion relative to the CDRs of SEQ ID NOS: 42-47 or SEQ ID NOS: 48-53.

9. The immune cell of any one of claims 1-6, wherein the extracellular ligand binding domain of the second receptor comprises a polypeptide sequence selected from the polypeptide sequence disclosed in Table 5; or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

10. The immune cell of any one of claims 1-6, wherein the extracellular ligand binding domain of the second receptor comprises any one of SEQ ID NOS: 30-41, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

11. The immune cell of any one of claims 1-10, wherein the first receptor is a chimeric antigen receptor (CAR).

12. The immune cell of any one of claims 1-11, wherein the extracellular ligand binding domain of the first receptor comprises complementarity determining regions (CDRs) CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, CDR-H3 as disclosed Table 2; or CDR sequences having at most 1, 2, or 3 substitutions, deletions, or insertions relative to the CDRs of Table 2.

13. The immune cell of any one of claims 1-11, wherein the extracellular ligand binding domain of the first receptor comprises a variable heavy (VH) portion comprising a sequence set forth in Table 3 and a variable light (VL) portion comprising a sequence set forth in Table 4; or a sequence having at least 80%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

14. The immune cell of any one of claims 1-13, wherein the extracellular ligand binding domain of the first receptor comprises a variable heavy (VH) portion comprising SEQ ID NO: 233 or a sequence having at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% identity thereto, and a variable light (VL) portion comprising SEQ ID NO: 279 or a sequence having 85%, at least 90%, at least 95%, at least 97%, or at least 99% identity thereto.

15. The immune cell of any one of claims 1-13, wherein the extracellular ligand binding domain of the first receptor comprises a sequence selected from the group consisting of SEQ ID NOS: 3-6, 80 and 154-215, or a sequence having at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% identity thereto.

16. The immune cell of any one of claims 1-13, wherein the extracellular ligand binding domain of the first receptor comprises an scFv sequence of SEQ ID NO: 171; or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

17. The immune cell of any one of claims 1-16, wherein the first receptor comprises a hinge domain, a transmembrane domain and an intracellular domain.

18. The immune cell of claim 17, wherein the hinge domain comprises a CD8α hinge domain.

19. The immune cell of claim 18, wherein the CD8α hinge domain comprises a sequence of SEQ ID NO: 7, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

20. The immune cell of any one of claims 11-19, wherein the transmembrane domain comprises a CD28 transmembrane domain.

21. The immune cell of claim 20, wherein the CD28 transmembrane domain comprises a sequence of SEQ ID NO: 11, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

22. The immune cell of any one of claims 11-21, wherein the intracellular domain comprises a CD28 co-stimulatory domain, a 4-1BB co-stimulatory domain, and a CD3ζ activation domain.

23. The immune cell of claim 22, wherein the intracellular domain comprises a sequence of SEQ ID NO: 285, or a sequence having at least 85%, at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

24. The immune cell of any one of claims 1-23, wherein the first receptor comprises a sequence of SEQ ID NO: 303, or a sequence having at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

25. The immune cell of any one of claims 1-24, wherein the second receptor comprises a LILRB1 intracellular domain or a functional variant thereof.

26. The immune cell of claim 25, wherein the LILRB1 intracellular domain comprises a sequence at least 90%, at least 95%, at least 97%, at least 99%, or is identical to SEQ ID NO: 70.

27. The immune cell of any one of claims 1-26, wherein the second receptor comprises a LILRB1 transmembrane domain or a functional variant thereof.

28. The immune cell of claim 27, wherein the LILRB1 transmembrane domain or a functional variant thereof comprises a sequence at least 90%, at least 95%, at least 97%, at least 99% or is identical to SEQ ID NO: 74.

29. The immune cell of any one of claims 1-28, wherein the second receptor comprises a LILRB1 hinge domain or functional variant thereof.

30. The immune cell of claim 29, wherein the LILRB1 hinge domain comprises a sequence at least 90%, at least 95%, at least 97%, at least 99% or is identical to SEQ ID NO: 73.

31. The immune cell of any one of claims 1-30, wherein the second receptor comprises a LILRB1 intracellular domain, a LILRB1 transmembrane domain, a LILRB1 hinge domain, a functional variant of any of these, or combinations thereof.

32. The immune cell of claim 31, wherein the LILRB1 hinge domain, LILRB1 intracellular domain and LILRB1 transmembrane domain comprises SEQ ID NO: 71 or a sequence at least 90%, at least 95%, at least 97%, at least 99% or is identical to SEQ ID NO: 71.

33. The immune cell of any one of claims 1-32, wherein the second receptor comprises a sequence of SEQ ID NO: 348, or a sequence having at least 90%, at least 95%, at least 97%, or at least 99% identity thereto.

34. The immune cell of any one of claims 1-33, wherein the MSLN+ cancer cell is a mesothelioma cancer cell, an ovarian cancer cell, a cervical cancer cell, a colorectal cancer cell, an esophageal cancer cell, a head and neck cancer cell, a kidney cancer cell, an uterine cancer cell, a gastric cancer cell, a pancreatic cancer cell, a lung cancer cell, a colorectal cancer cell or a cholangiocarcinoma cell.

35. The immune cell of claim 34, wherein the MSLN+ cancer cell is a mesothelioma cancer cell, an ovarian cancer cell, a cervical cell, a uterine cancer cell, a gastric cancer cell, a pancreatic cancer cell or a lung adenocarcinoma cell.

36. The immune cell of any one of claims 1-35, wherein the MSLN+ cancer cell is a MSLN+/HLA-A*02– cancer cell that does not express HLA-A*02.

37. The immune cell of claim 36, wherein the MSLN+/HLA-A*02– cancer cell is derived from a MSLN+/HLA-A*02+ cell by loss of heterozygosity at HLA-A leading to loss of HLA-A*02.

38. The immune cell of any one of claims 1-37, wherein the first receptor and the second receptor together specifically activate the immune cell in the presence of the MSLN+/HLA-A*02- cancer cell having loss of heterozygosity.

39. The immune cell of any one of claims 1-38, wherein the first receptor and the second receptor together do not specifically activate the immune cell in the presence of an MSLN+ cell that has not lost HLA-A*02 by loss of heterozygosity.

40. The immune cell of any one of claims 1-39, wherein the immune cell is a T cell.

41. The immune cell of claim 40, wherein the T cell is a CD8+ CD4- T cell.

42. The immune cell of any one of claims 1-41, wherein expression and/or function of a MHC Class I gene has been reduced or eliminated.

43. The immune cell of claim 42, wherein the MHC Class I gene is beta-2-microglobulin (B2M).

44. The immune cell of claim 43, further comprising a polynucleotide comprising an interfering RNA, the interfering RNA comprising a sequence complementary to a sequence of a B2M mRNA.

45. The immune cell of claim 44, wherein the interfering RNA comprises a sequence selected from the group of sequences set forth in Table 13, or a sequence having at most 1, 2, 3, or 4 substitutions, insertions or deletions relative thereto.

46. The immune cell of claim 44 or 45, wherein the interfering RNA is capable of inducing RNAi-mediated degradation of the B2M mRNA.

47. The immune cell of claim 46, wherein the interfering RNA is a short hairpin RNA (shRNA).

48. The immune cell of claim 47, wherein the shRNA comprises:

a. a first sequence, having from 5' end to 3' end a sequence complementary to a sequence of the B2M mRNA; and
b. a second sequence, having from 5' end to 3' end a sequence complementary to the first sequence,

wherein the first sequence and the second sequence form the shRNA.

49. The immune cell of claim 47 or 48, wherein the shRNA is encoded by a sequence comprising a sequence of GCACTCAAAGCTTGTTAAGATCGAAATCTTAACAAGCTTTGAGTGC (SEQ ID NO: 349) or GTTAACTTCCAATTTACATACCGAAGTATGTAAATTGGAAGTTAAC (SEQ ID NO: 350), or a sequence having at least 80%, at least 90%, or at least 95% identity thereto.

50. The immune cell of claim 43, comprising one or more modifications to a sequence encoding B2M, wherein the one or more modifications reduce the expression and/or eliminate the function of B2M.

51. The immune cell of claim 50, wherein the one or more modifications comprise one or more inactivating mutations of the endogenous gene encoding B2M.

52. The immune cell of claim 51, wherein the one or more inactivating mutations comprise a deletion, an insertion, a substitution, or a frameshift mutation.

53. The immune cell of any one of claims 51 or 52, wherein the one or more inactivating mutations are introduced with a nucleic acid guided endonuclease in a complex with at least one guide nucleic acid (gNA) that specifically targets a sequence of the endogenous gene encoding B2M.

54. The immune cell of claim 53, wherein the gNA comprises a sequence selected from the group of sequences set forth in Table 12, or a sequence having at most 1, 2, 3, or 4 substitutions, insertions or deletions relative thereto.

55. The immune cell of claim 42, wherein the MHC Class I gene is HLA-A*02.

56. The immune cell of claim 55, further comprising a polynucleotide comprising an interfering RNA, comprising a sequence complementary to a sequence of an HLA-A*02 mRNA.

57. The immune cell of claim 56, wherein the interfering RNA is capable of inducing RNA interference (RNAi)-mediated degradation of the HLA-A*02 mRNA.

58. The immune cell of claim 57, wherein the interfering RNA is a short hairpin RNA (shRNA) comprising:

a. a first sequence, having from 5' end to 3' end a sequence complementary to a sequence of the HLA-A*02 mRNA; and
b. a second sequence, having from 5' end to 3' end a sequence complementary to the first sequence,

wherein the first sequence and the second sequence form the shRNA.

59. The immune cell of claim 55, comprising one or more modifications to a sequence of an endogenous gene encoding HLA-A*02, wherein the one or modifications reduce the expression and/or eliminate the function of HLA-A*02.

60. The immune cell of claim 59, wherein the one or more modifications comprise one or more inactivating mutations of the endogenous gene encoding HLA-A*02.

61. The immune cell of claim 59 or 60, wherein the one or more inactivating mutations are introduced with a nucleic acid guided endonuclease in a complex with at least one guide nucleic acid (gNA) that specifically targets a sequence of the endogenous gene encoding HLA-A*02.

62. The immune cell of any one of claims 1-61, wherein the first receptor comprises a sequence of SEQ ID NO: 164, and the second receptor comprises a sequence of SEQ ID NO: 52, or sequences having at least 90%, at least 95%, at least 97% or at least 99% identity thereto.

63. The immune cell of claim 62, comprising an shRNA encoded by a sequence comprising GCACTCAAAGCTTGTTAAGATCGAAATCTTAACAAGCTTTGAGTGC (SEQ ID NO: 349) or GTTAACTTCCAATTTACATACCGAAGTATGTAAATTGGAAGTTAAC (SEQ ID NO: 350) or a sequence having at least 80%, at least 90%, or at least 95% identity thereto.

64. The immune cell of claim 62 or 63, wherein the first receptor and second receptor are encoded by a single polynucleotide, and wherein the sequences encoding the first and second receptors are separated by a sequence encoding a self-cleaving polypeptide.

65. The immune cell of claim 63, wherein the self-cleaving polypeptide comprises a T2A self-cleaving polypeptide comprising a sequence of GSGEGRGSLLTCGDVEENPGP (SEQ ID NO: 351).

66. The immune cell of any one of claims 1-65, wherein the immune cell is autologous.

67. The immune cell of any one of claims 1-65, wherein the immune cell is allogeneic.

68. A pharmaceutical composition, comprising a therapeutically effective amount of the immune cells of any one of claims 1-67.

69. The pharmaceutical composition of claim 68, further comprising a pharmaceutically acceptable carrier, diluent or excipient.

70. The pharmaceutical composition of claim 68 or 69, for use as a medicament in the treatment of MSLN+ cancer.

71. A polynucleotide or polynucleotide system, comprising one or more polynucleotides comprising polynucleotide sequences encoding:

a. a first receptor, comprising an extracellular ligand binding domain specific to Mesothelin (MSLN); and
b. a second receptor, comprising an extracellular ligand binding domain specific to a non-target antigen that has been lost in a MSLN+ cancer cell,

wherein the first receptor is an activator receptor responsive to MSLN on the MSLN+ cancer cell; and wherein the second receptor is an inhibitory receptor responsive to the non-target antigen.

72. A polynucleotide or polynucleotide system, comprising one or more polynucleotides comprising polynucleotide sequences encoding the first receptor and the second receptor for use in generating the immune cells of any one of claims 1-67.

73. The polynucleotide or polynucleotide system of claim 71 or 72, comprising a sequence encoding an shRNA specific to B2M.

74. The polynucleotide or polynucleotide system of claim 73, wherein the sequences encoding the first receptor, the second receptor and the shRNA specific to B2M are encoded by the same polynucleotide.

75. The polynucleotide or polynucleotide system of claims 73 or 74, wherein

a. the sequence encoding the shRNA specific to B2M comprises GCACTCAAAGCTTGTTAAGATCGAAATCTTAACAAGCTTTGAGTGC

(SEQ ID NO: 349) or GTTAACTTCCAATTTACATACCGAAGTATGTAAATTGGAAGTTAAC (SEQ ID NO: 350) or a sequence having at least 80%, at least 90%, or at least 95% identity thereto;

b. the sequence encoding the first receptor comprises a sequence encoding a polypeptide comprising a of SEQ ID NO: 303, or a sequence having at least 80%, at least 90%, or at least 95% identity thereto; and

c. the sequence encoding the second receptor comprises a sequence encoding a polypeptide comprising a sequence of SEQ ID NO: 348, or a sequence having at least 80%, at least 90%, or at least 95% identity thereto.

76. A vector, comprising the one or more polynucleotides of any one of claims 71-75.

77. A method of killing a MSLN+ cancer cell having loss of heterozygosity at an MHC class I locus, comprising administering to the subject an effective amount of the immune cell of any one of claims 1-65 or the pharmaceutical composition of any one of claims 66-68.

78. A method of treating MSLN+ cancer in a subject having a MSLN+ tumor having loss of heterozygosity at an MHC class I locus, comprising administering to the subject an effective amount of the immune cell of any one of claims 1-67 or the pharmaceutical composition of any one of claims 68-70.

79. A method of treating a cancer in a subject comprising:

a. determining HLA-A genotype or expression of normal cells and a plurality of cancer cells of the subject;

b. optionally, determining the expression of MSLN in a plurality of cancer cells of the subject; and

c. administering to the subject an effective amount of the immune cell of any one of claims 1-65 or the pharmaceutical composition of any one of claims 66-68 if the normal cells express HLA-A*02 and the plurality of cancer cells do not express HLA-A*02, and the plurality of cancer cells are MSLN-positive.

80. The method of claim 79, wherein the subject is a heterozygous HLA-A*02 patient with a malignancy that expresses MSLN (MSLN+) and has lost HLA-A*02 expression.

81. The method of claim 79, wherein the subject is a heterozygous HLA-A*02 patient with recurrent unresectable or metastatic solid tumors that express MSLN and have lost HLA-A*02 expression.

82. The method of any one of claims 79-81, wherein the cancer comprises mesothelioma cancer, ovarian cancer, cervical cancer, colorectal cancer, esophageal cancer, head and neck

cancer, kidney cancer, uterine cancer, gastric cancer, pancreatic cancer, lung cancer, colorectal cancer, or cholangiocarcinoma.

83. The method of any one of claims 82, wherein the cancer has relapsed in a subject, the cancer is refractory to one or more prior administered anticancer therapies, and/or the cancer is metastatic.

84. The method of any one of claims 79-83, wherein the cancer cells comprise MSLN+/HLA-A*02– cancer cells that do not express HLA-A*02.

85. The method of claim 84, wherein the MSLN+/HLA-A*02– cancer cells are derived from a MLSN+/HLA-A*02+ cell by loss of heterozygosity at HLA-A leading to loss of HLA-A*02.

86. The method of any one of claims 79-85, wherein the first receptor and the second receptor together specifically activate the immune cell in the presence of the MSLN+/HLA-A*02- cancer cells.

87. The method of any one of claims 79-86, wherein the first receptor and the second receptor together do not specifically activate the immune cell in the presence of a MSLN+ cell that has not lost HLA-A*02.

88. The method of any one of claims 79-87, wherein administration of the immune cell of any one of claims 1-58 or the pharmaceutical composition of any one of claims 59-61 reduces the size of a tumor in the subject.

89. The method of claim 88, wherein the tumor is reduced by about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%.

90. The method of claim 88, wherein the tumor is eliminated.

91. The method of claim 88 or claim 89, wherein administration of the immune cell or the pharmaceutical composition arrests the growth of a tumor in the subject.

92. The method of any one of claims 79-91, wherein administration of the immune cell or the pharmaceutical composition reduces the number of tumors in the subject.

93. The method of any one of claims 79-92, wherein administration of the immune cell or the pharmaceutical composition results in selective killing of a cancer cell but not a normal cell in the subject.

94. The method of claim 93, wherein at least about 60% of the cells killed are cancer cells, about 65% of the cells killed are cancer cells, about 70% of the cells killed are cancer cells, about 75% of the cells killed are cancer cells, about 80% of the cells killed are cancer cells,

about 85% of the cells killed are cancer cells, about 90% of the cells killed are cancer cells, about 95% of the cells killed are cancer cells, or about 100% of the cells killed are cancer cells.

95. The method of claim 93, wherein administration of the immune cell or pharmaceutical composition results in the killing of at least about 40%, about 50%, about 60%, about 70%, about 80%, about 90% or all of the cancer cells of the subject.

96. The method of any one of claims 79-95, wherein administration of the immune cell or the pharmaceutical composition results in fewer side effects for the subject than administration of an otherwise equivalent immune cell comprising the first activator receptor but no second inhibitory receptor.

97. A method of making a plurality of immune cells, comprising:

a. providing a plurality of immune cells, and
b. transforming the plurality of immune cells with the polynucleotide system of any one of claim 71-75, or the vector of claim 76.

98. A kit comprising the immune cell of any one of claims 1-67 or the pharmaceutical composition of any one of claims 68-708.

99. The kit of claim 98, further comprising instructions for use.

FIG. 1

	Colon adenocarcinoma	Ovarian	Lung Adenocarcinoma	Pancreatic Adenocarcinoma	Mesothelioma
Gene	TCGA-COADREAD-Xena-Median-FPKM (383 samples)	TCGA-OV-Xena-Median-FPKM (427 samples)	TCGA-LUAD-Xena-Median-FPKM (515 samples)	TCGA-PAAD-Xena-Median-FPKM (179 samples)	TCGA-MESO-Xena-Median-FPKM (87 samples)
VASN	1.7	5.1	3.5	3.7	5.1
TUSC3	1.8	5.0	4.8	4.9	5.3
VSIG4	1.8	3.8	4.5	4.0	5.0
CTXN1	0.3	6.6	2.1	2.1	5.0
NPR1	-0.4	5.2	1.2	1.3	5.5
HAS1	-3.0	-3.6	-2.7	-0.6	5.7
CD200	1.7	3.9	2.0	2.7	5.7
LRRN4*	-4.0	0.5	1.3	-1.8	5.0
UPK3B*	-1.5	6.3	0.7	0.6	9.2
PTGIS	-0.2	1.8	1.6	3.2	6.9
SCARA3	0.7	5.7	2.0	3.2	5.7
UPK1B	-10.0	2.4	-4.3	0.9	6.7
CLIC3	1.7	3.6	3.7	4.4	5.6

FIG. 2

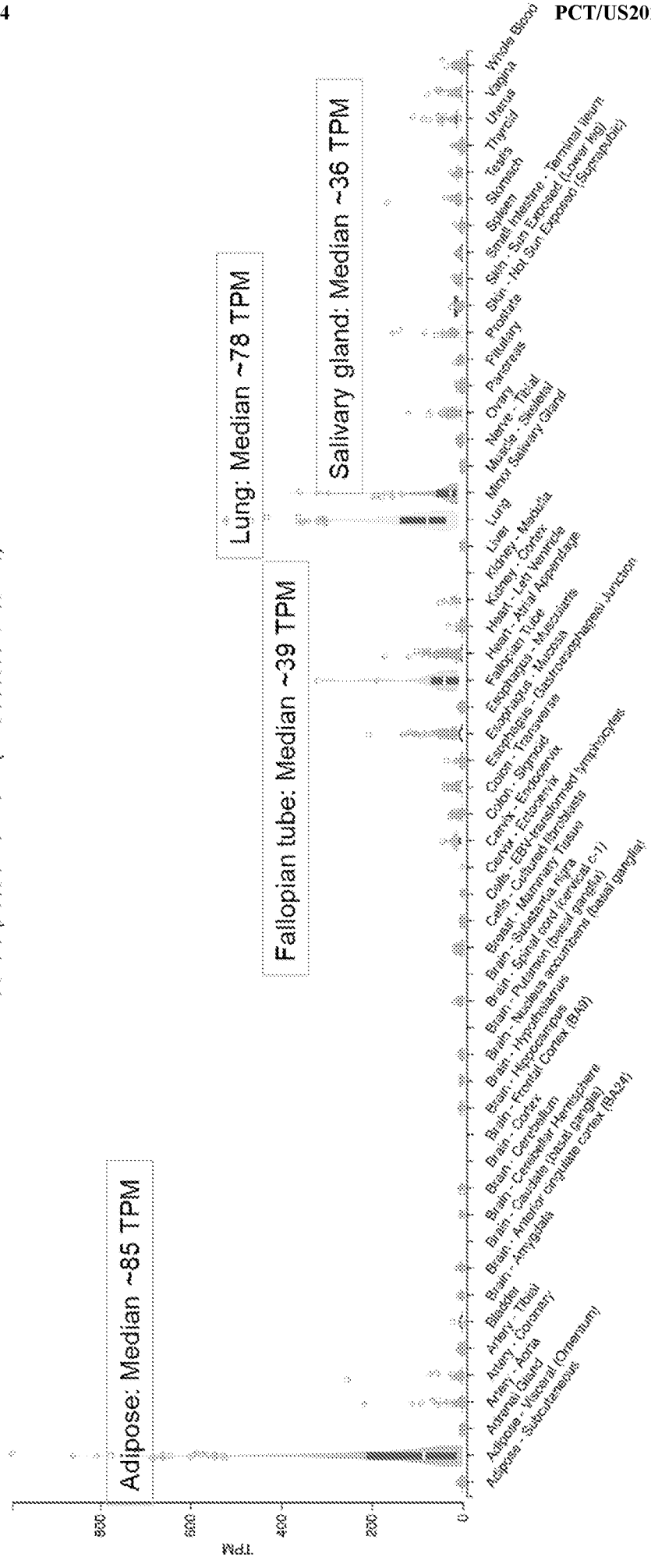

Gene expression for MSLN (ENSG00000102854.15)
TPM
Adipose: Median ~85 TPM
Fallopian tube: Median ~39 TPM
Lung: Median ~78 TPM
Salivary gland: Median ~36 TPM
Adipose - Subcutaneous
Adipose - Visceral (Omentum)
Adrenal Gland
Artery - Aorta
Artery - Coronary
Artery - Tibial
Bladder
Brain - Amygdala
Brain - Anterior cingulate cortex (BA24)
Brain - Caudate (basal ganglia)
Brain - Cerebellar Hemisphere
Brain - Cerebellum
Brain - Cortex
Brain - Frontal Cortex (BA9)
Brain - Hippocampus
Brain - Hypothalamus
Brain - Nucleus accumbens (basal ganglia)
Brain - Putamen (basal ganglia)
Brain - Spinal cord (cervical c-1)
Brain - Substantia nigra
Breast - Mammary Tissue
Cells - Cultured fibroblasts
Cells - EBV-transformed lymphocytes
Cervix - Ectocervix
Cervix - Endocervix
Colon - Sigmoid
Colon - Transverse
Esophagus - Gastroesophageal Junction
Esophagus - Mucosa
Esophagus - Muscularis
Fallopian Tube
Heart - Atrial Appendage
Heart - Left Ventricle
Kidney - Cortex
Kidney - Medulla
Liver
Lung
Minor Salivary Gland
Muscle - Skeletal
Nerve - Tibial
Ovary
Pancreas
Pituitary
Prostate
Skin - Not Sun Exposed (Suprapubic)
Skin - Sun Exposed (Lower leg)
Small Intestine - Terminal Ileum
Spleen
Stomach
Testis
Thyroid
Uterus
Vagina
Whole Blood

FIG. 3

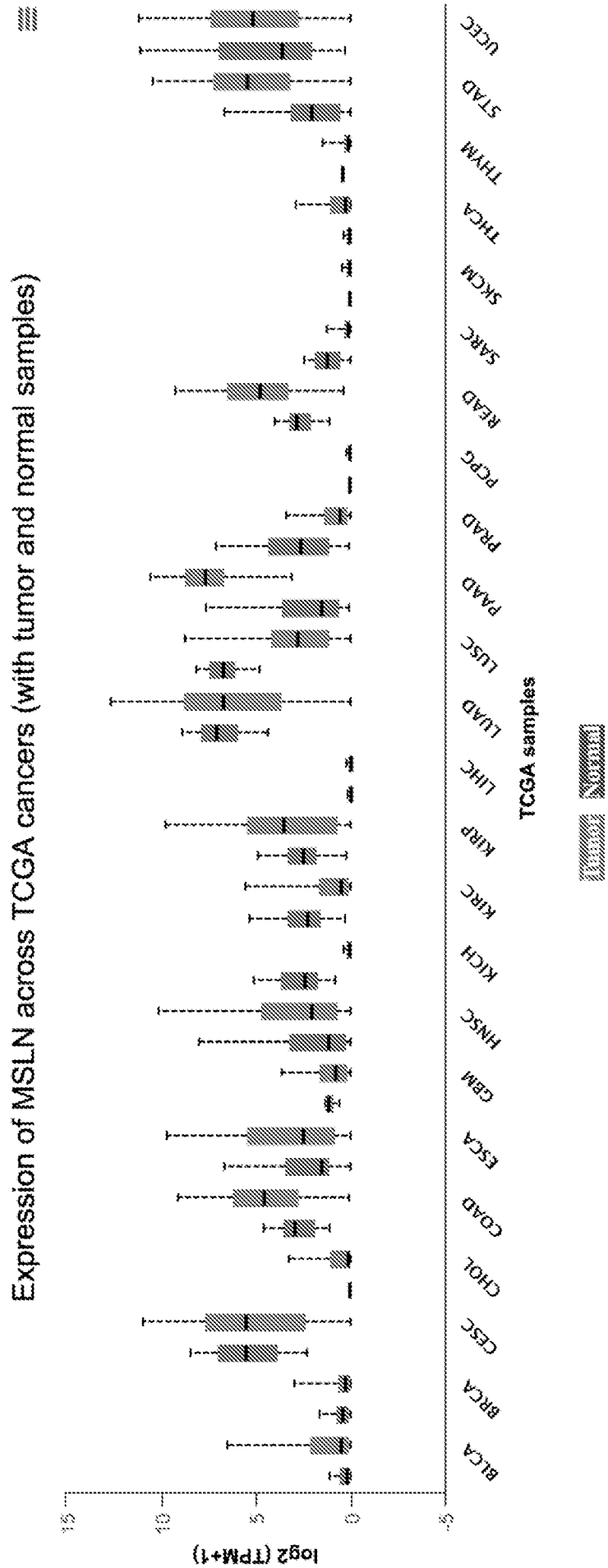

Expression of MSLN across TCGA cancers (with tumor and normal samples)
Tumor
Normal
log2 (TPM+1)
15
10
5
0
TCGA samples
BLCA
BRCA
CESC
CHOL
COAD
ESCA
GBM
HNSC
KICH
KIRC
KIRP
LIHC
LUAD
LUSC
PAAD
PRAD
PCPG
READ
SARC
SKCM
THCA
THYM
STAD
UCEC

FIG. 4

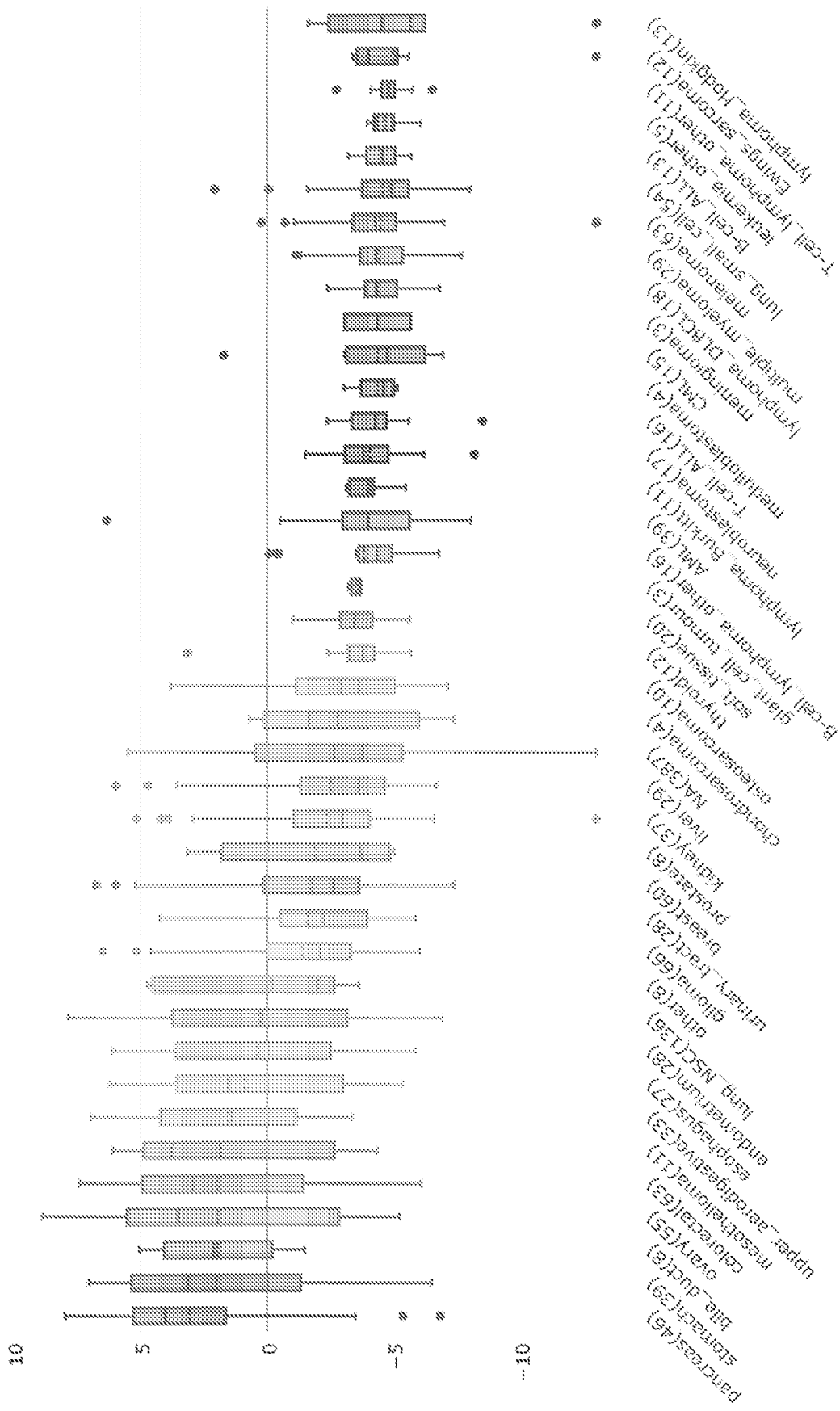

mRNA expression (RNAseq): MSLN
10
5
0
−5
−10
pancreas(46)
stomach(39)
bile_duct(8)
ovary(55)
colorectal(63)
mesothelioma(11)
esophagus(33)
endometrium(28)
lung_NSC(135)
other(8)
glioma(66)
urinary_tract(28)
breast(60)
prostate(8)
kidney(37)
liver(29)
UA(52)
chondrosarcoma(4)
osteosarcoma(10)
thyroid(12)
soft_tissue(30)
plant_cell_tumour(3)
lymphoma_other(16)
AML(39)
lymphoma_Burkitt(11)
neuroblastoma(7)
T-cell_ALL(16)
medulloblastoma(4)
CNS(15)
meningioma(3)
lymphoma_DLBCL(18)
multiple_myeloma(29)
melanoma(63)
lung_small_cell(54)
leukemia_other(13)
CML(6)
lymphoma_Hodgkin(12)
T-cell_lymphoma_other(12)

FIG. 5

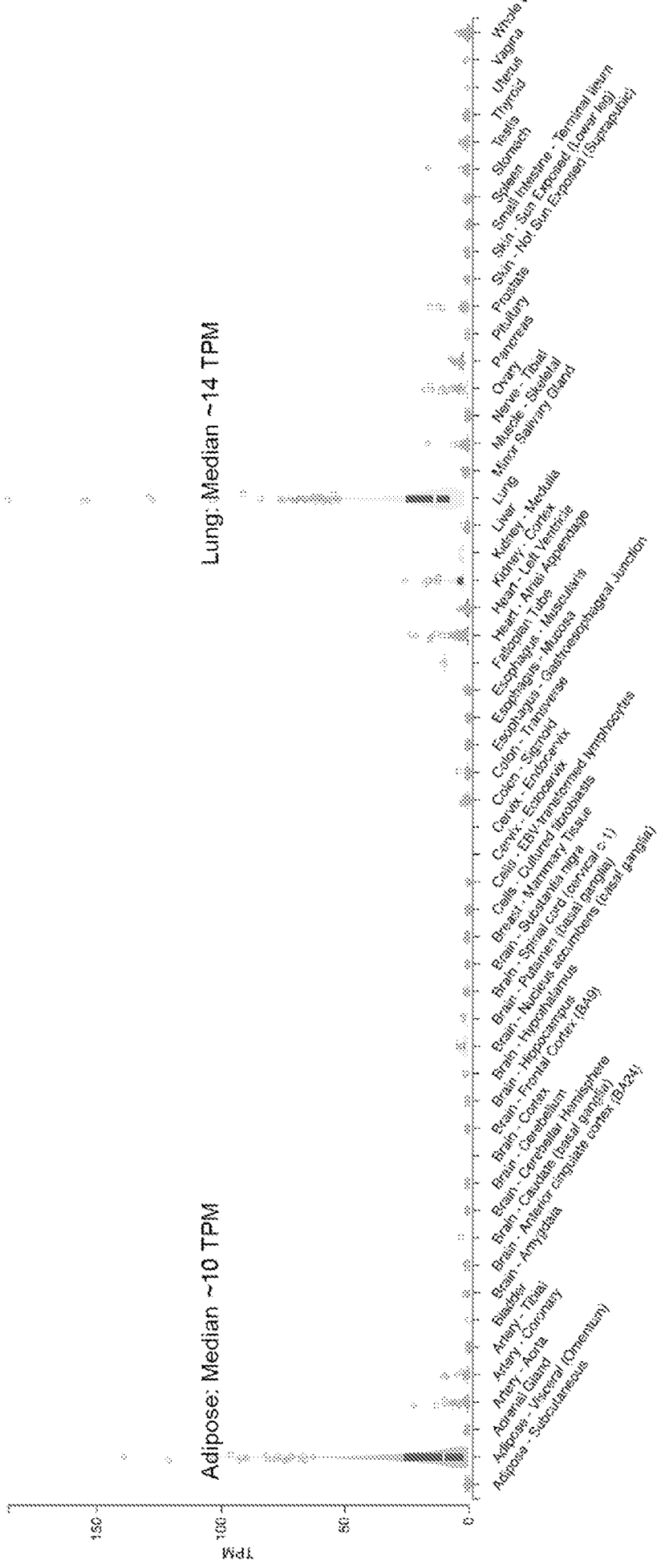

Gene expression for LRRN4 (ENSG00000125872.7)
Adipose: Median ~10 TPM
Lung: Median ~14 TPM
TPM
150
100
50
0
Adipose - Subcutaneous
Adipose - Visceral (Omentum)
Adrenal Gland
Artery - Aorta
Artery - Coronary
Artery - Tibial
Bladder
Brain - Amygdala
Brain - Anterior cingulate cortex (BA24)
Brain - Caudate (basal ganglia)
Brain - Cerebellar Hemisphere
Brain - Cerebellum
Brain - Cortex
Brain - Frontal Cortex (BA9)
Brain - Hippocampus
Brain - Hypothalamus
Brain - Nucleus accumbens (basal ganglia)
Brain - Putamen (basal ganglia)
Brain - Spinal cord (cervical c-1)
Brain - Substantia nigra
Breast - Mammary Tissue
Cells - Cultured fibroblasts
Cells - EBV-transformed lymphocytes
Cervix - Ectocervix
Cervix - Endocervix
Colon - Sigmoid
Colon - Transverse
Esophagus - Gastroesophageal Junction
Esophagus - Mucosa
Esophagus - Muscularis
Fallopian Tube
Heart - Atrial Appendage
Heart - Left Ventricle
Kidney - Cortex
Kidney - Medulla
Liver
Lung
Minor Salivary Gland
Muscle - Skeletal
Nerve - Tibial
Ovary
Pancreas
Pituitary
Prostate
Skin - Not Sun Exposed (Suprapubic)
Skin - Sun Exposed (Lower leg)
Small Intestine - Terminal Ileum
Spleen
Stomach
Testis
Thyroid
Uterus
Vagina
Whole Blood

FIG. 6

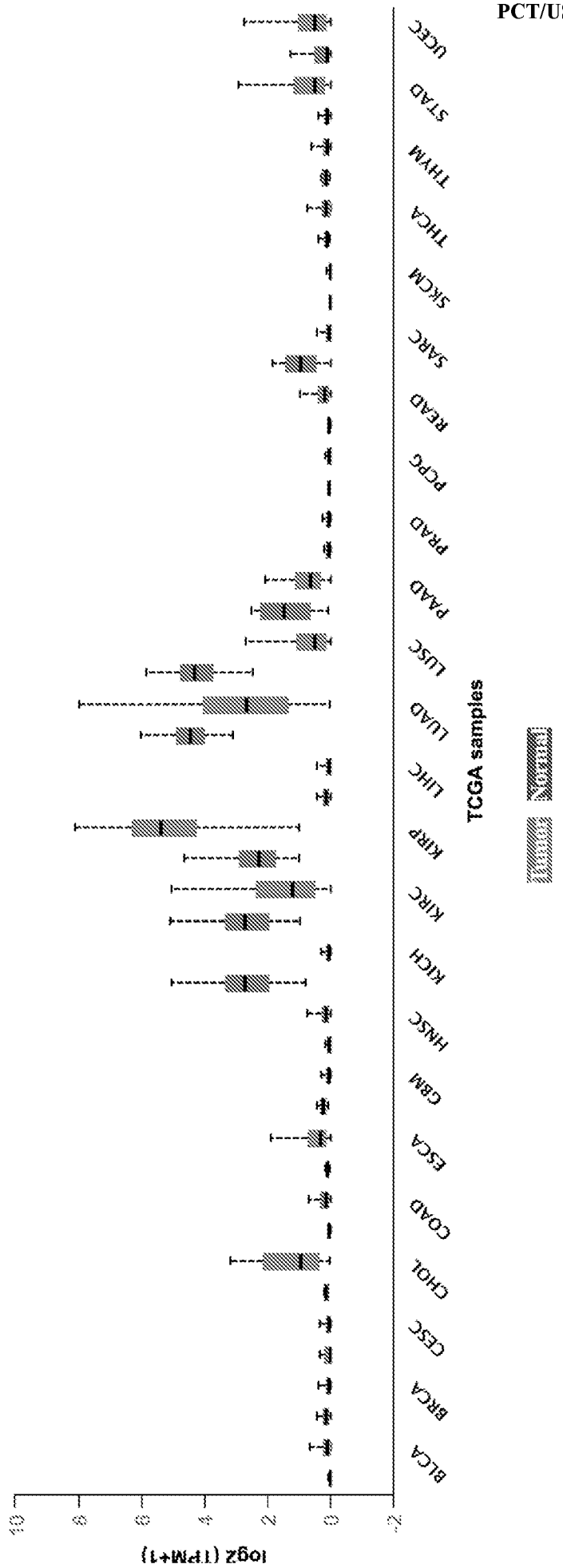

Expression of LRRN4 across TCGA cancers (with tumor and normal samples)
log2 (TPM+1)
10
8
6
4
2
0
-2
TCGA samples
Tumor
Normal
BLCA
BRCA
CESC
CHOL
COAD
ESCA
GBM
HNSC
KICH
KIRC
KIRP
LIHC
LUAD
LUSC
PAAD
PRAD
PCPG
READ
SARC
SKCM
THCA
THYM
STAD
UCEC

FIG. 7

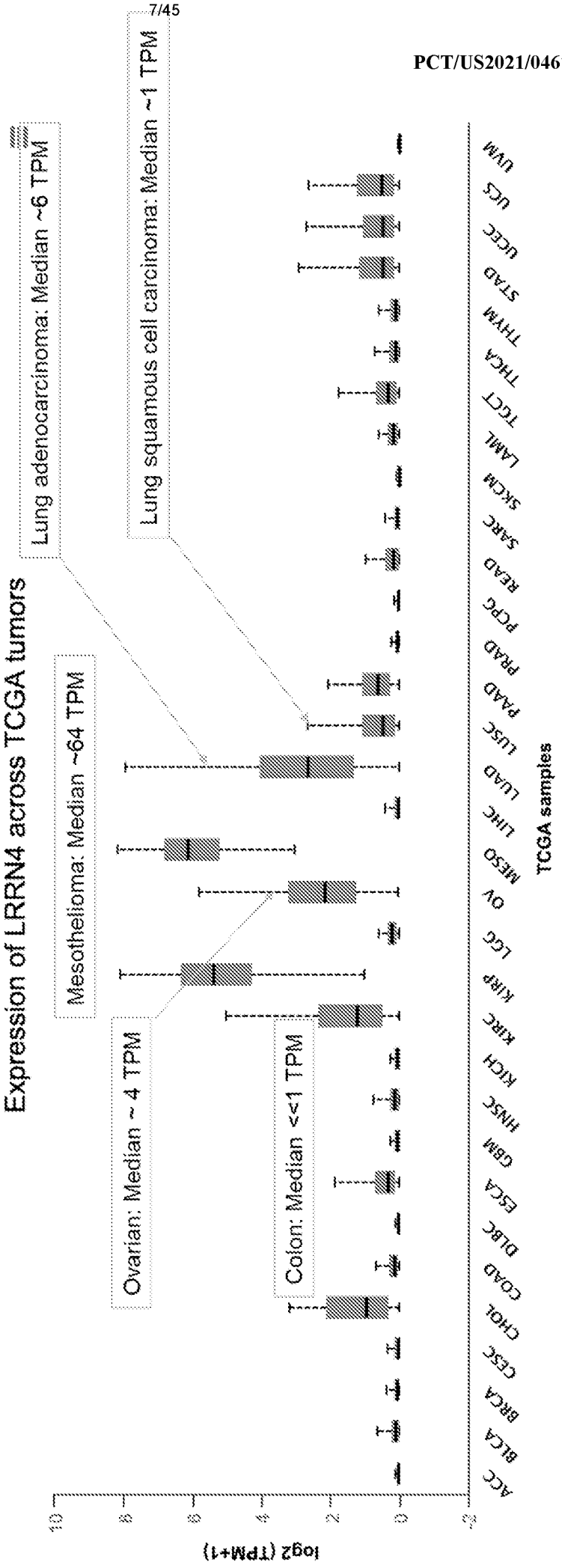

Expression of LRRN4 across TCGA tumors
Lung adenocarcinoma: Median ~6 TPM
Lung squamous cell carcinoma: Median ~1 TPM
Mesothelioma: Median ~64 TPM
Ovarian: Median ~ 4 TPM
Colon: Median <<1 TPM
log2 (TPM+1)
10
8
6
4
2
0
-2
TCGA samples
ACC
BLCA
BRCA
CESC
CHOL
COAD
DLBC
ESCA
GBM
HNSC
KICH
KIRC
KIRP
LCC
OV
MESO
LIHC
LUAD
LUSC
PAAD
PRAD
PCPG
READ
SARC
SKCM
LAML
TGCT
THCA
THYM
STAD
UCEC
UCS
UVM

FIG. 8

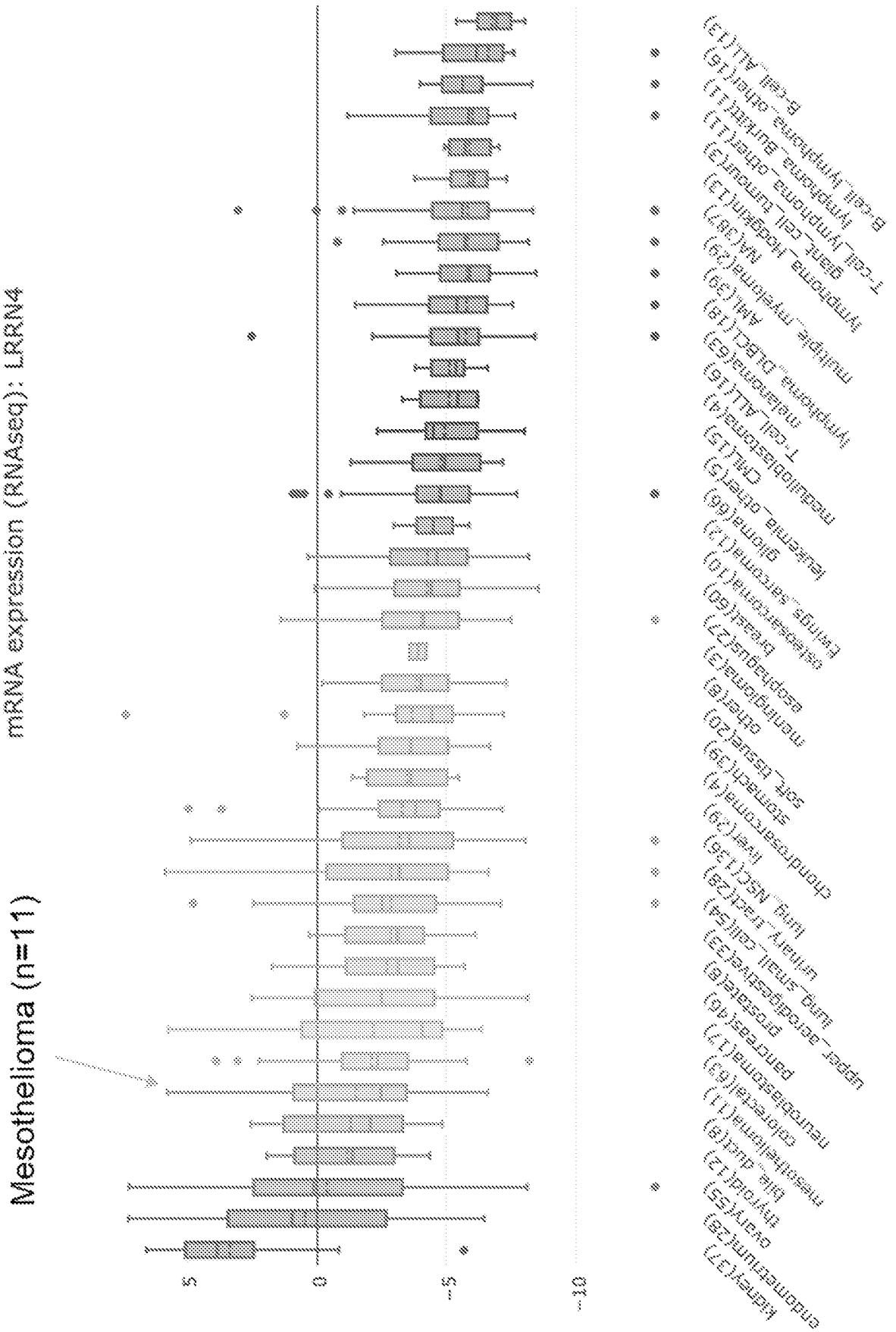

mRNA expression (RNAseq): LRRN4
Mesothelioma (n=11)
5
0
−5
−10
kidney(37)
endometrium(28)
ovary(55)
bile_duct(12)
mesothelioma(9)
colorectal(11)
neuroblastoma(69)
pancreas(17)
prostate(46)
upper_aerodigestive(35)
lung_small_cell(54)
urinary_tract(28)
lung_NSCC(136)
liver(29)
chondrosarcoma(4)
stomach(39)
soft_tissue(20)
mononuclear(8)
other(8)
esophagus(3)
breast(27)
osteosarcoma(60)
glioma(10)
ewings_sarcoma(11)
leukemia_other(6)
glioma(6)
medulloblastoma(5)
CML(15)
T-cell_ALL(4)
malignant(63)
lymphoma_DLBCL(19)
AML(39)
multiple_myeloma(39)
NA(987)
lymphoma_Hodgkin(13)
germ_cell_tumour(3)
lymphoma_other(11)
lymphoma_Burkitt(11)
T-cell_lymphoma(15)
B-cell_lymphoma_other(16)
B-cell_ALL(13)

FIG. 9

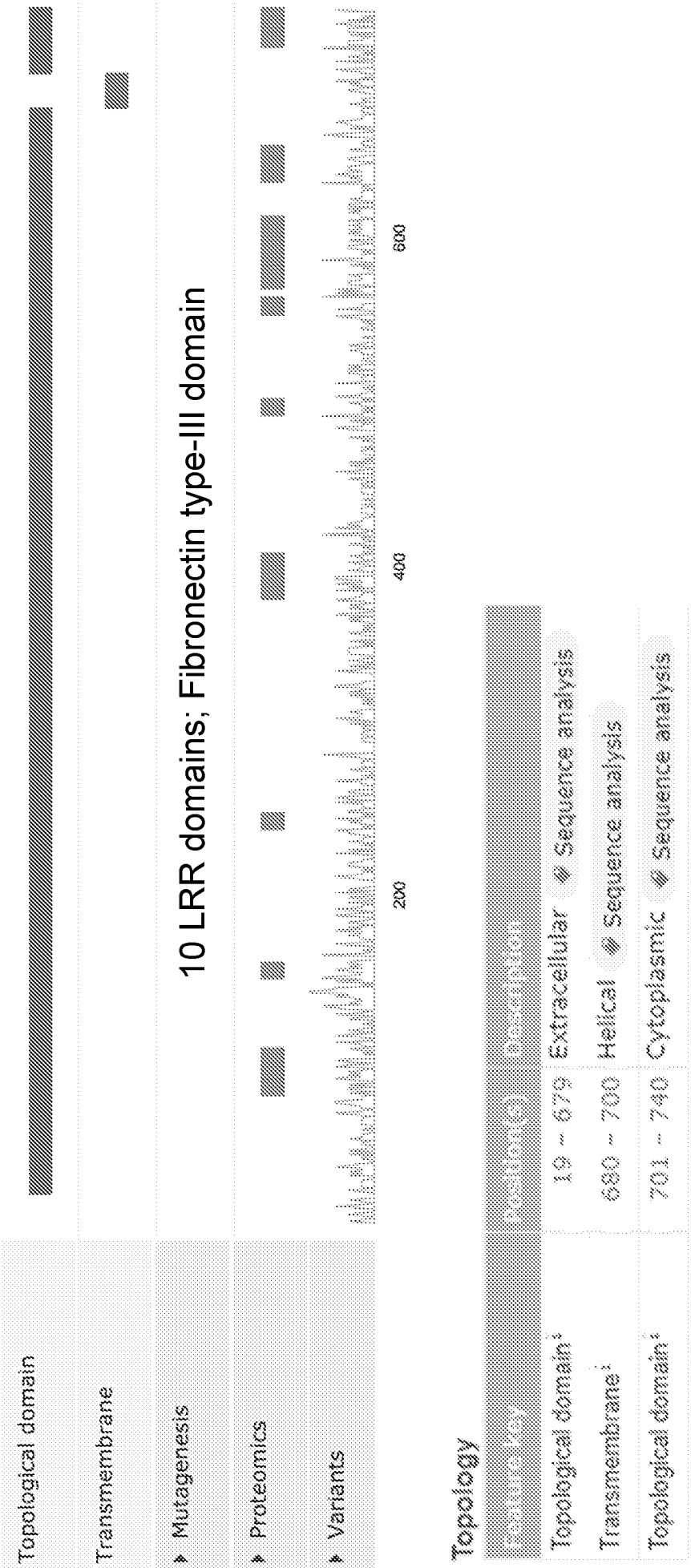

Topological domain
Transmembrane
Mutagenesis
Proteomics
Variants
10 LRR domains; Fibronectin type-III domain
200
400
600
Topology
FEATURE KEY
POSITION(S)
DESCRIPTION
Topological domain
19 - 679
Extracellular
Sequence analysis
Transmembrane
680 - 700
Helical
Sequence analysis
Topological domain
701 - 740
Cytoplasmic
Sequence analysis

FIG. 10A

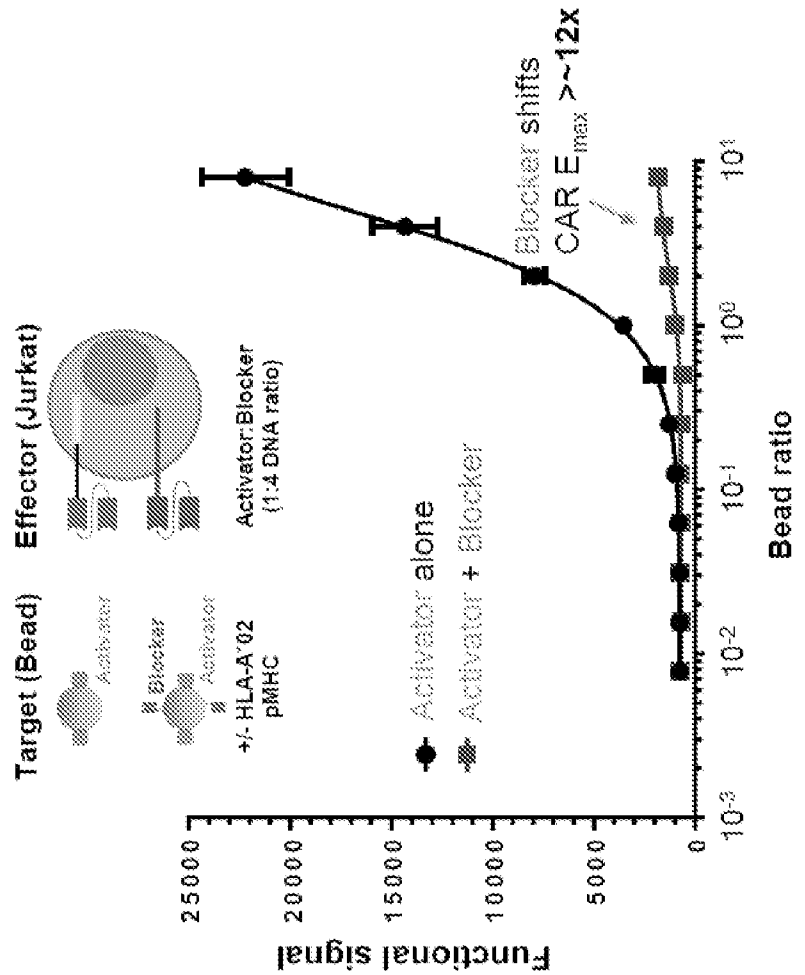
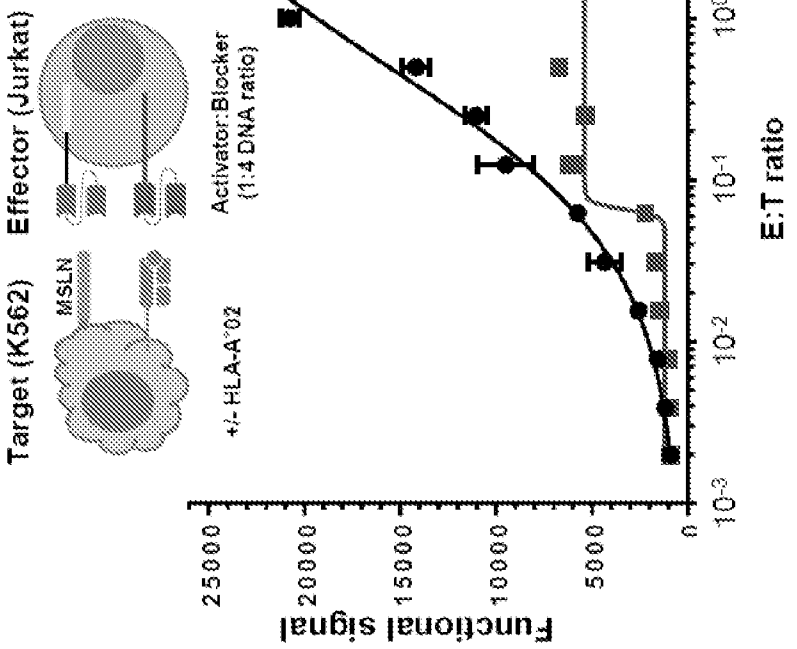
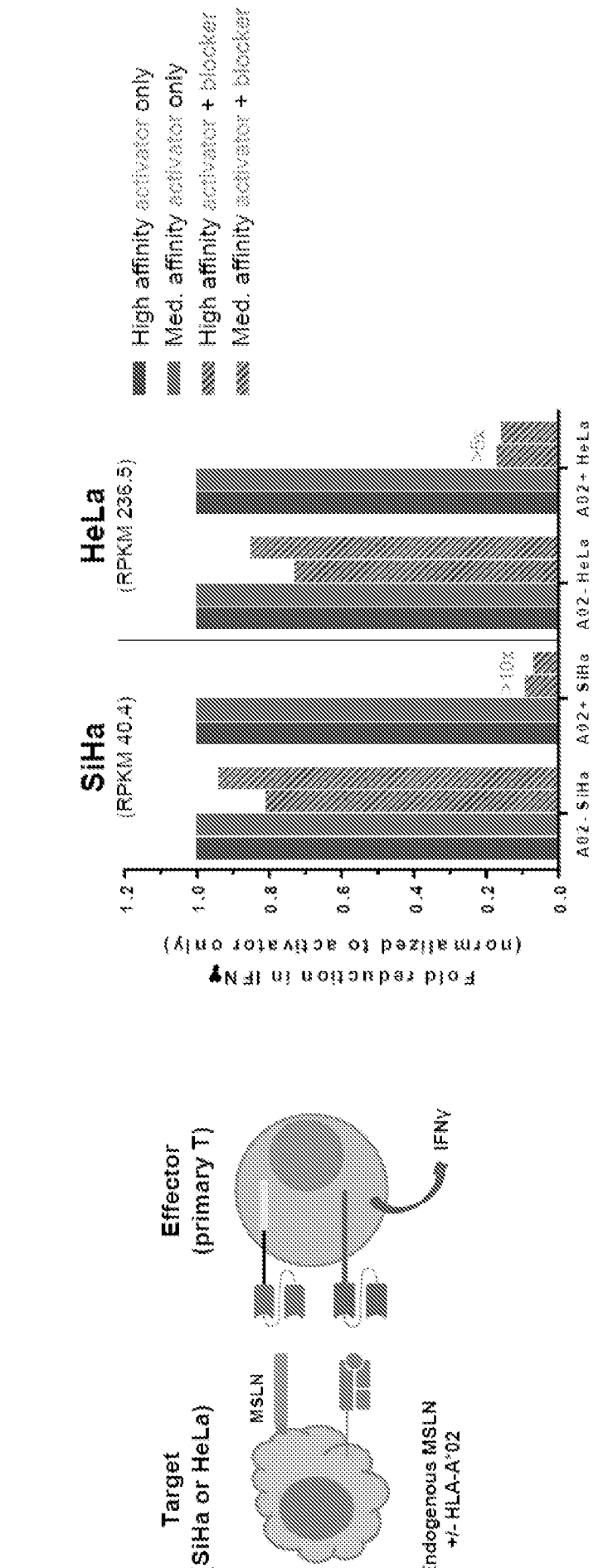


FIG. 10B



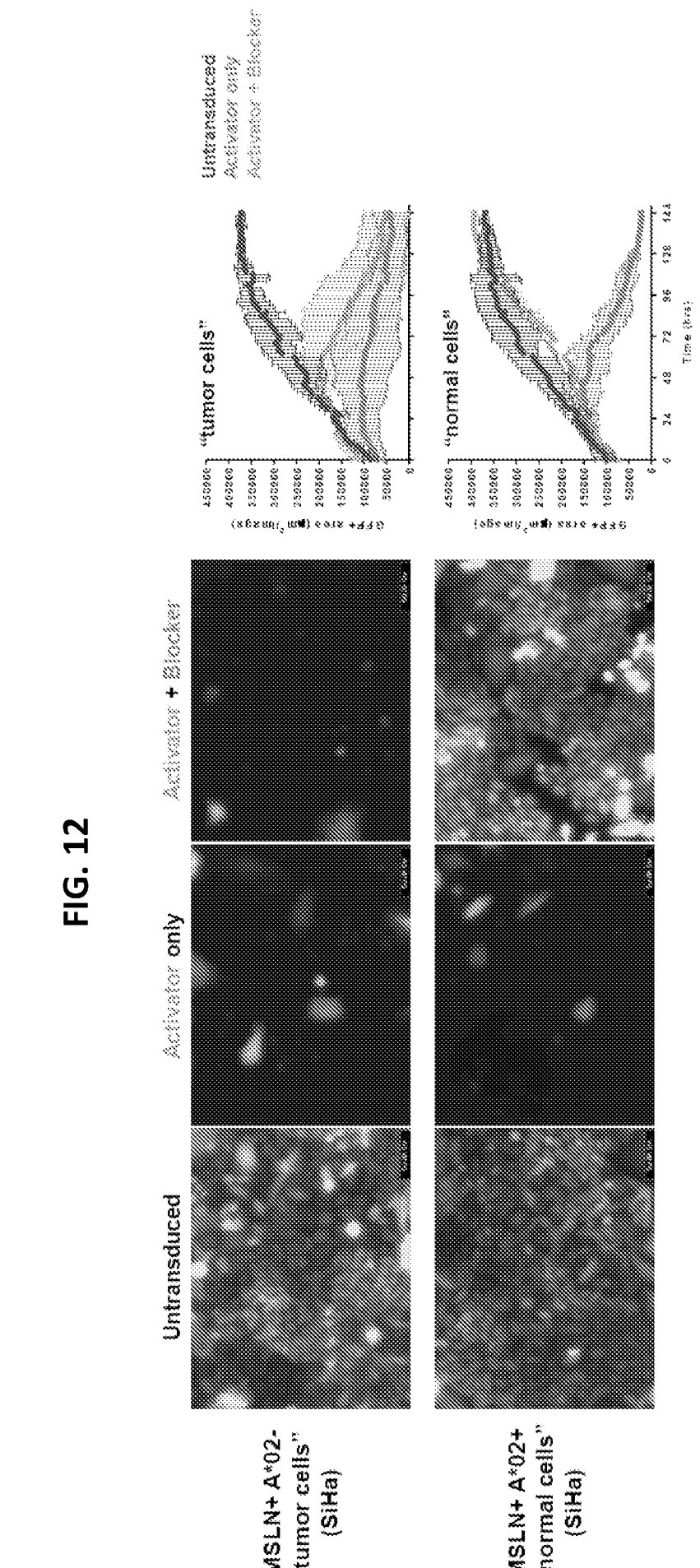
Activator = MSLN CAR; Blocker = A2-LIR-1

FIG. 11



Activator = MSLN CAR; Blocker = A2-LIR-1

FIG. 12



Activator = MSLN CAR; Blocker = A2-LIR-1

FIG. 13

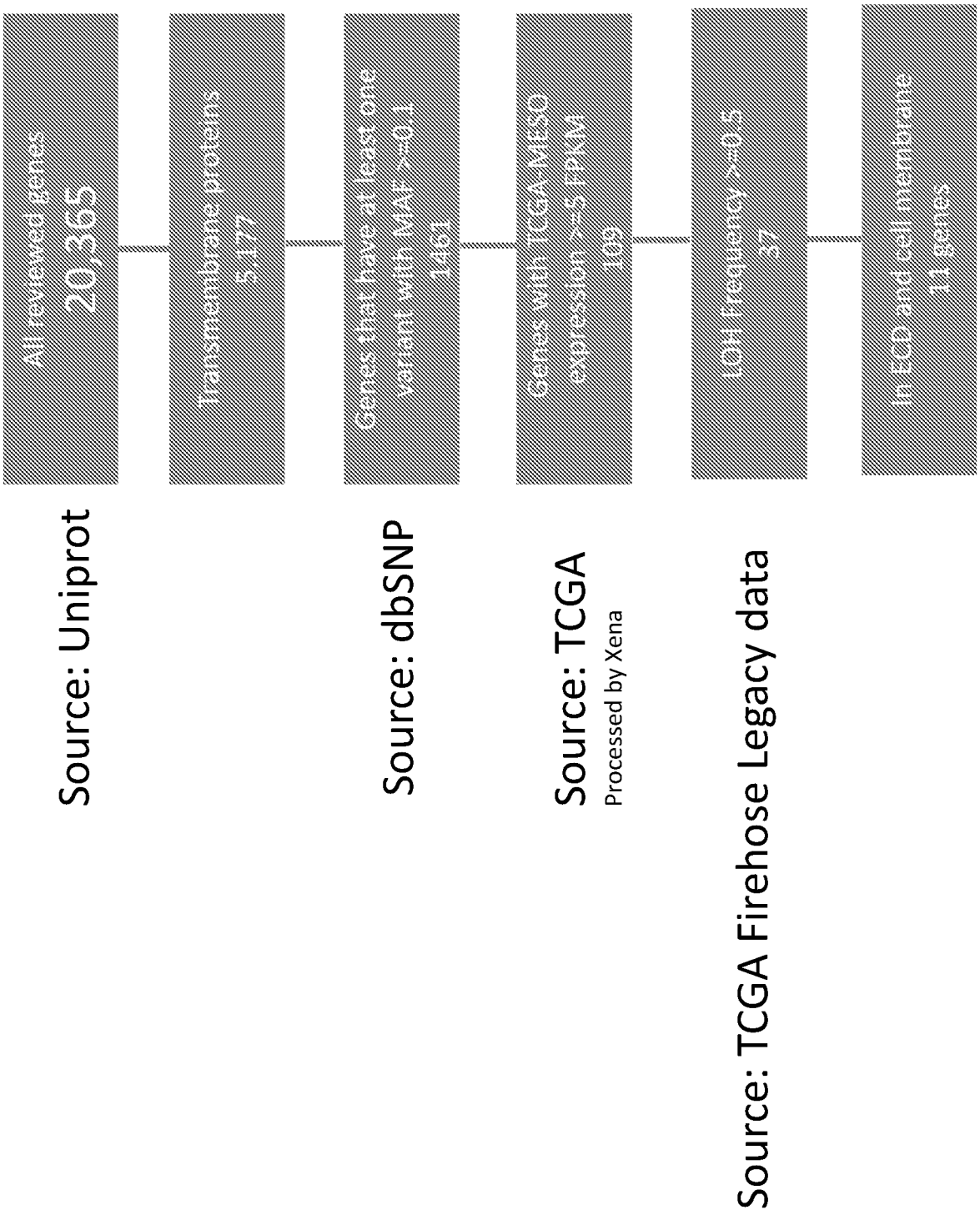
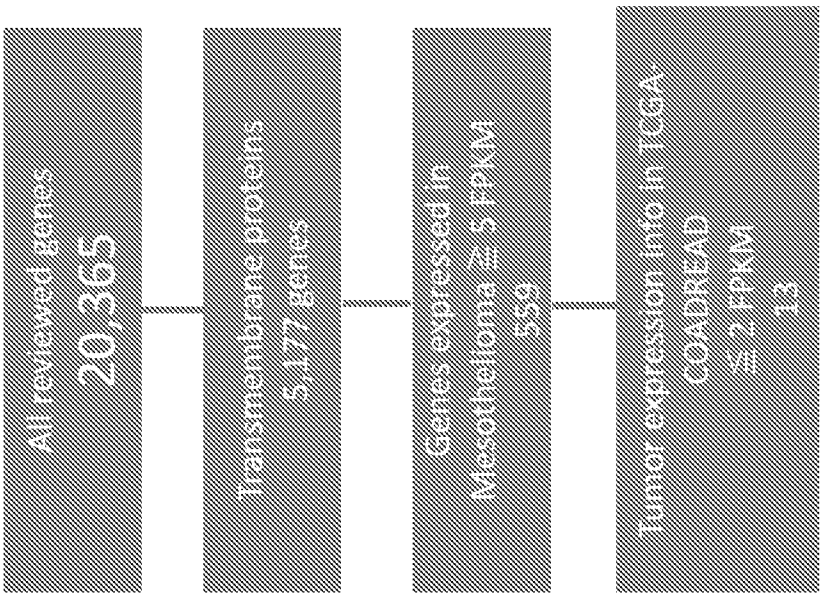

All reviewed genes
20,365
Source: Uniprot
Transmembrane proteins
5,177
Genes that have at least one
variant with MAF >=0.1
1461
Source: dbSNP
Genes with TCGA-MESO
expression >=5 FPKM
109
Source: TCGA
Processed by Xena
10% frequency >=0.5
37
In ECP and cell membrane
11 genes
Source: TCGA Firehose Legacy data

FIG. 14



Source: Uniprot

FIG. 15A

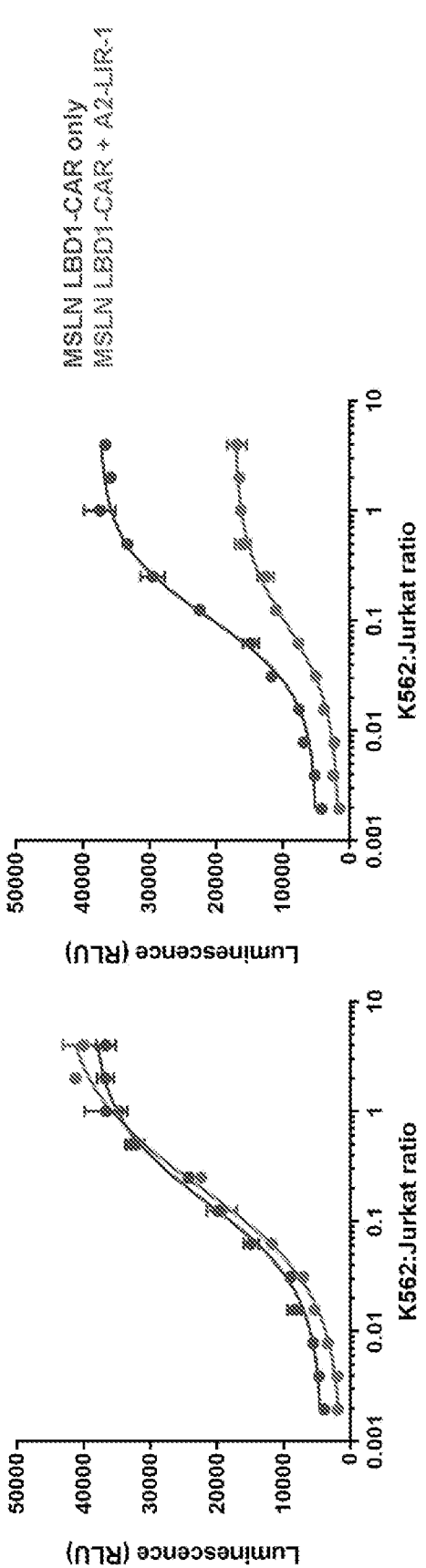


FIG. 15B

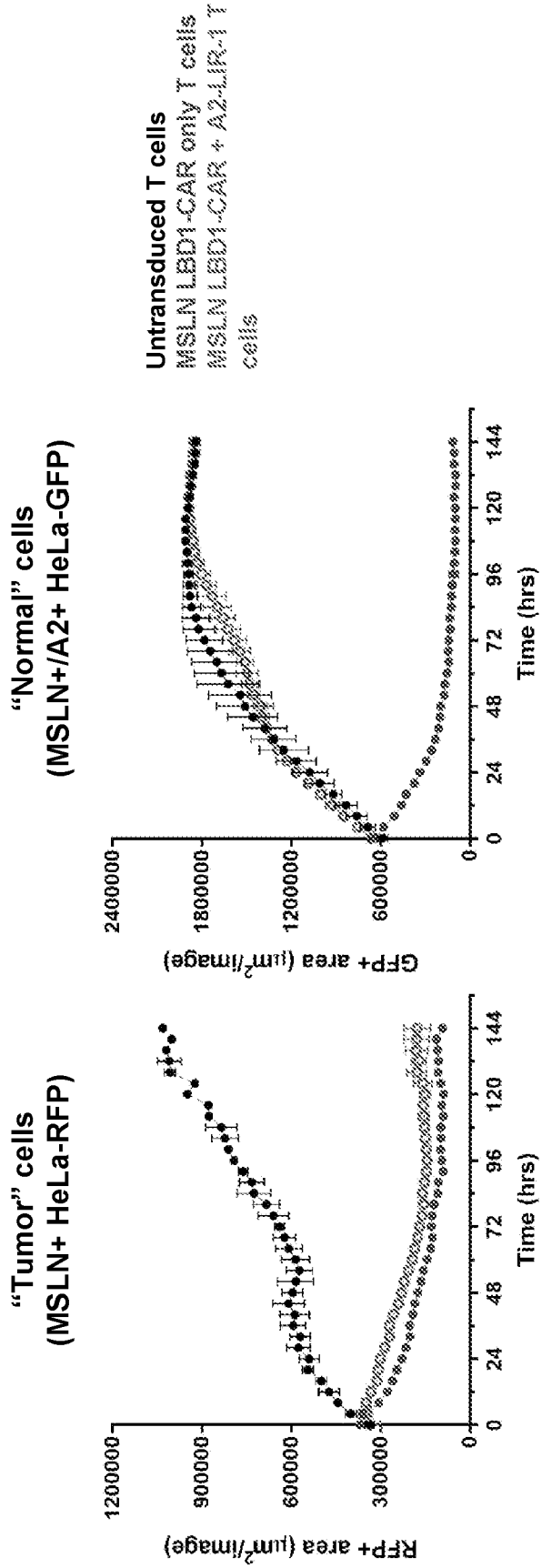


FIG. 15C

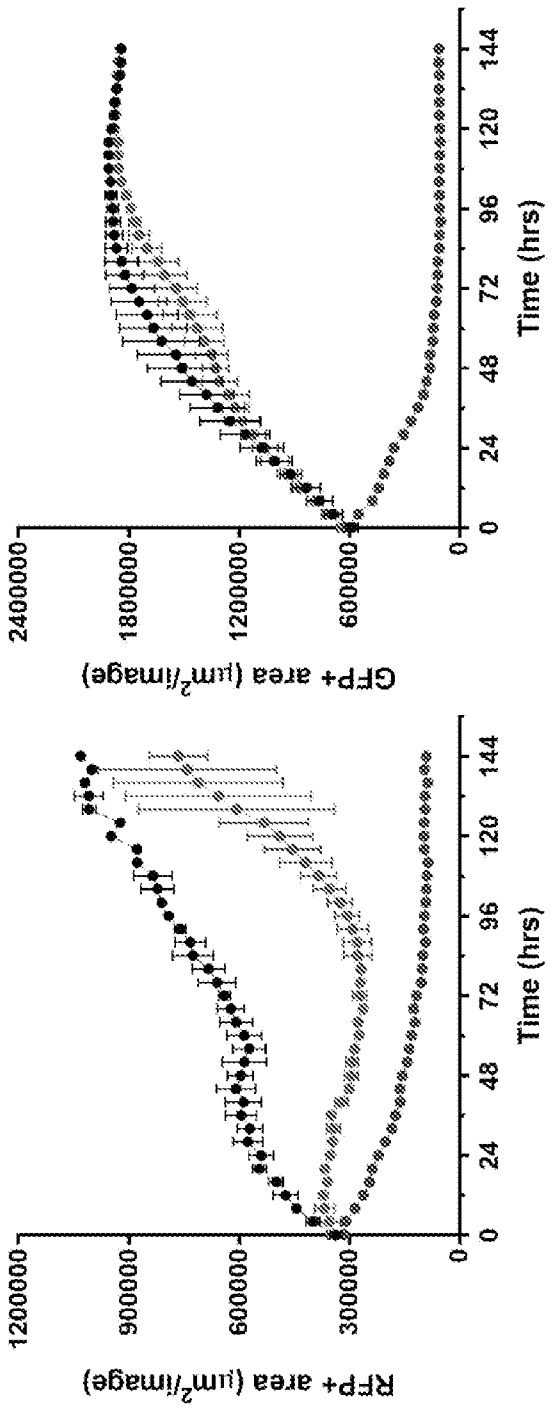

Untransduced T cells
MSLN LBD2-CAR only T cells
MSLN LBD2-CAR + A2-LIR-1 T cells
GFP+ area (μm²/image)
2400000
1800000
1200000
600000
0
0
24
48
72
96
120
144
Time (hrs)
RFP+ area (μm²/image)
1200000
900000
600000
300000
0
0
24
48
72
96
120
144
Time (hrs)

FIG. 16

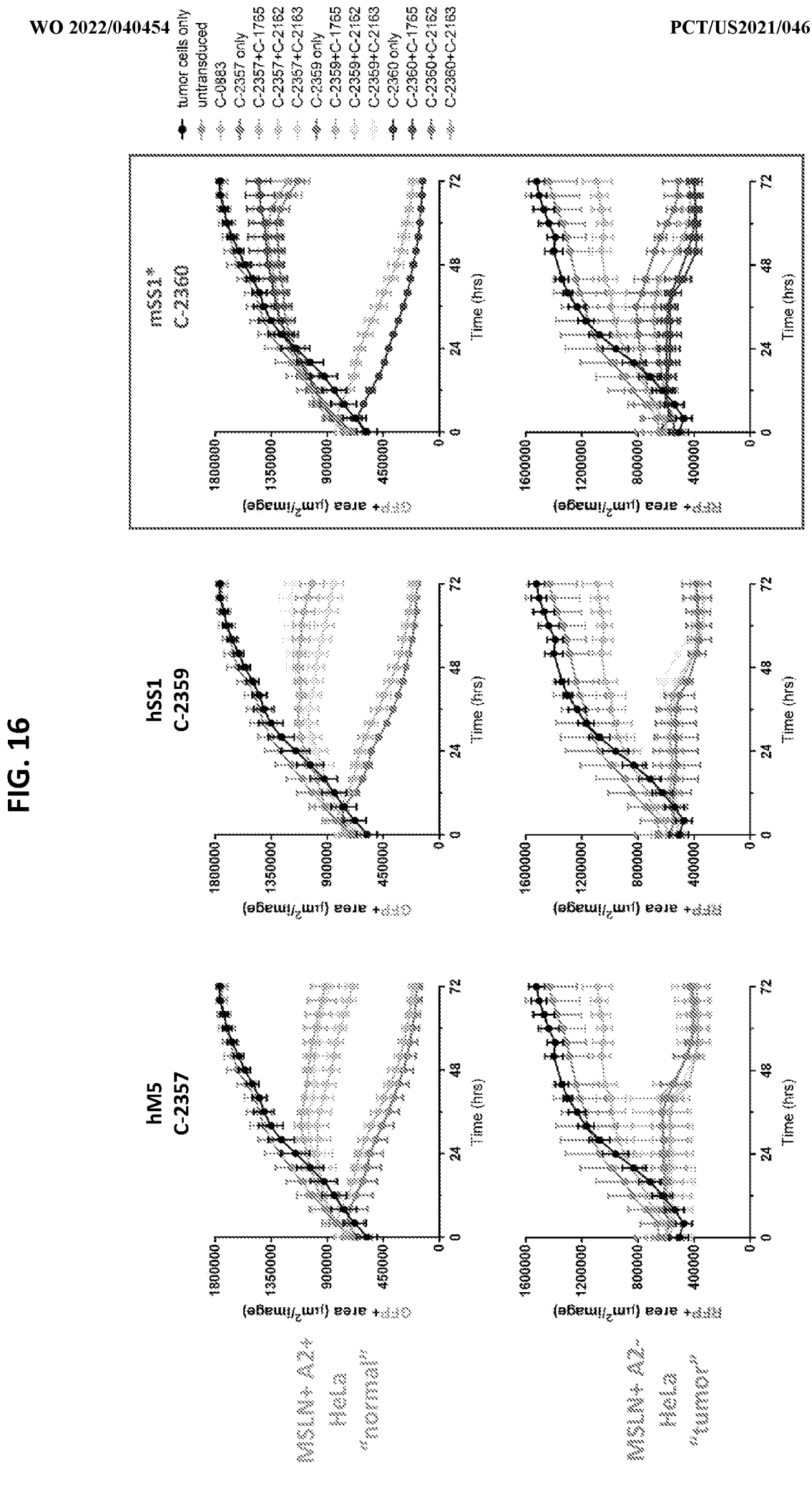

tumor cells only
untransduced
C-0883
C-2357 only
C-2357+C-1765
C-2357+C-2162
C-2357+C-2163
C-2359 only
C-2359+C-1765
C-2359+C-2162
C-2359+C-2163
C-2360 only
C-2360+C-1765
C-2360+C-2162
C-2360+C-2163
mSS1*
C-2360
hSS1
C-2359
hM5
C-2357
MSLN+ A2+
Hela
"normal"
MSLN+ A2-
Hela
"tumor"
GFP+ area (μm²/image)
RFP+ area (μm²/image)
Time (hrs)
0
24
48
72
450000
900000
1350000
1800000
400000
800000
1200000
1600000

FIG. 17

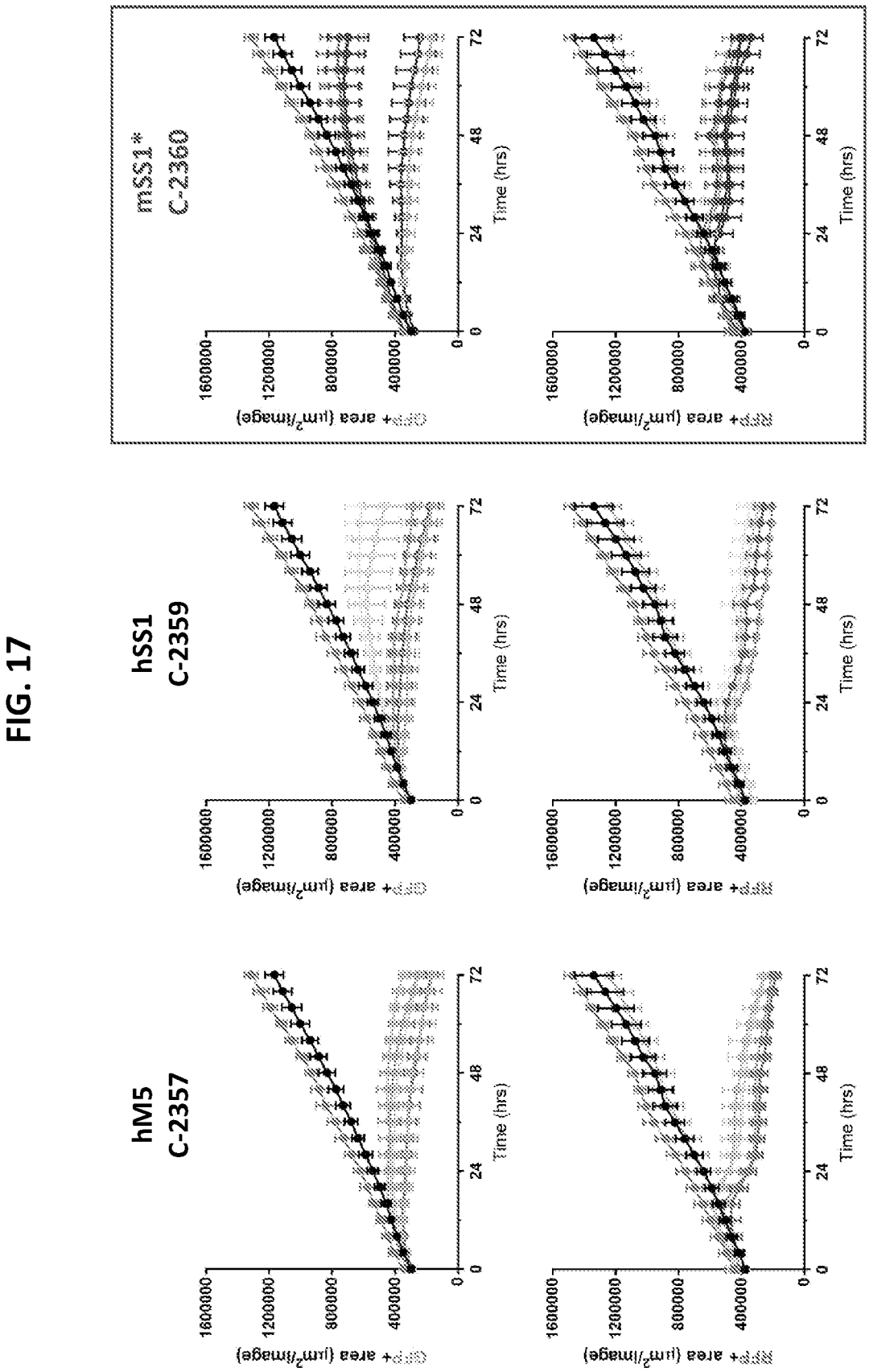

tumor cells only
untransduced
C-0883
C-2357 only
C-2357+C-1765
C-2357+C-2162
C-2357+C-2163
C-2359 only
C-2359+C-1765
C-2359+C-2162
C-2359+C-2163
C-2360 only
C-2360+C-1765
C-2360+C-2162
C-2360+C-2163
mSS1*
C-2360
hSS1
C-2359
hM5
C-2357
MSLN+ A2+
Capan-2
"normal"
MSLN+ A2-
Capan-2
"tumor"
GFP+ area (µm²/image)
Time (hrs)
0
24
48
72
400000
800000
1200000
1600000

FIG. 18

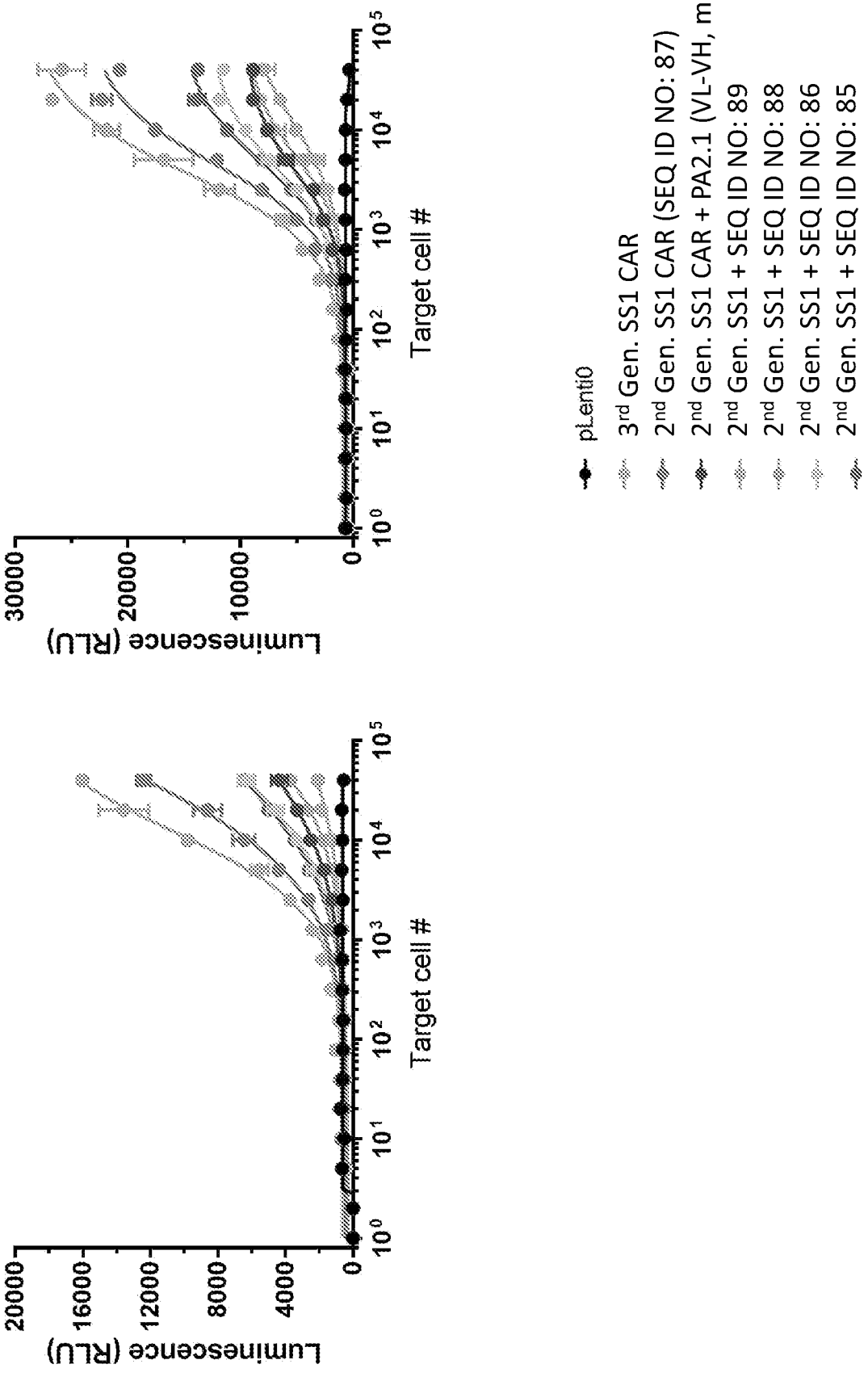

Native MSLN+ A2+
HCT116 WT
HeLa + A2
Luminescence (RLU)
Target cell #
pLenti0
3rd Gen. SS1 CAR
2nd Gen. SS1 CAR (SEQ ID NO: 87)
2nd Gen. SS1 CAR + PA2.1 (VL-VH, mouse)
2nd Gen. SS1 + SEQ ID NO: 89
2nd Gen. SS1 + SEQ ID NO: 88
2nd Gen. SS1 + SEQ ID NO: 86
2nd Gen. SS1 + SEQ ID NO: 85

FIG. 19

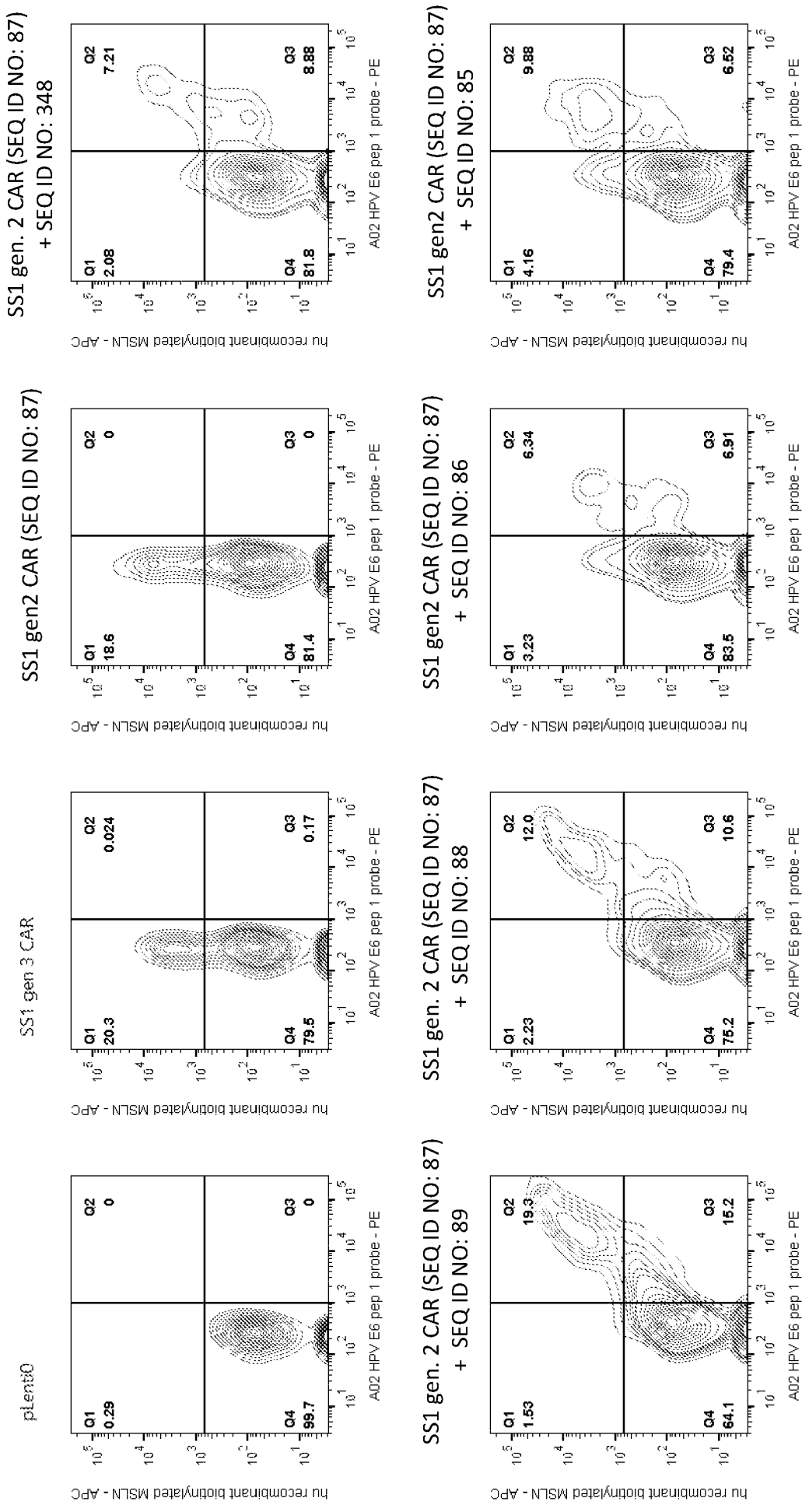

plenti0
SS1 gen 3 CAR
SS1 gen2 CAR (SEQ ID NO: 87)
SS1 gen. 2 CAR (SEQ ID NO: 87) + SEQ ID NO: 348
SS1 gen2 CAR (SEQ ID NO: 87) + SEQ ID NO: 85
SS1 gen2 CAR (SEQ ID NO: 87) + SEQ ID NO: 86
SS1 gen. 2 CAR (SEQ ID NO: 87) + SEQ ID NO: 88
SS1 gen. 2 CAR (SEQ ID NO: 87) + SEQ ID NO: 89
Q1 0.29
Q2 0
Q4 99.7
Q3 0
Q1 20.3
Q2 0.024
Q4 79.5
Q3 0.17
Q1 18.6
Q2 0
Q4 81.4
Q3 0
Q1 2.08
Q2 7.21
Q4 81.8
Q3 8.88
Q1 3.23
Q2 6.34
Q4 83.5
Q3 6.91
Q1 4.16
Q2 9.88
Q4 79.4
Q3 6.52
Q1 2.23
Q2 12.0
Q4 75.2
Q3 10.6
Q1 1.53
Q2 19.3
Q4 64.1
Q3 15.2
hu recombinant biotinylated MSLN - APC
A02 HPV E6 pep 1 probe - PE

FIG. 20A

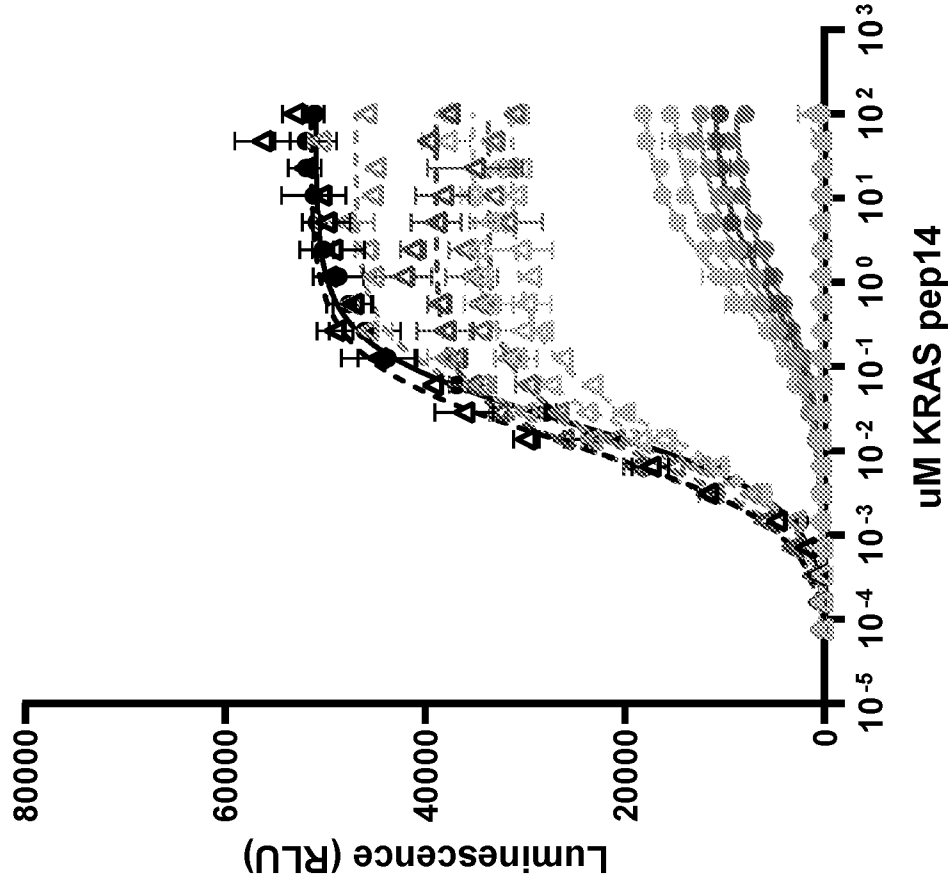
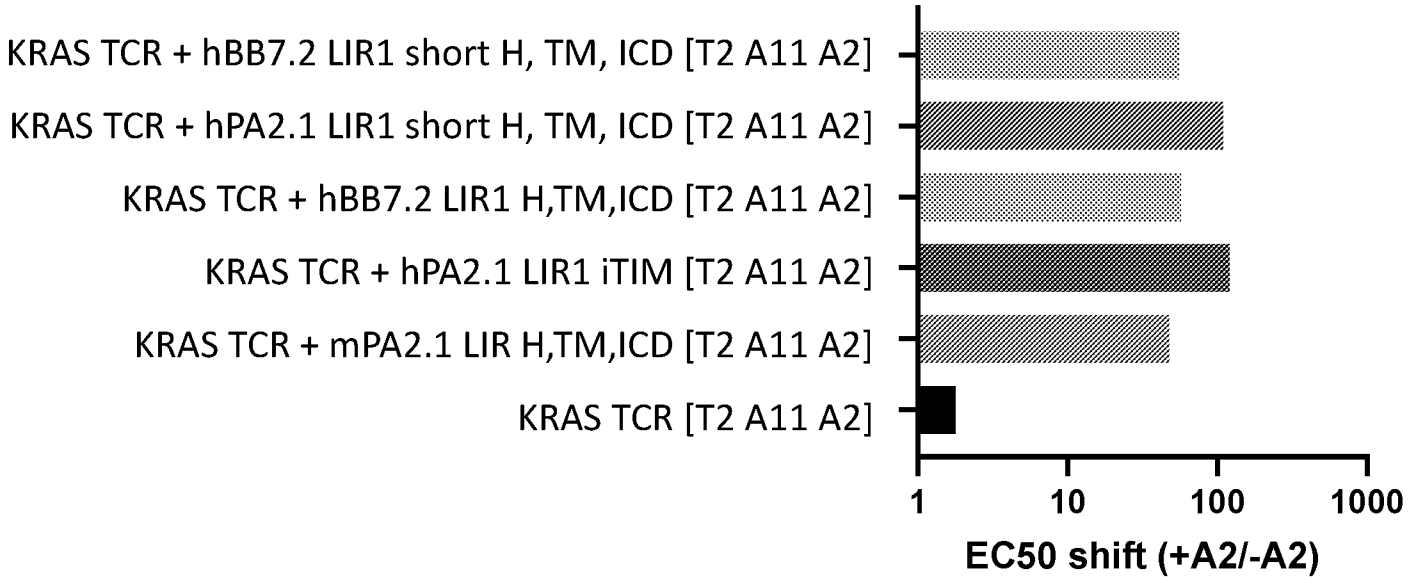

pLenti [T2 A11]
KRAS TCR [T2 A11]
KRAS TCR + mPA2.1 LIR H,TM,ICD [T2 A11]
KRAS TCR + hPA2.1 LIR1 iTIM (SEQ ID NO: 89) [T2 A11]
KRAS TCR + hBB7.2 LIR1 H,TM,ICD [T2 A11]
KRAS TCR + hPA2.1 LIR1 short H, TM, ICD (SEQ ID NO: 90) [T2 A11]
KRAS TCR + hBB7.2 LIR1 short H, TM, ICD [T2 A11]
pLenti [T2 A11 A2]
KRAS TCR [T2 A11 A2]
KRAS TCR + mPA2.1 LIR H,TM,ICD [T2 A11 A2]
KRAS TCR + hPA2.1 LIR1 iTIM (SEQ ID NO: 89) [T2 A11 A2]
KRAS TCR + hBB7.2 LIR1 H,TM,ICD [T2 A11 A2]
KRAS TCR + hPA2.1 LIR1 short H, TM, ICD (SEQ ID NO: 90) [T2 A11 A2]
KRAS TCR + hBB7.2 LIR1 short H, TM, ICD [T2 A11 A2]
Luminescence (RLU)
80000
60000
40000
20000
0
10-5 10-4 10-3 10-2 10-1 100 101 102 103
uM KRAS pep14

FIG. 20B



PA2.1 scFv LIR1 HTICD	Mouse PA2.1	**YGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV**
BB7.2.6 scFv LIR1 HTICD	hPBB7.2.6	**YGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV**
BB7.2.6 scFv LIR1 sHTICD	hPBB7.2.6	**VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV**
PA2.1.14 scFv LIR1 iTIM	hPA2.1.14	**YGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV**
PA2.1.14 scFv LIR1 sHTICD	hPA2.1.14	**VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV**

FIG. 21A

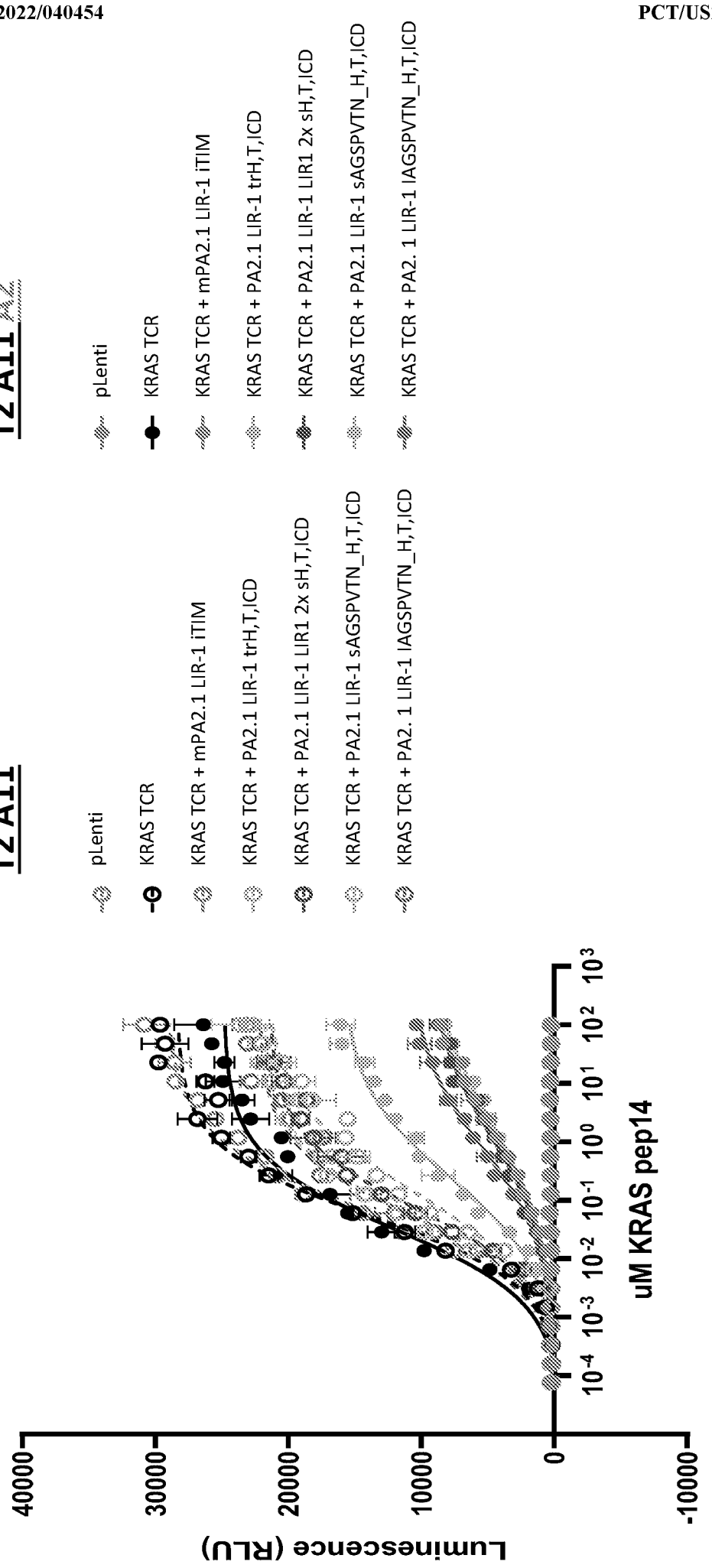
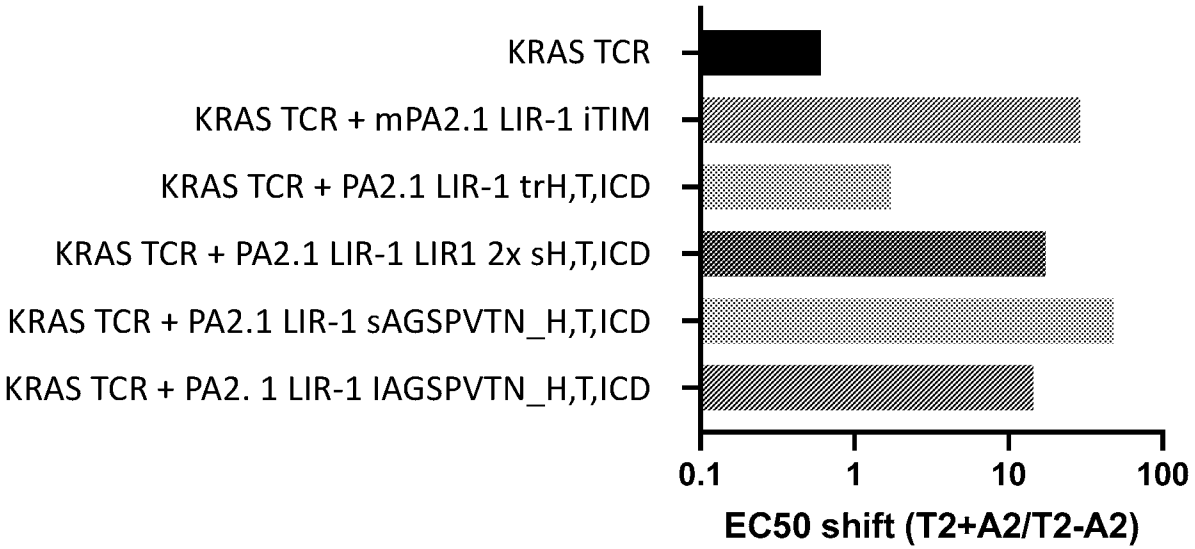

T2 A11
pLenti
KRAS TCR
KRAS TCR + mPA2.1 LIR-1 iTIM
KRAS TCR + PA2.1 LIR-1 trH,T,ICD
KRAS TCR + PA2.1 LIR-1 LIR1 2x sH,T,ICD
KRAS TCR + PA2.1 LIR-1 sAGSPVTN_H,T,ICD
KRAS TCR + PA2. 1 LIR-1 IAGSPVTN_H,T,ICD
T2 A11 A2
pLenti
KRAS TCR
KRAS TCR + mPA2.1 LIR-1 iTIM
KRAS TCR + PA2.1 LIR-1 trH,T,ICD
KRAS TCR + PA2.1 LIR-1 LIR1 2x sH,T,ICD
KRAS TCR + PA2.1 LIR-1 sAGSPVTN_H,T,ICD
KRAS TCR + PA2. 1 LIR-1 IAGSPVTN_H,T,ICD
Luminescence (RLU)
40000
30000
20000
10000
0
-10000
10-4 10-3 10-2 10-1 100 101 102 103
uM KRAS pep14

FIG. 21B



blocker	hinge	length
mPA2.1_scFv LIR1 iTIM	LIR1	64
PA2.1_scFv LIR1 trHTICD	LIR1 trunc	32
PA2.1_scFv LIR1 2x sH TICD	2x LIR1 short	85
PA2.1_scFv sAGSPVTN_H LIR1 TICD	sAGSPVTN	67
PA2.1_scFv lAGSPVTN_H LIR1 TICD	lAGSPVTN	75

mPA2.1_scFv LIR1 iTIM	SS**YGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV**VIGIL
PA2.1_scFv LIR1 trHTICD	SS**TTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV**VIGIL
PA2.1_scFv sAGSPVTN_H LIR1 TICD	SS**AGSGGSGGSGGSPVPSTPPTPSPSTPPTPSPSGGSGNSSGSGGSPVPSTPPTPSPSTPPTPSPSASV**VIGIL
PA2.1_scFv lAGSPVTN_H LIR1 TICD	SS**AGSGGSGGSGGSPVPSTPPTNSSSTPPTPSPSPVPSTPPTNSSSTPPTPSPSPVPSTPPTNSSSTPPTPSPSASV**VIGIL
PA2.1_scFv LIR1 2x sH TICD	SS**VVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGR HLGV**VIGIL

FIG. 22A

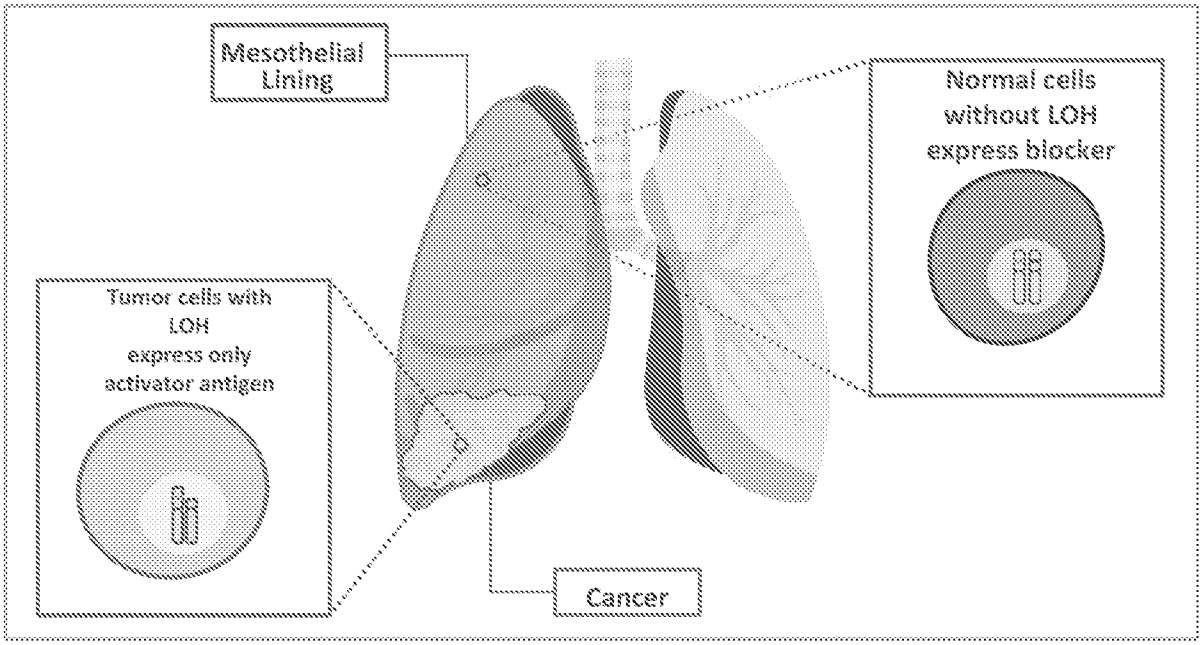


FIG. 22B

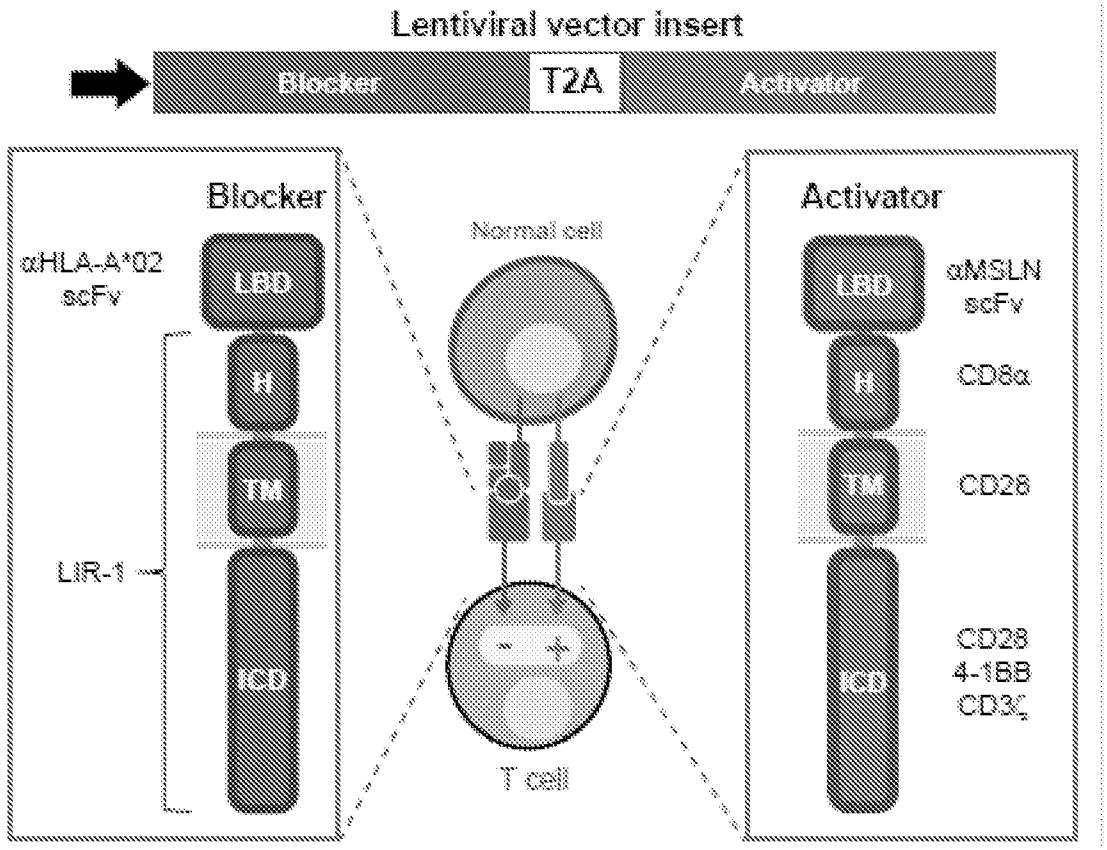


FIG. 23A

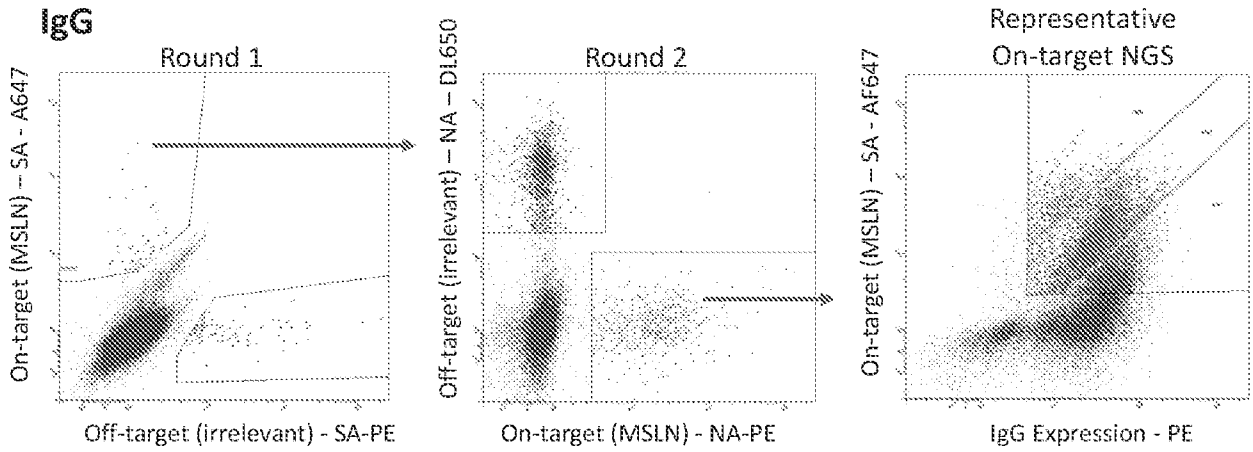


FIG. 23B

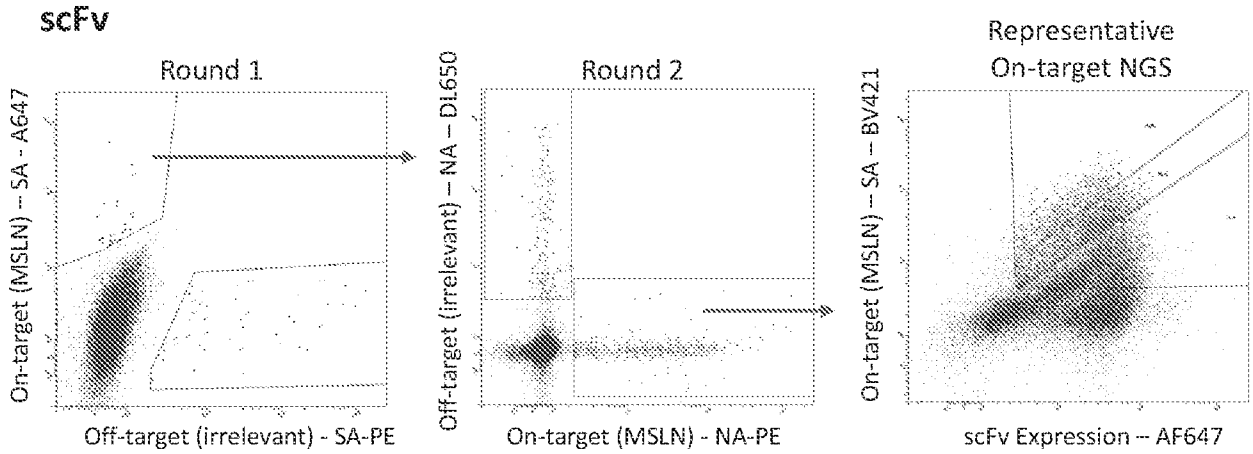


FIG. 23C

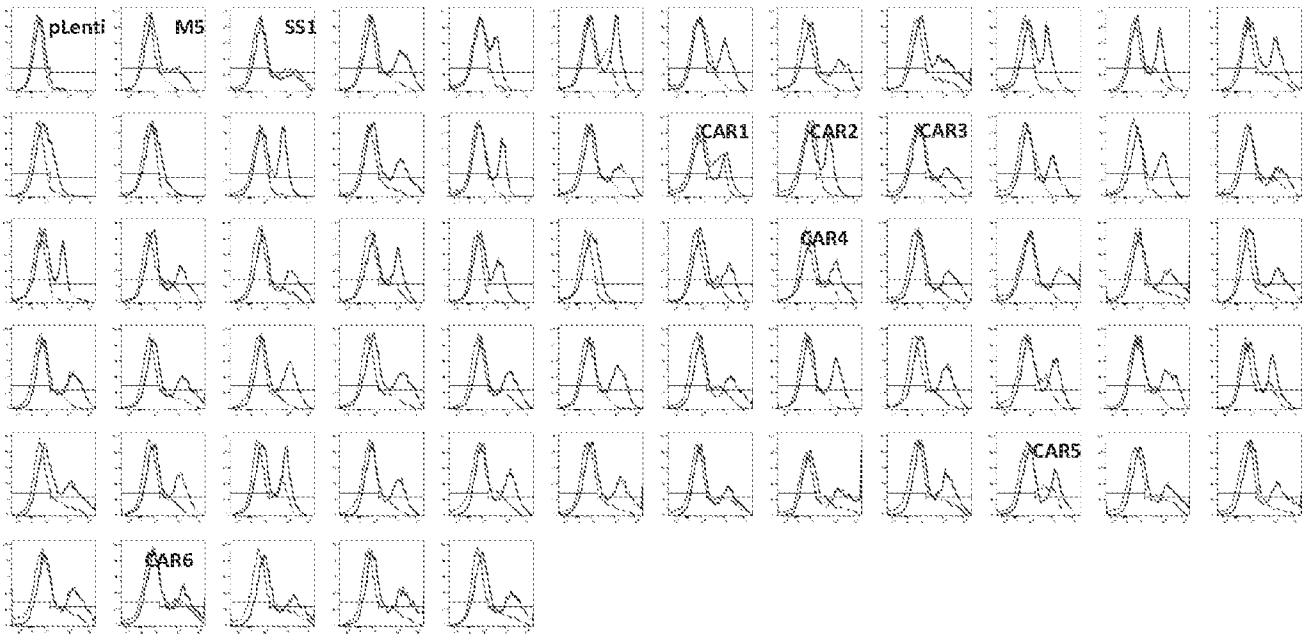
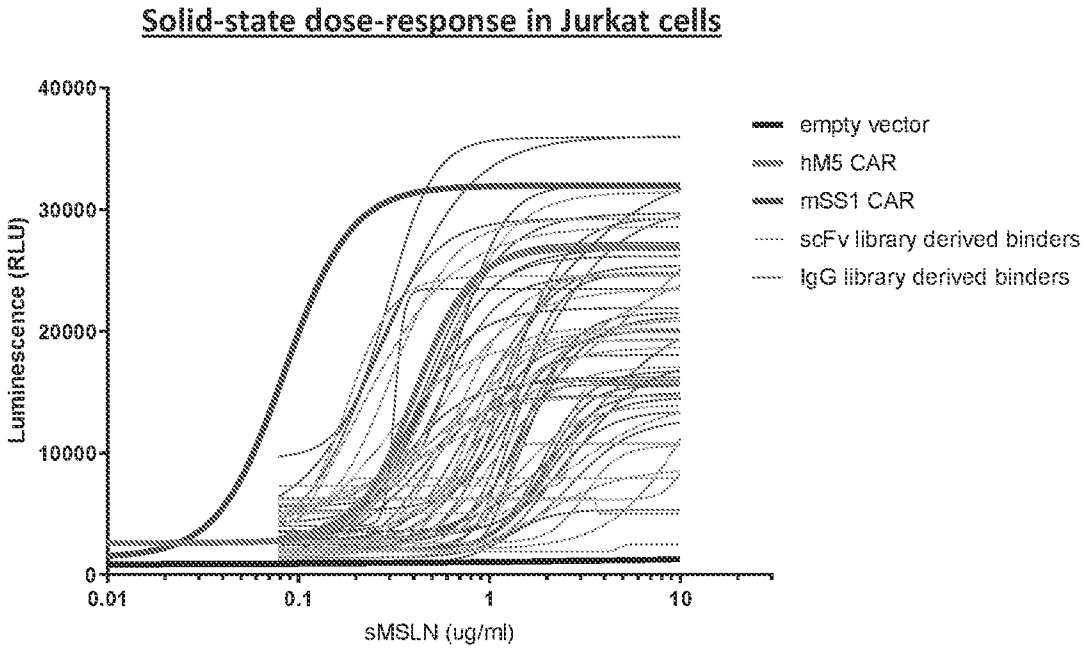
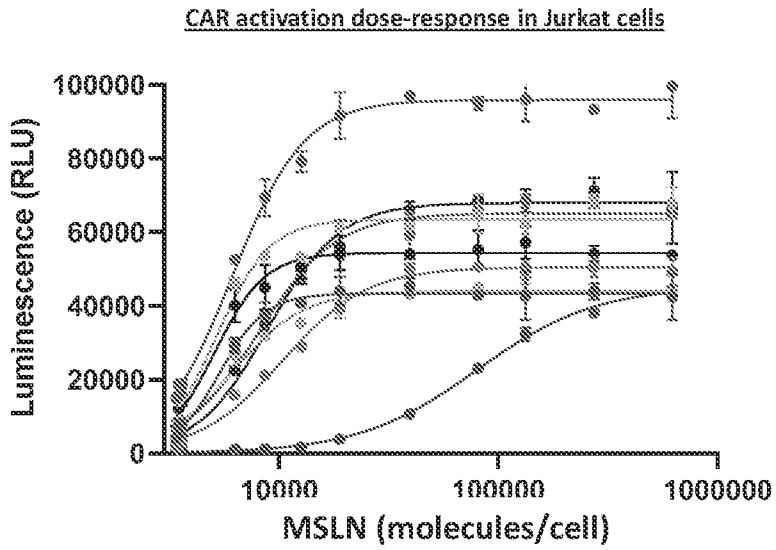


FIG. 23D



FIGs. 24A



	Source	EC_{50} (molecule/cell)	E_{max} (RLU)
⁘	CAR1	5,700	45,000
⁘	CAR2	<3,000	96,000
⁘	CAR3	3,100	63,000
⁘	CAR4	<3,000	53,000
⁘	CAR5	<3,000	65,000
⁘	CAR6	3,100	68,000
⁘	M5	3,500	42,000
⁘	SS1	6,000	51,000
⁘	m912	80,000	42,000

FIGs. 24B

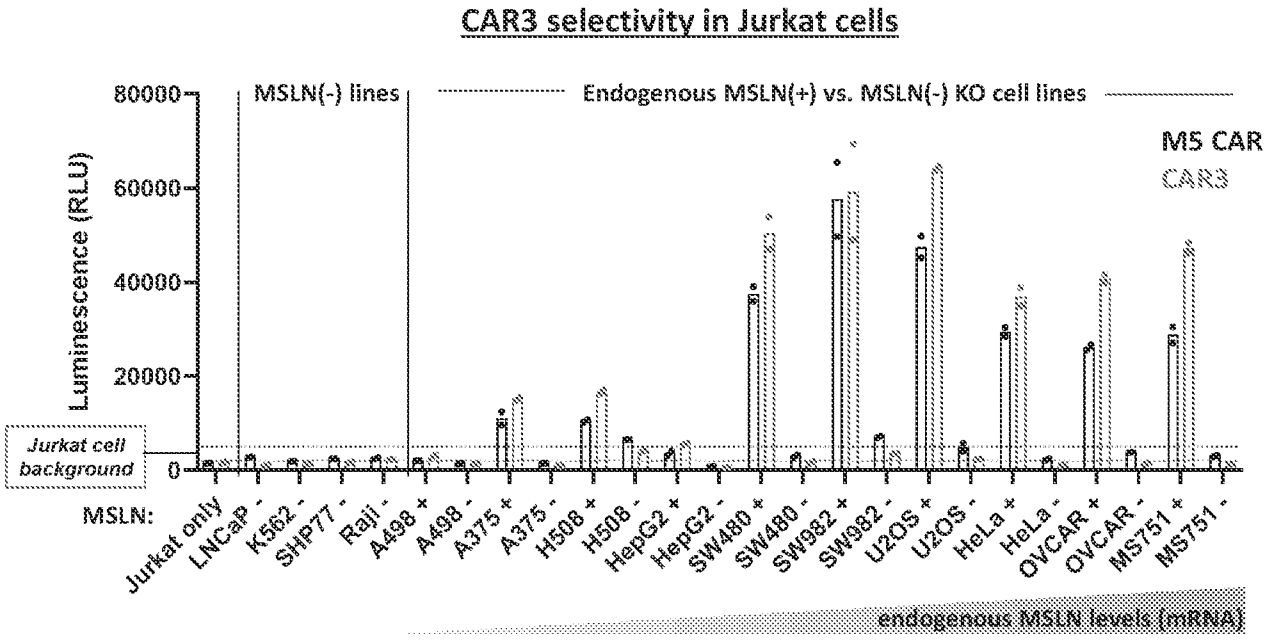


FIG. 25A

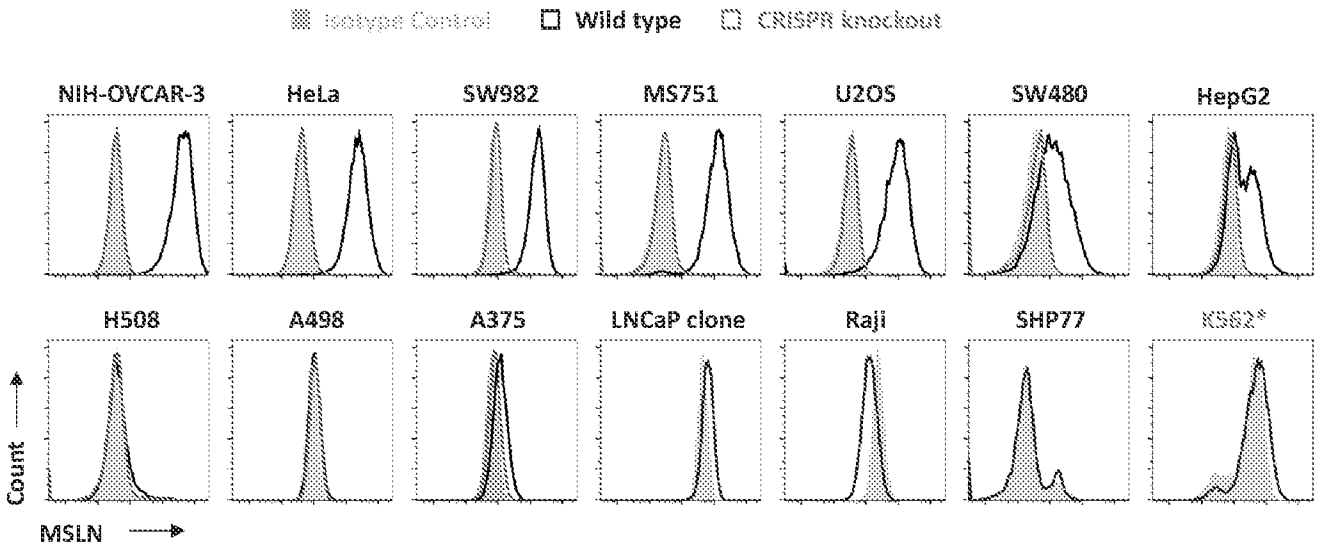


FIG. 25B

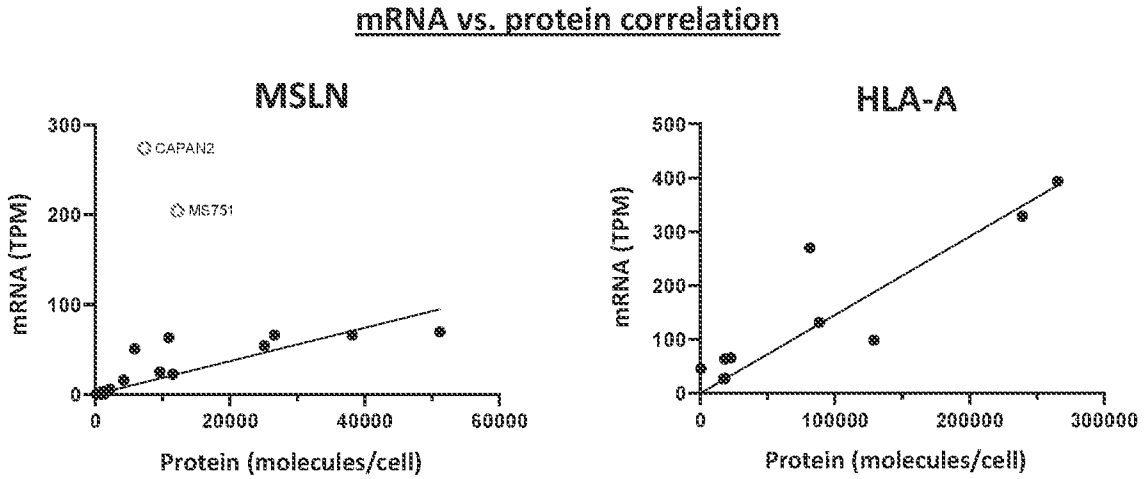


FIG. 26A

	mRNA			Protein		
Tumor cell line	**MSLN (TPM)**	**HLA-A (TPM)**	**A*02:MSLN ratio**	**MSLN (#mol/cell)**	**A*02 (#mol/cell)**	**A*02:MSLN ratio**
MS751 (cervix; A*02:01, A*24:02)	205	156	0.4	12,000	28,000	2.3
MS751 (transduced with A*02)	205	438	2.1	12,000	301,000	25
HeLa (cervix; A*68:02, A*68:02; transduced with A*02)	66	85	na	27,000	740,000	27
NIH-OVCAR-3 (ovary; A*02:01, A*29:02)	70	81	0.6	51,000	25,000	0.5
U2OS (bone; A*02:01, A*32:01)	25	108	2.2	9,600	18,000	1.9
SW982 (synovium; A*02:01, A*02:01)	22	533	24	12,000	240,000	20
Tumor	**MSLN (TPM)**	**A*02 (TPM)**	**A*02:MSLN ratio**			
Lung adenocarcinoma	371	LOH	na			
Mesothelioma	784	LOH	na			
Ovarian	511	LOH	na			
Normal tissue (GTex)	**MSLN (TPM)**	**HLA-A (TPM)**	**A*02:MSLN ratio**			
Lung	88	1934	22			

FIG. 26B

MSLN expression (molecules/cell) in cell lines used in study

	Cell line	Avg	Stan dev
1	NIH-OVCAR-3	51,000	12,000
2	HeLa	27,000	1,900
3	SW982	12,000	730
4	MS751	12,000	1,700
5	U2OS	9,600	2,800
6	SW480	2,200	1,200
7	HEPG2	1,900	120
8	H508	1,000	400
9	LnCAP cloneFGC	930	220
10	A498	820	39
11	A375	630	170
12	Raji	180	5
13	SHP77	180	-
14	K562	n/a	n/a

FIG. 27A

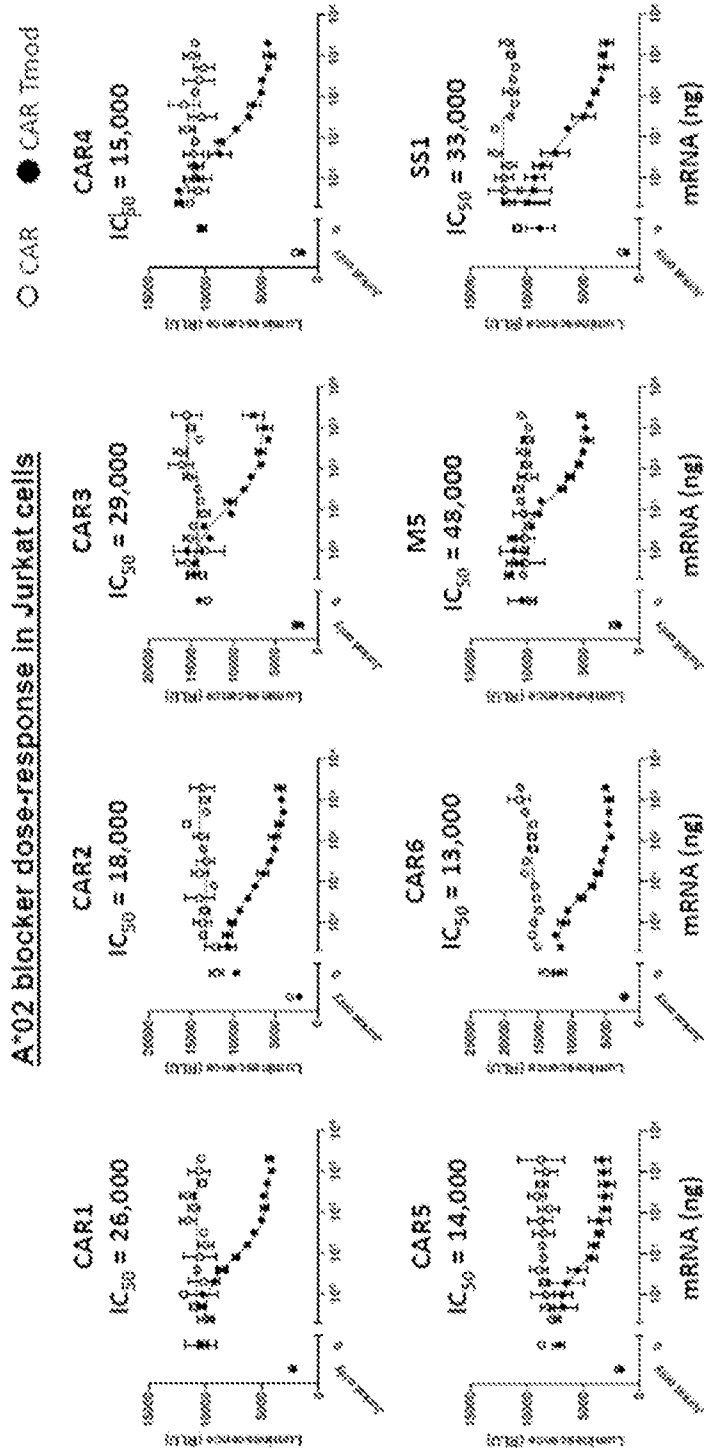
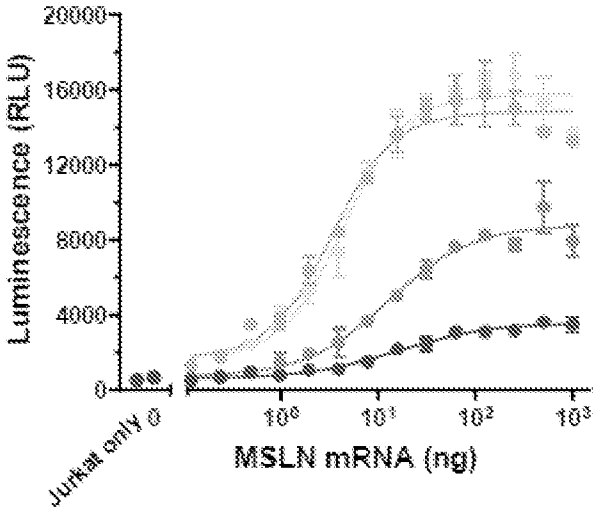
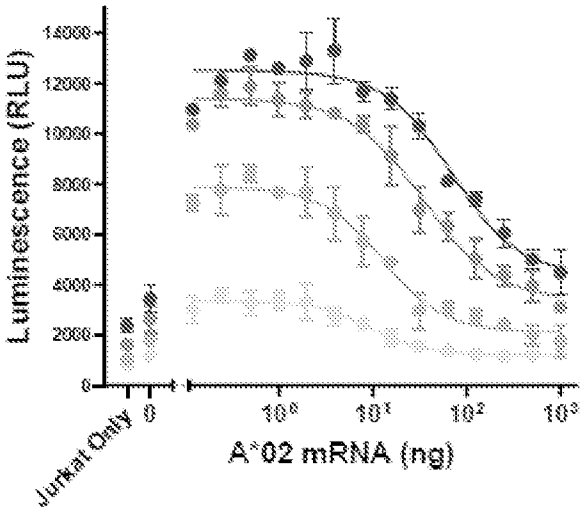

A*02 blocker dose-response in Jurkat cells
CAR
CAR Tmod
CAR1
IC50 = 26,000
CAR2
IC50 = 18,000
CAR3
IC50 = 29,000
CAR4
IC50 = 15,000
CAR5
IC50 = 14,000
CAR6
IC50 = 13,000
M5
IC50 = 48,000
SS1
IC50 = 33,000
mRNA (ng)

FIG. 27B



	A*02 mRNA (ng)	EC_{50} (molecules/cell)	E_{max} (RLU)
●	1000	42,000	3,500
●	50	26,000	7,200
●	2.5	9,000	11,000
●	0	7,700	12,000

FIG. 27C



	MSLN mRNA (ng)	IC50 (molecules/cell)	Imax (RLU)
●	250	182,000	4,400
●	50	60,000	3,400
●	10	12,000	2,100
●	2	7,400	1,200

FIG. 28A

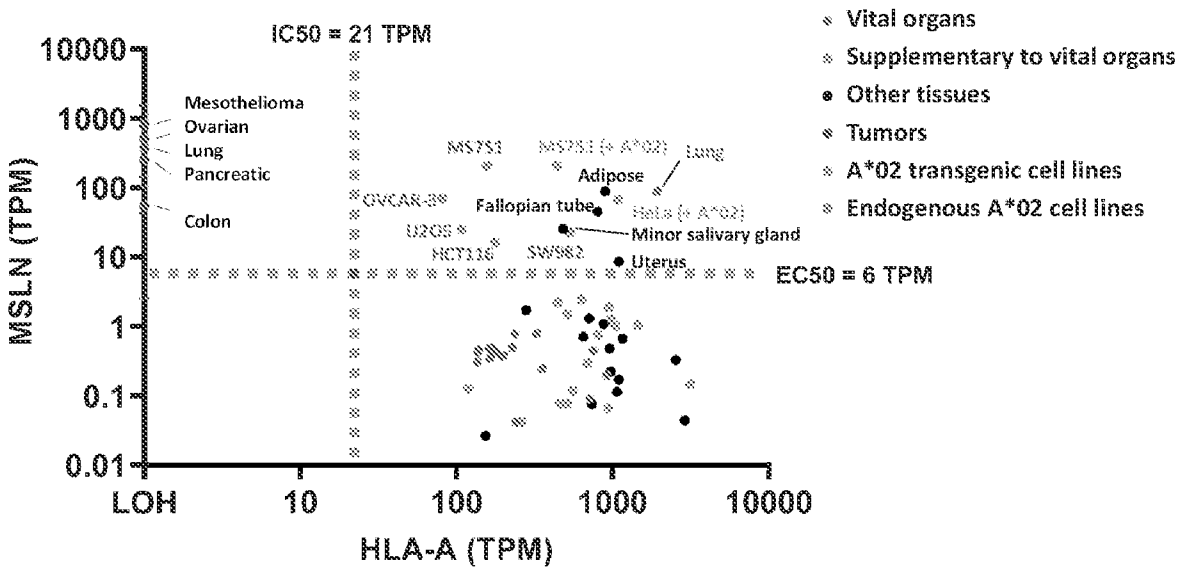
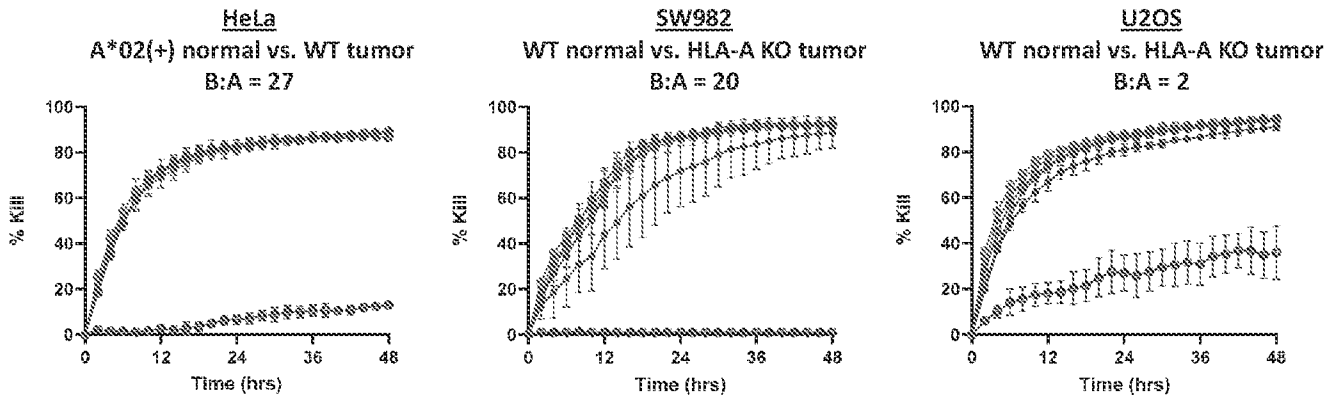


FIG. 28B



MS CAR; CAR3; CAR3 Tmod; Tumor target (solid); Normal target (open)

FIG. 29A

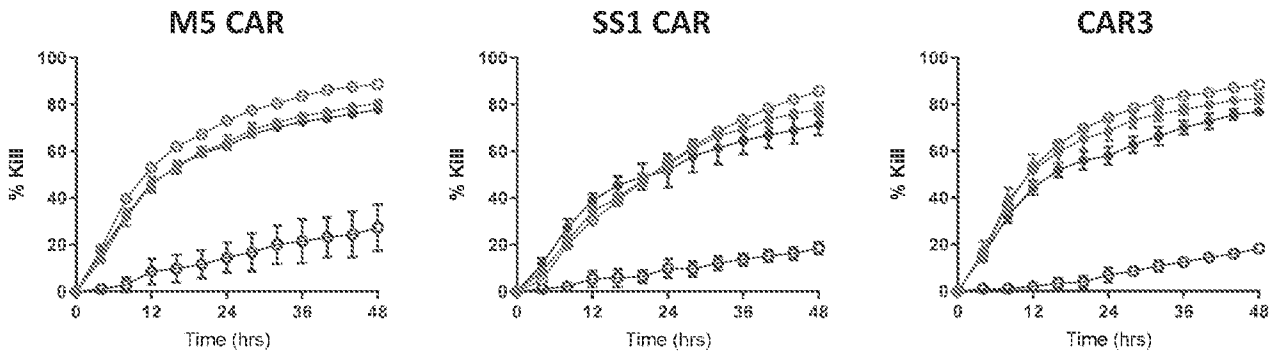


FIG. 29B

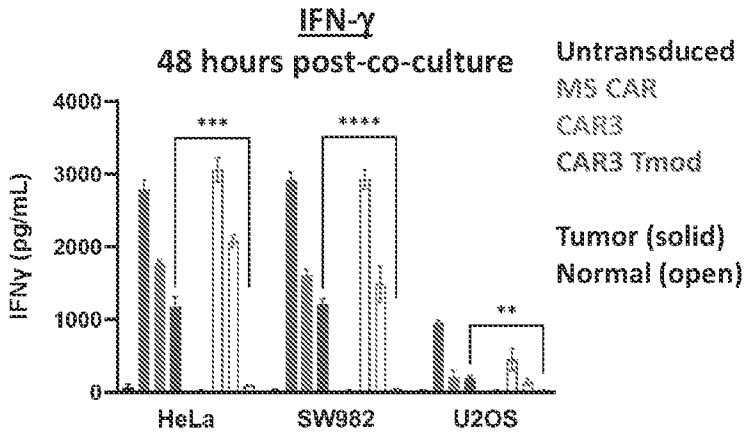


FIG. 30A

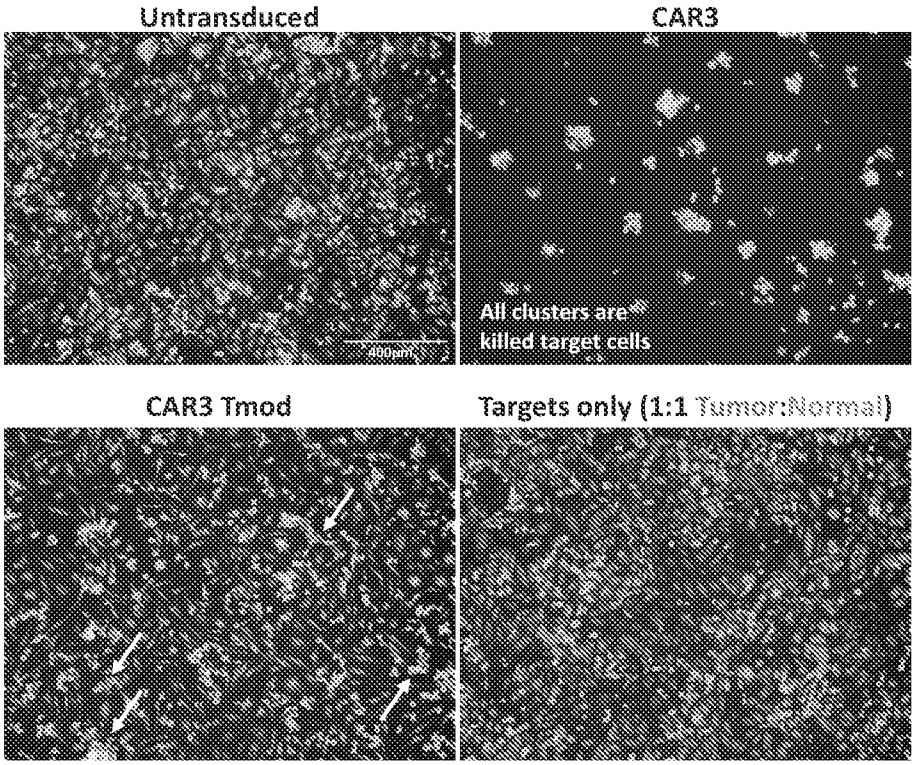


FIG. 30B

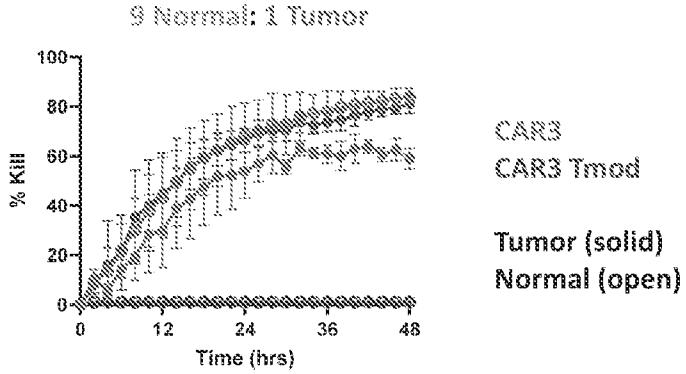


FIG. 31A

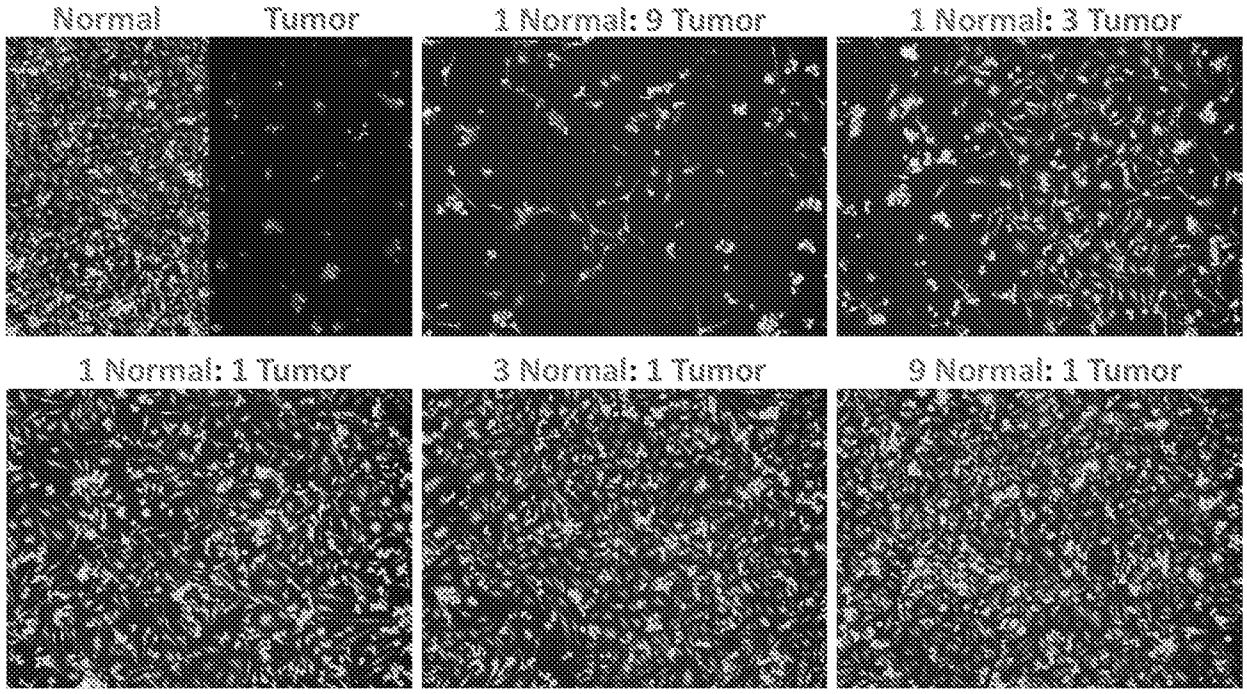


FIG. 31B

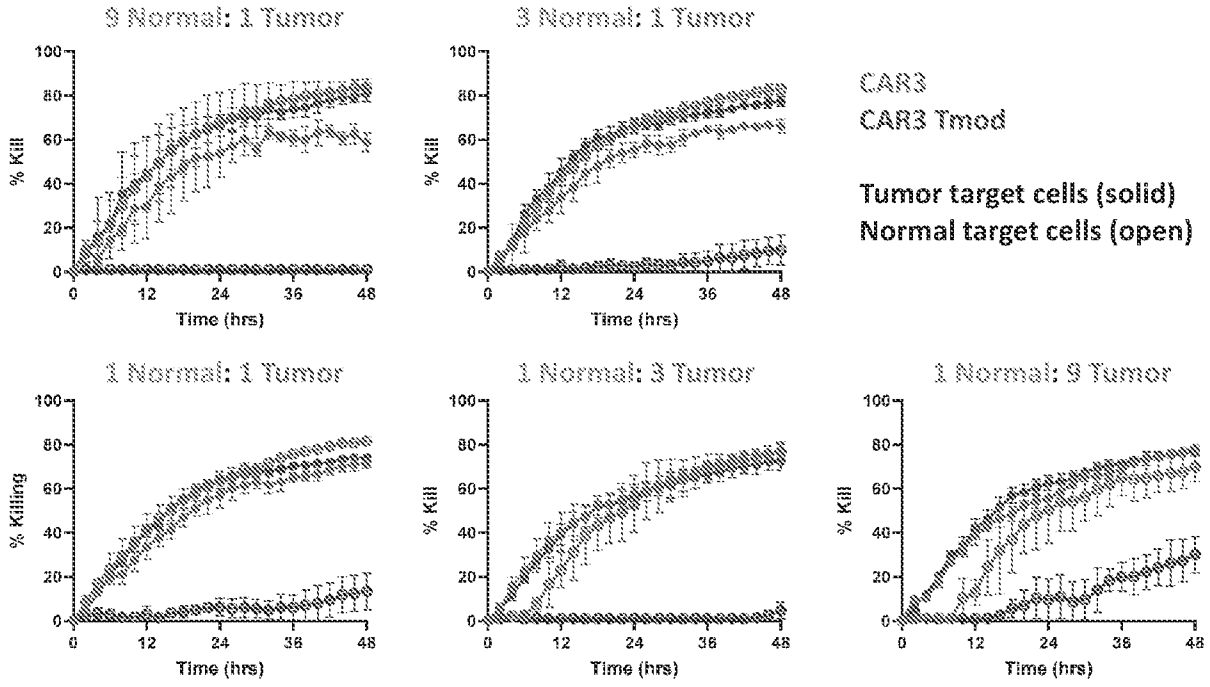


FIG. 32A

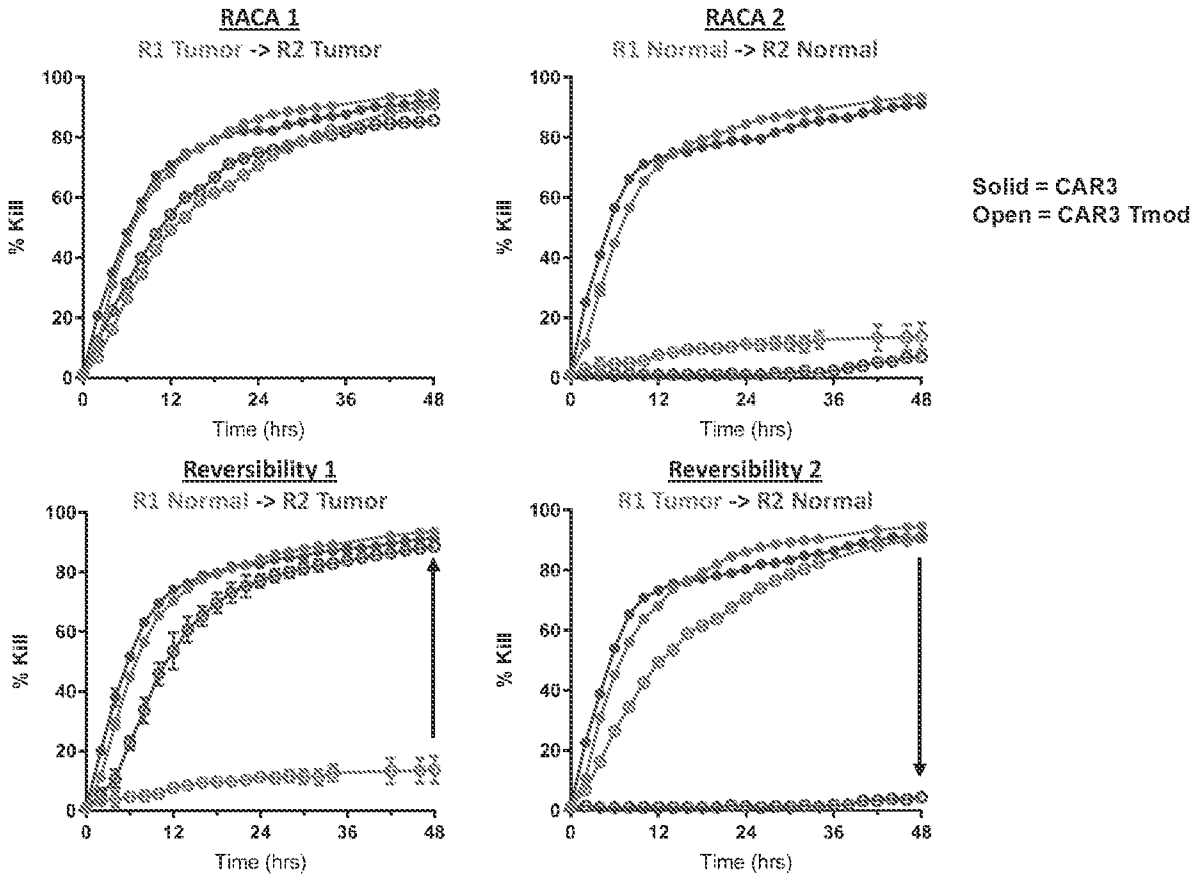


FIG. 32B

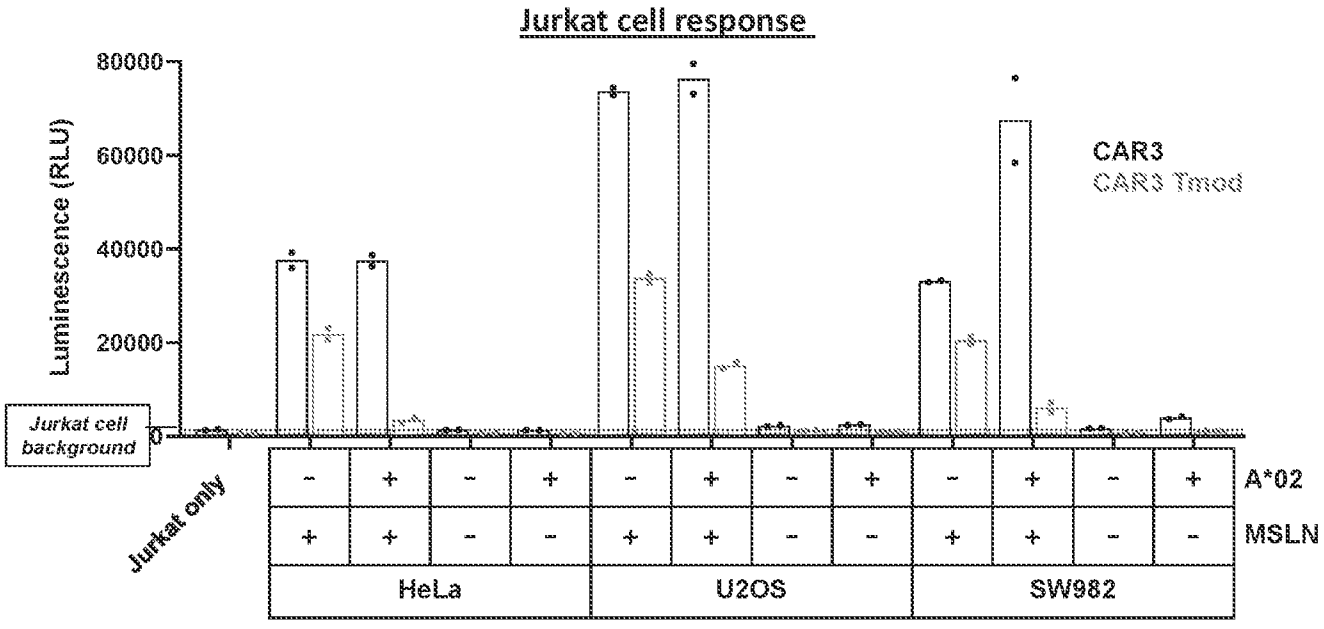


FIG. 33A

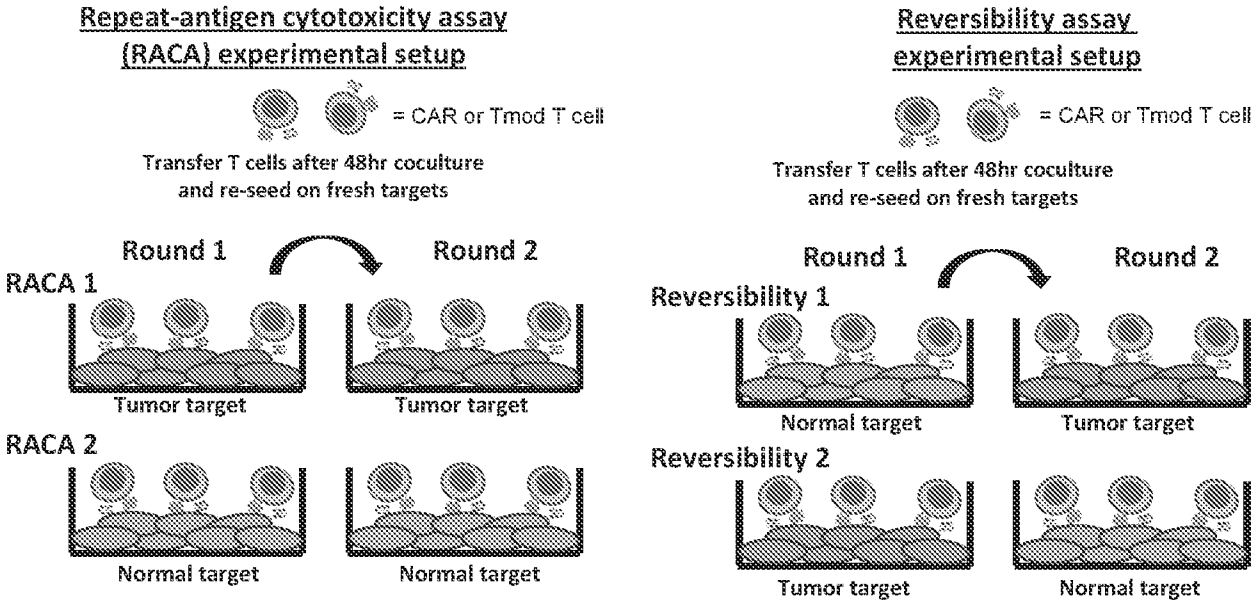


FIG. 33B

Cytotoxicity assays +/- sMSLN

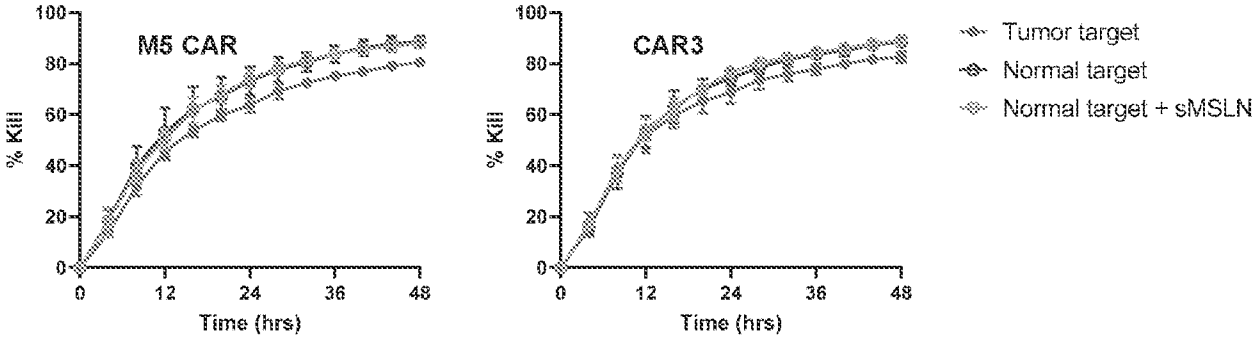


FIG. 33C

sMSLN-stained CAR(+) Jurkat cells

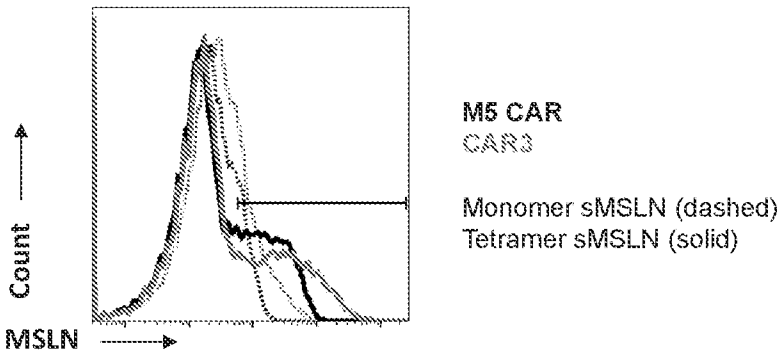


FIG. 34A

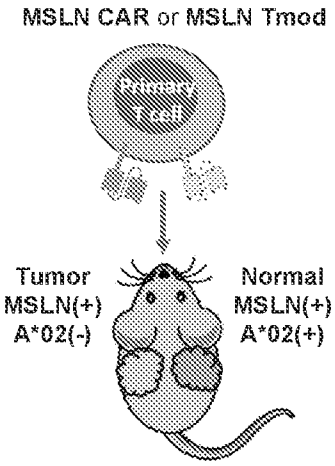


FIG. 34B

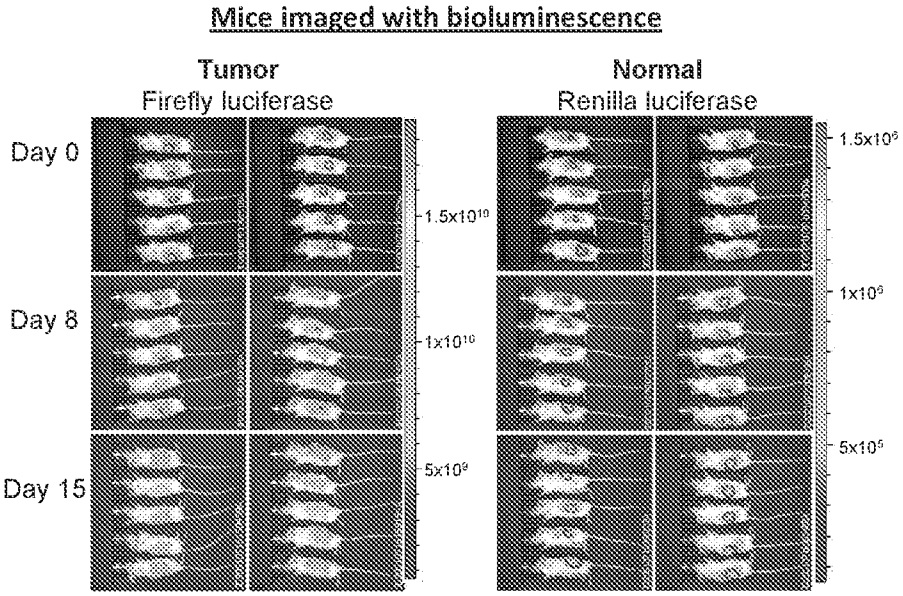


FIG. 34C

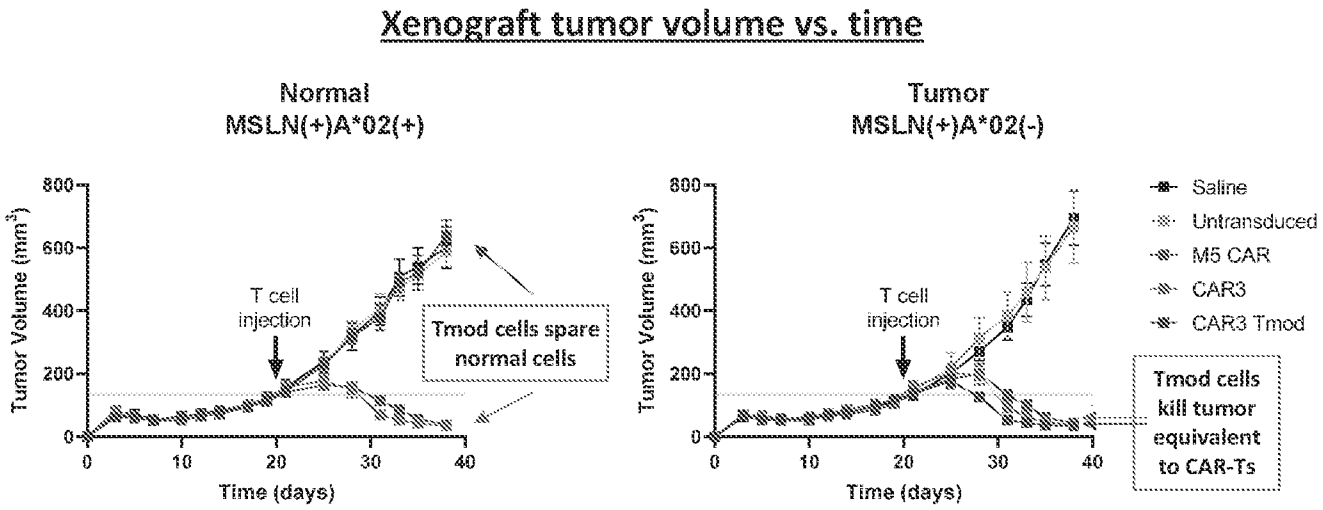


FIG. 35A

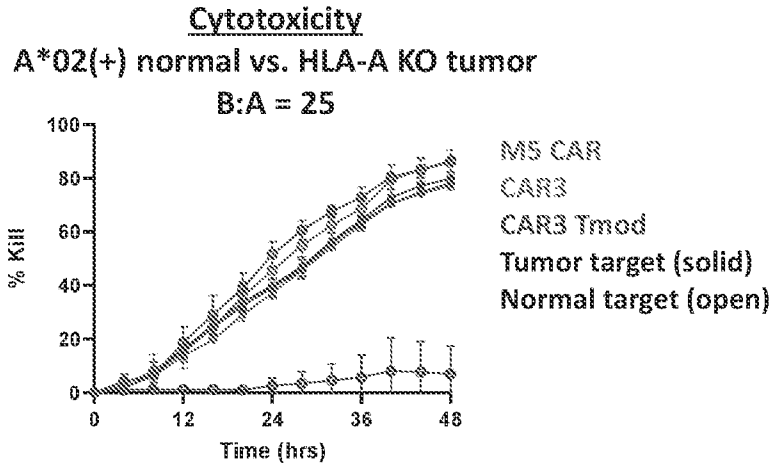


FIG. 35B

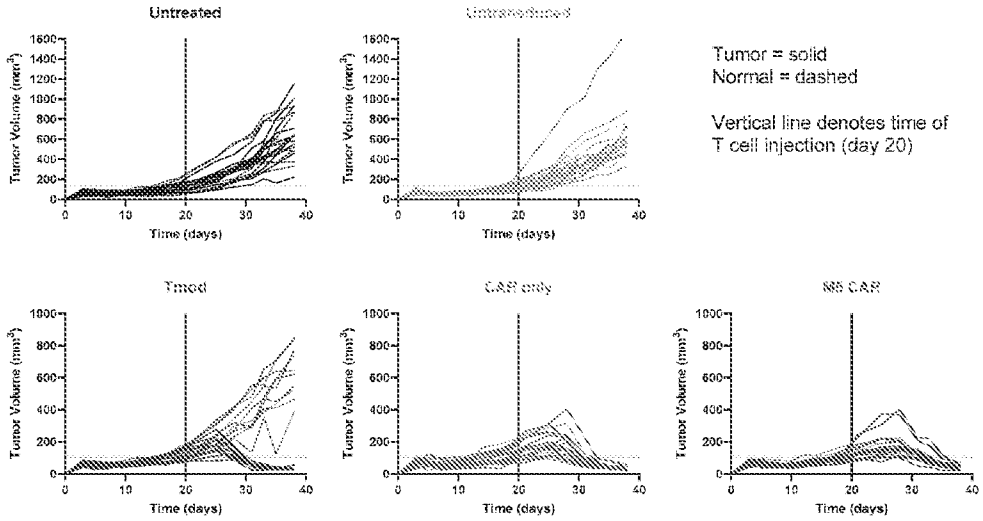


FIG. 35C

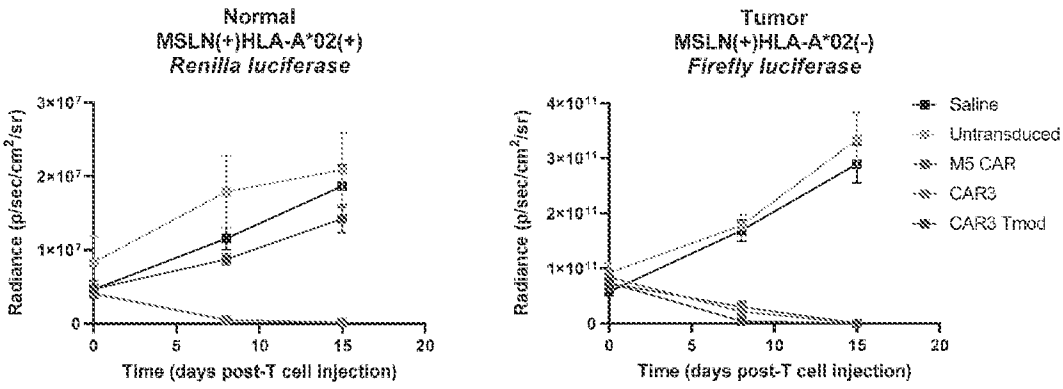


FIG. 36

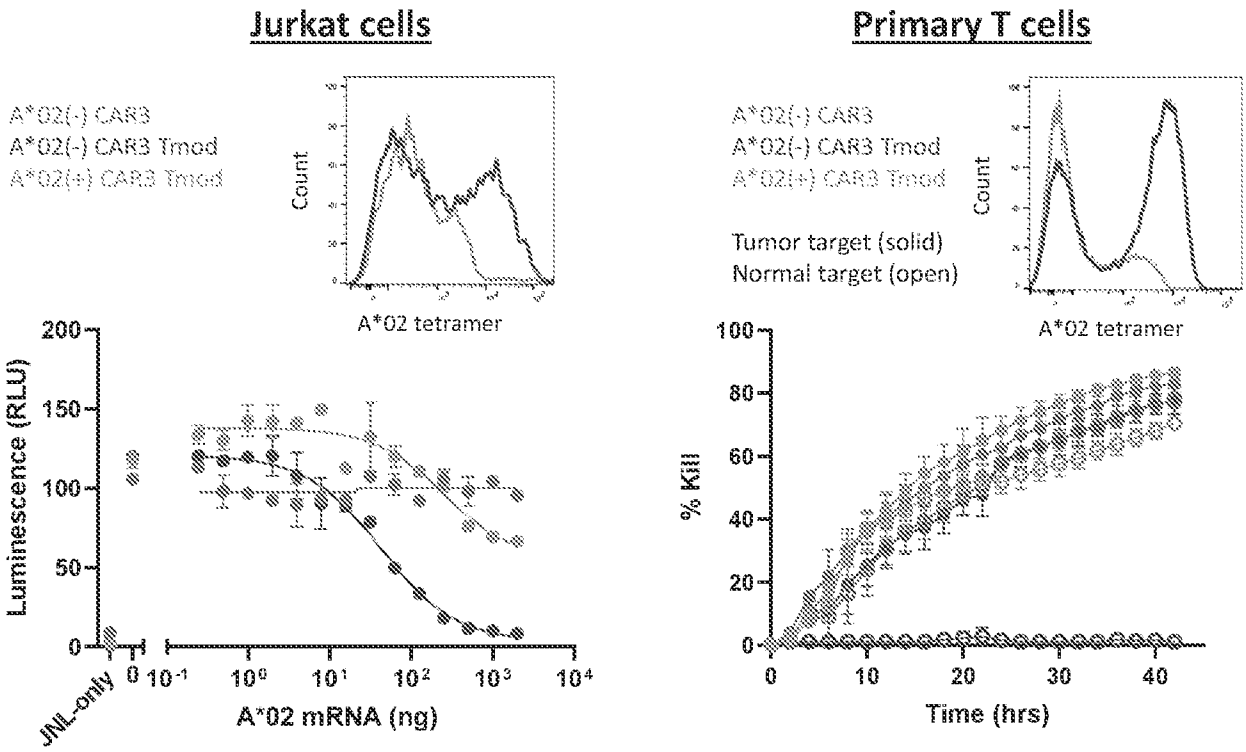

Jurkat cells
A*02(-) CAR3
A*02(-) CAR3 Tmod
A*02(+) CAR3 Tmod
Count
A*02 tetramer
Luminescence (RLU)
200
150
100
50
0
JNL-only
0
10⁻¹
10⁰
10¹
10²
10³
10⁴
A*02 mRNA (ng)
Primary T cells
A*02(-) CAR3
A*02(-) CAR3 Tmod
A*02(+) CAR3 Tmod
Tumor target (solid)
Normal target (open)
Count
A*02 tetramer
% Kill
100
80
60
40
20
0
0
10
20
30
40
Time (hrs)

FIG. 37A

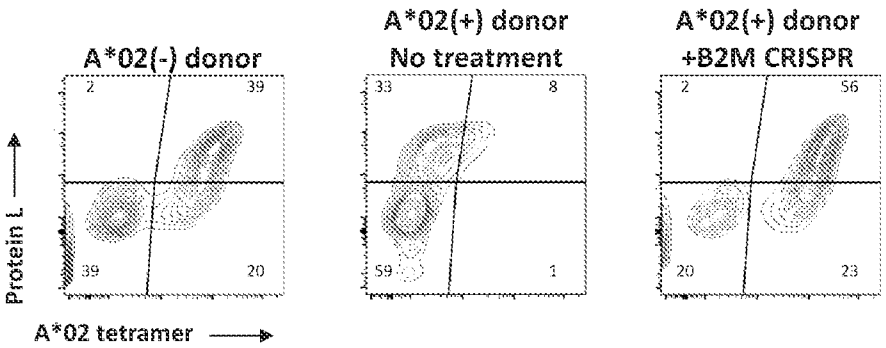


FIG. 37B

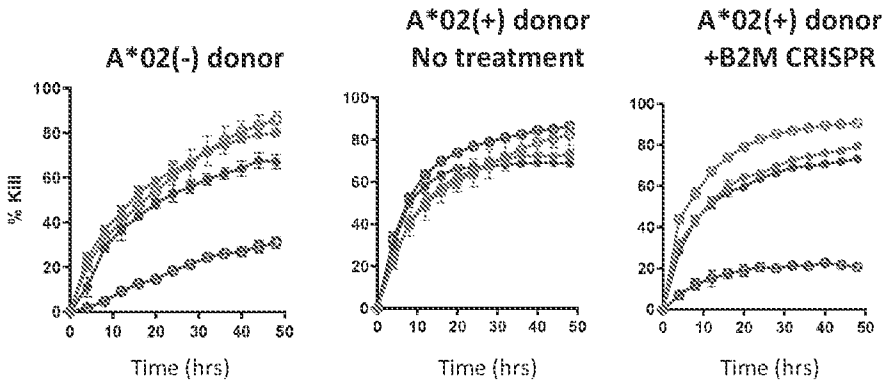


FIG. 37C

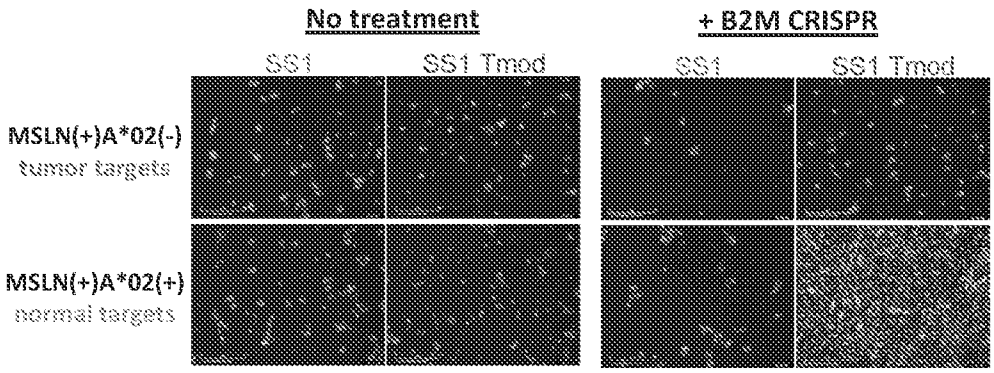


FIG. 38A

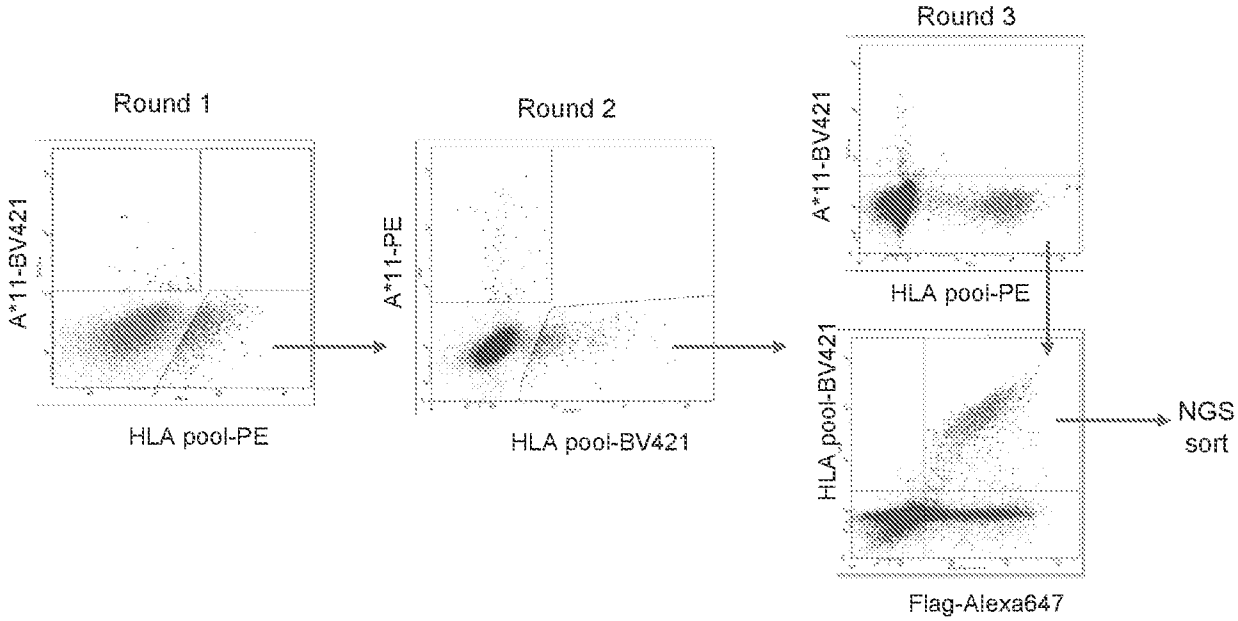


FIG. 38B

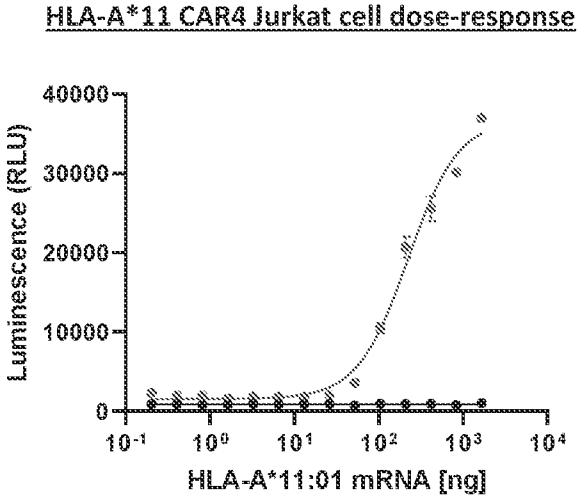


FIG. 39A

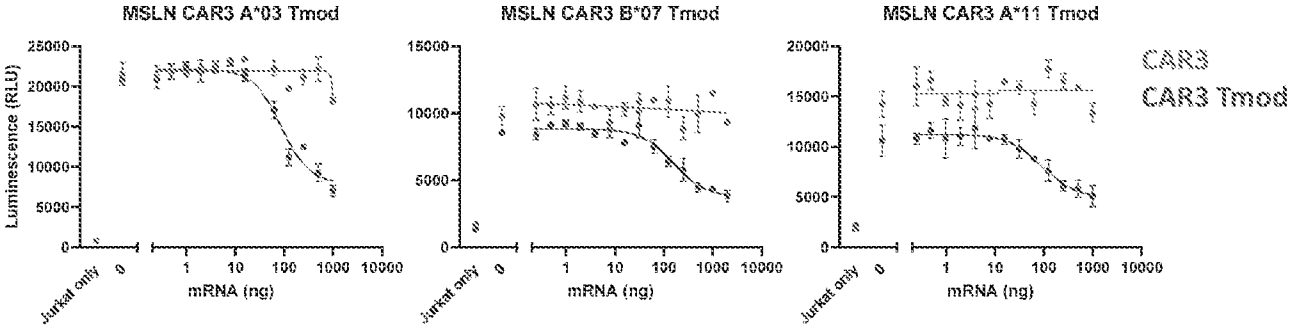


FIG. 39B

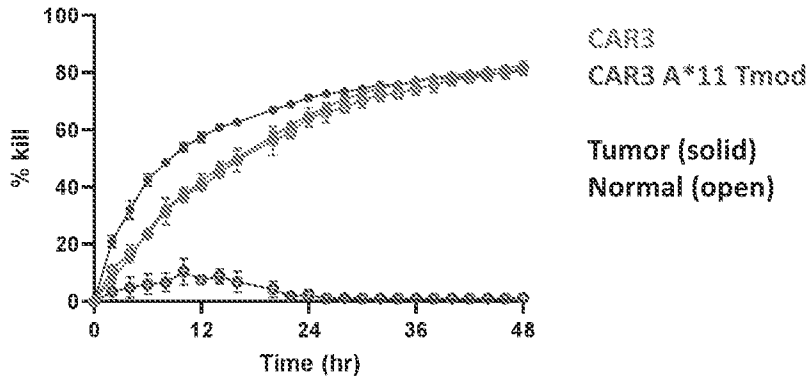
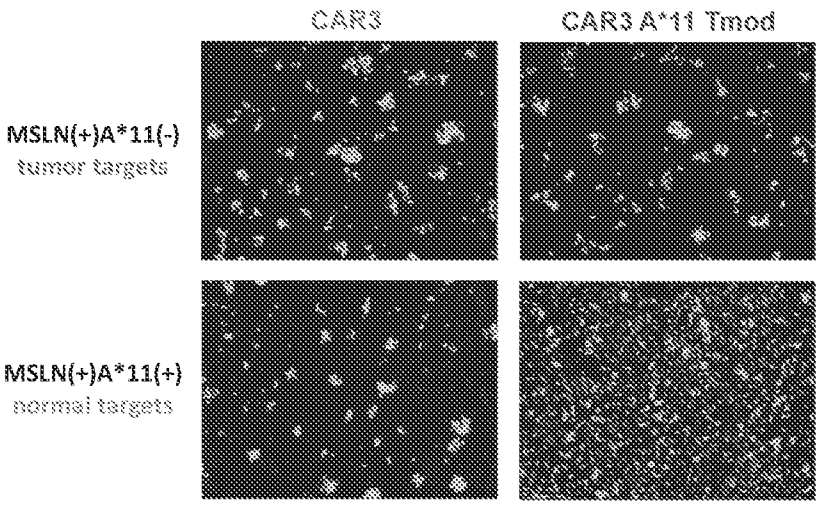


FIG. 39C



SEQUENCE LISTING

<110> A2 BIOTHERAPEUTICS, INC.

<120> COMPOSITIONS AND METHODS FOR TREATING MESOTHELIN POSITIVE CANCERS

<130> A2BI-019/03WO 331656-2068

<150> US 63/085,971
<151> 2020-09-30

<150> US 63/068,245
<151> 2020-08-20

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<170> PatentIn version 3.5

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        35                  40                  45


Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
    50                  55                  60


Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65                  70                  75                  80


Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
                85                  90                  95


Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
            100                 105                 110


Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
```

```
        115                 120                 125

Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
    130                 135                 140

Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145                 150                 155                 160

Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
                165                 170                 175

Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
            180                 185                 190

Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
        195                 200                 205

Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
    210                 215                 220

Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225                 230                 235                 240

Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
                245                 250                 255

Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
            260                 265                 270

Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
        275                 280                 285

Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
    290                 295                 300

Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305                 310                 315                 320

Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
                325                 330                 335
```

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Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
            340                 345                 350

Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
        355                 360                 365

Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
    370                 375                 380

Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385                 390                 395                 400

Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp
                405                 410                 415

Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr
            420                 425                 430

Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu
        435                 440                 445

Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp
    450                 455                 460

Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala
465                 470                 475                 480

Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile
                485                 490                 495

Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser
            500                 505                 510

Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr
        515                 520                 525

Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly
    530                 535                 540

Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg
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545 550 555 560

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565 570 575

Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser
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Met Gln Glu Ala Leu Ser Gly Thr Pro Cys Leu Leu Gly Pro Gly Pro
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Val Leu Thr Val Leu Ala Leu Leu Leu Ala Ser Thr Leu Ala
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20 25 30

Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35 40 45

Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50 55 60

Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65 70 75 80

Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85 90 95

Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100 105 110

```
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
        115                 120                 125

Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
    130                 135                 140

Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145                 150                 155                 160

Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
                165                 170                 175

Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
            180                 185                 190

Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
        195                 200                 205

Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
    210                 215                 220

Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225                 230                 235                 240

Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
                245                 250                 255

Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
            260                 265                 270

Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
        275                 280                 285

Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
    290                 295                 300

Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305                 310                 315                 320

Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
                325                 330                 335
```

```
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
            340                 345                 350

Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
        355                 360                 365

Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
    370                 375                 380

Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385                 390                 395                 400

Val Asn Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu
                405                 410                 415

Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
            420                 425                 430

Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
        435                 440                 445

Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
    450                 455                 460

Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
465                 470                 475                 480

Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
                485                 490                 495

Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
            500                 505                 510

Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
        515                 520                 525

Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
    530                 535                 540
```

```
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
545                 550                 555                 560


Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
                565                 570                 575


Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
            580                 585                 590


Gly Tyr Leu Val Leu Asp Leu Ser Met Gln Glu Ala Leu Ser Gly Thr
        595                 600                 605


Pro Cys Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu
    610                 615                 620


Leu Ala Ser Thr Leu Ala
625                 630
```

<210> 3
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 3

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Glu Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Asp Ile Val Met Thr Gln Ser Ser Ser Leu Ser Ala
    130                 135                 140

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
145                 150                 155                 160

Arg Tyr Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                165                 170                 175

Leu Leu Ile Tyr Thr Ala Ser Ile Leu Gln Asn Gly Val Pro Ser Arg
            180                 185                 190

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
        195                 200                 205

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Thr Tyr Thr
    210                 215                 220

Thr Pro Asp Phe Gly Pro Gly Thr Lys Val Glu Ile Lys
225                 230                 235
```

<210> 4
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 4

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg Ala Pro Gly Ala
1               5                   10                  15
```

```
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Phe Thr Phe Arg Gly Tyr
            20                  25                  30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Asn Pro Ser Gly Gly Ser Arg Ala Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Thr Ala Ser Cys Gly Gly Asp Cys Tyr Tyr Leu Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Pro Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Glu Asn Val Asn Ile Trp Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ser Ser Ser
            180                 185                 190

Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Ala
        195                 200                 205

Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Tyr Gln Ser Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240
```

Thr Lys Val Glu Ile Lys
245

<210> 5
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 5

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys Phe
50 55 60

Arg Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser
145 150 155 160

```
Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Arg Leu Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Trp Ser Gly Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu
225                 230                 235                 240

Ile Lys
```

<210> 6
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 6

```
Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
            20                  25                  30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35                  40                  45

Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys Phe
    50                  55                  60

Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85                  90                  95

Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Glu Leu Thr Gln Ser Pro
    130                 135                 140

Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Ser
145                 150                 155                 160

Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Ser Gly
                165                 170                 175

Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly
            180                 185                 190

Val Pro Gly Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser Tyr Ser Leu
        195                 200                 205

Thr Ile Ser Ser Val Glu Ala Glu Asp Asp Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Trp Ser Gly Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu
225                 230                 235                 240

Ile Lys
```

<210> 7
<211> 45
<212> PRT
<213> Unknown

<220>
<223> CD8alpha hinge

<400> 7

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
35 40 45

<210> 8
<211> 135
<212> DNA
<213> Unknown

<220>
<223> encodes CD8alpha hinge

<400> 8
accacgacgc cagcgccgcg accaccaaca ccggcgccca ccatcgcgtc gcagcccctg 60

tccctgcgcc cagaggcgtg ccggccagcg gcgggggggcg cagtgcacac gagggggctg 120

gacttcgcct gtgat 135

<210> 9
<211> 41
<212> PRT
<213> Unknown

<220>
<223> CD28 hinge

<400> 9

Cys Thr Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys
1 5 10 15

Ser Asn Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser
20 25 30

Pro Leu Phe Pro Gly Pro Ser Lys Pro
35 40

<210> 10
<211> 123

<212> DNA
<213> Unknown

<220>
<223> encodes CD28 hinge

<400> 10
tgtaccattg aagttatgta tcctcctcct tacctagaca atgagaagag caatggaacc 60

attatccatg tgaaagggaa acacctttgt ccaagtcccc tatttcccgg accttctaag 120

ccc 123

<210> 11
<211> 27
<212> PRT
<213> Unknown

<220>
<223> CD28 transmembrane domain

<400> 11

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
1 5 10 15

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
20 25

<210> 12
<211> 81
<212> DNA
<213> Unknown

<220>
<223> encodes CD28 transmembrane domain

<400> 12
ttctgggtgc tggtcgttgt gggcggcgtg ctggcctgct acagcctgct ggtgacagtg 60

gccttcatca tcttttgggt g 81

<210> 13
<211> 25
<212> PRT
<213> Unknown

<220>
<223> IL-2Rbeta transmembrane domain

<400> 13

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

Phe Ile Ile Leu Val Tyr Leu Leu Ile
20 25

<210> 14
<211> 75
<212> DNA
<213> Unknown

<220>
<223> encodes IL-2Rbeta transmembrane domain

<400> 14
attccgtggc tcggccacct cctcgtgggc ctcagcgggg cttttggctt catcatctta 60

gtgtacttgc tgatc 75

<210> 15
<211> 112
<212> PRT
<213> Unknown

<220>
<223> CD3zeta activation domain

<400> 15

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys 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> 16
<211> 336
<212> DNA
<213> Unknown

<220>
<223> encodes CD3zeta activation domain

<400> 16

```
agagtgaagt tcagcaggag cgcagacgcc cccgcgtaca agcagggcca gaaccagctc       60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gcgtagaggc      120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat      180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc      240

cggaggggca aggggcacga tggcctttac cagggactca gtacagccac caaggacacc      300

tacgacgccc ttcacatgca ggccctgccc cctcgc                                336
```

<210> 17
<211> 43
<212> PRT
<213> Unknown

<220>
<223> CD3zeta activation domain

<400> 17

```
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 His Met Gln Ala Leu Pro Pro Arg
        35                  40
```

<210> 18
<211> 129

<212> DNA
<213> Unknown

<220>
<223> encodes CD3zeta activation domain

<400> 18
agagtgaagt tcagcaggag cgcagacgcc cccgcgtacc agcagggcca gaaccagctc 60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttgcacat gcaggccctg 120

ccccctcgc 129

<210> 19
<211> 41
<212> PRT
<213> Unknown

<220>
<223> CD28 co-stimulatory domain

<400> 19

Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
1 5 10 15

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
20 25 30

Pro Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 20
<211> 123
<212> DNA
<213> Unknown

<220>
<223> encodes CD28 co-stimulatory domain

<400> 20
aggagcaagc ggagcagact gctgcacagc gactacatga acatgacccc ccggaggcct 60

ggccccaccc ggaagcacta ccagccctac gcccctccca gggatttcgc cgcctaccgg 120

agc 123

<210> 21
<211> 23

<212> PRT
<213> Unknown

<220>
<223> TCR alpha transmembrane domain

<400> 21

Val Ile Gly Phe Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu
1   5   10   15

Leu Met Thr Leu Arg Leu Trp
            20

<210> 22
<211> 69
<212> DNA
<213> Unknown

<220>
<223> encodes TCR alpha transmembrane domain

<400> 22
gtgattgggt tccgaatcct cctcctgaaa gtggccgggt ttaatctgct catgacgctg   60

cggctgtgg   69

<210> 23
<211> 23
<212> PRT
<213> Unknown

<220>
<223> TCR beta transmembrane domain

<400> 23

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
1   5   10   15

Leu Val Ser Ala Leu Val Leu
            20

<210> 24
<211> 69
<212> DNA
<213> Unknown

<220>

<223> encodes TCR beta transmembrane domain

<400> 24
accatcctct atgagatctt gctagggaag gccaccttgt atgccgtgct ggtcagtgcc 60

ctcgtgctg 69

<210> 25
<211> 10
<212> PRT
<213> Unknown

<220>
<223> TCR beta intracellular domain

<400> 25

Met Ala Met Val Lys Arg Lys Asp Ser Arg
1 5 10

<210> 26
<211> 30
<212> DNA
<213> Unknown

<220>
<223> encodes TCR beta intracellular domain

<400> 26
atggccatgg tcaagagaaa ggattccaga 30

<210> 27
<211> 532
<212> PRT
<213> Homo sapiens

<400> 27

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

Leu Gly Ala Leu Phe Pro Gly Pro Gly Asn Ala Gln Thr Ser Val Ser
            20 25 30

Pro Ser Lys Val Ile Leu Pro Arg Gly Gly Ser Val Leu Val Thr Cys
        35 40 45

Ser Thr Ser Cys Asp Gln Pro Lys Leu Leu Gly Ile Glu Thr Pro Leu

```
    50                  55                  60

Pro Lys Lys Glu Leu Leu Leu Pro Gly Asn Asn Arg Lys Val Tyr Glu
65                  70                  75                  80

Leu Ser Asn Val Gln Glu Asp Ser Gln Pro Met Cys Tyr Ser Asn Cys
                85                  90                  95

Pro Asp Gly Gln Ser Thr Ala Lys Thr Phe Leu Thr Val Tyr Trp Thr
            100                 105                 110

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

Lys Asn Leu Thr Leu Arg Cys Gln Val Glu Gly Gly Ala Pro Arg Ala
    130                 135                 140

Asn Leu Thr Val Val Leu Leu Arg Gly Glu Lys Glu Leu Lys Arg Glu
145                 150                 155                 160

Pro Ala Val Gly Glu Pro Ala Glu Val Thr Thr Thr Val Leu Val Arg
                165                 170                 175

Arg Asp His His Gly Ala Asn Phe Ser Cys Arg Thr Glu Leu Asp Leu
            180                 185                 190

Arg Pro Gln Gly Leu Glu Leu Phe Glu Asn Thr Ser Ala Pro Tyr Gln
        195                 200                 205

Leu Gln Thr Phe Val Leu Pro Ala Thr Pro Pro Gln Leu Val Ser Pro
    210                 215                 220

Arg Val Leu Glu Val Asp Thr Gln Gly Thr Val Val Cys Ser Leu Asp
225                 230                 235                 240

Gly Leu Phe Pro Val Ser Glu Ala Gln Val His Leu Ala Leu Gly Asp
                245                 250                 255

Gln Arg Leu Asn Pro Thr Val Thr Tyr Gly Asn Asp Ser Phe Ser Ala
            260                 265                 270
```

```
Lys Ala Ser Val Ser Val Thr Ala Glu Asp Glu Gly Thr Gln Arg Leu
        275                 280                 285

Thr Cys Ala Val Ile Leu Gly Asn Gln Ser Gln Glu Thr Leu Gln Thr
    290                 295                 300

Val Thr Ile Tyr Ser Phe Pro Ala Pro Asn Val Ile Leu Thr Lys Pro
305                 310                 315                 320

Glu Val Ser Glu Gly Thr Glu Val Thr Val Lys Cys Glu Ala His Pro
                325                 330                 335

Arg Ala Lys Val Thr Leu Asn Gly Val Pro Ala Gln Pro Leu Gly Pro
            340                 345                 350

Arg Ala Gln Leu Leu Leu Lys Ala Thr Pro Glu Asp Asn Gly Arg Ser
        355                 360                 365

Phe Ser Cys Ser Ala Thr Leu Glu Val Ala Gly Gln Leu Ile His Lys
    370                 375                 380

Asn Gln Thr Arg Glu Leu Arg Val Leu Tyr Gly Pro Arg Leu Asp Glu
385                 390                 395                 400

Arg Asp Cys Pro Gly Asn Trp Thr Trp Pro Glu Asn Ser Gln Gln Thr
                405                 410                 415

Pro Met Cys Gln Ala Trp Gly Asn Pro Leu Pro Glu Leu Lys Cys Leu
            420                 425                 430

Lys Asp Gly Thr Phe Pro Leu Pro Ile Gly Glu Ser Val Thr Val Thr
        435                 440                 445

Arg Asp Leu Glu Gly Thr Tyr Leu Cys Arg Ala Arg Ser Thr Gln Gly
    450                 455                 460

Glu Val Thr Arg Lys Val Thr Val Asn Val Leu Ser Pro Arg Tyr Glu
465                 470                 475                 480

Ile Val Ile Ile Thr Val Val Ala Ala Ala Val Ile Met Gly Thr Ala
```

485 490 495

Gly Leu Ser Thr Tyr Leu Tyr Asn Arg Gln Arg Lys Ile Lys Lys Tyr
500 505 510

Arg Leu Gln Gln Ala Gln Lys Gly Thr Pro Met Lys Pro Asn Thr Gln
515 520 525

Ala Thr Pro Pro
530

<210> 28
<211> 271
<212> PRT
<213> Homo sapiens

<400> 28

Met Pro Glu Ala Pro Pro Leu Leu Leu Ala Ala Val Leu Leu Gly Leu
1 5 10 15

Val Leu Leu Val Val Leu Leu Leu Leu Leu Arg His Trp Gly Trp Gly
20 25 30

Leu Cys Leu Ile Gly Trp Asn Glu Phe Ile Leu Gln Pro Ile His Asn
35 40 45

Leu Leu Met Gly Asp Thr Lys Glu Gln Arg Ile Leu Asn His Val Leu
50 55 60

Gln His Ala Glu Pro Gly Asn Ala Gln Ser Val Leu Glu Ala Ile Asp
65 70 75 80

Thr Tyr Cys Glu Gln Lys Glu Trp Ala Met Asn Val Gly Asp Lys Lys
85 90 95

Gly Lys Ile Val Asp Ala Val Ile Gln Glu His Gln Pro Ser Val Leu
100 105 110

Leu Glu Leu Gly Ala Tyr Cys Gly Tyr Ser Ala Val Arg Met Ala Arg
115 120 125

```
Leu Leu Ser Pro Gly Ala Arg Leu Ile Thr Ile Glu Ile Asn Pro Asp
    130                 135                 140

Cys Ala Ala Ile Thr Gln Arg Met Val Asp Phe Ala Gly Val Lys Asp
145                 150                 155                 160

Lys Val Thr Leu Val Val Gly Ala Ser Gln Asp Ile Ile Pro Gln Leu
                165                 170                 175

Lys Lys Lys Tyr Asp Val Asp Thr Leu Asp Met Val Phe Leu Asp His
            180                 185                 190

Trp Lys Asp Arg Tyr Leu Pro Asp Thr Leu Leu Leu Glu Glu Cys Gly
        195                 200                 205

Leu Leu Arg Lys Gly Thr Val Leu Leu Ala Asp Asn Val Ile Cys Pro
    210                 215                 220

Gly Ala Pro Asp Phe Leu Ala His Val Arg Gly Ser Ser Cys Phe Glu
225                 230                 235                 240

Cys Thr His Tyr Gln Ser Phe Leu Glu Tyr Arg Glu Val Val Asp Gly
                245                 250                 255

Leu Glu Lys Ala Ile Tyr Lys Gly Pro Gly Ser Glu Ala Gly Pro
            260                 265                 270
```

<210> 29
<211> 273
<212> PRT
<213> Homo sapiens

<400> 29

```
Met Ser Gly Ser Gln Ser Glu Val Ala Pro Ser Pro Gln Ser Pro Arg
1               5                   10                  15

Ser Pro Glu Met Gly Arg Asp Leu Arg Pro Gly Ser Arg Val Leu Leu
            20                  25                  30

Leu Leu Leu Leu Leu Leu Leu Val Tyr Leu Thr Gln Pro Gly Asn Gly
        35                  40                  45
```

```
Asn Glu Gly Ser Val Thr Gly Ser Cys Tyr Cys Gly Lys Arg Ile Ser
    50                  55                  60

Ser Asp Ser Pro Pro Ser Val Gln Phe Met Asn Arg Leu Arg Lys His
65                  70                  75                  80

Leu Arg Ala Tyr His Arg Cys Leu Tyr Tyr Thr Arg Phe Gln Leu Leu
                85                  90                  95

Ser Trp Ser Val Cys Gly Gly Asn Lys Asp Pro Trp Val Gln Glu Leu
            100                 105                 110

Met Ser Cys Leu Asp Leu Lys Glu Cys Gly His Ala Tyr Ser Gly Ile
        115                 120                 125

Val Ala His Gln Lys His Leu Leu Pro Thr Ser Pro Pro Ile Ser Gln
    130                 135                 140

Ala Ser Glu Gly Ala Ser Ser Asp Ile His Thr Pro Ala Gln Met Leu
145                 150                 155                 160

Leu Ser Thr Leu Gln Ser Thr Gln Arg Pro Thr Leu Pro Val Gly Ser
                165                 170                 175

Leu Ser Ser Asp Lys Glu Leu Thr Arg Pro Asn Glu Thr Thr Ile His
            180                 185                 190

Thr Ala Gly His Ser Leu Ala Ala Gly Pro Glu Ala Gly Glu Asn Gln
        195                 200                 205

Lys Gln Pro Glu Lys Asn Ala Gly Pro Thr Ala Arg Thr Ser Ala Thr
    210                 215                 220

Val Pro Val Leu Cys Leu Leu Ala Ile Ile Phe Ile Leu Thr Ala Ala
225                 230                 235                 240

Leu Ser Tyr Val Leu Cys Lys Arg Arg Arg Gly Gln Ser Pro Gln Ser
                245                 250                 255

Ser Pro Asp Leu Pro Val His Tyr Ile Pro Val Ala Pro Asp Ser Asn
```

260 265 270

Thr

<210> 30
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 30

Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Arg Thr Ser Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly
130 135 140

Ala Ser Val Arg Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser

145 150 155 160

Tyr His Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp
165 170 175

Ile Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met His Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Ser Val Thr Val Ser Ser
245

<210> 31
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 31

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

His Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Glu Ile Val Leu Thr Gln Ser Pro Gly
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ser
145 150 155 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Lys Val Ser
180 185 190

Asn Arg Phe Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala
210 215 220

Val Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 32
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 32

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


His Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
    50                  55                  60


Lys Gly Lys Ala Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


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


Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser
145                 150                 155                 160


Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175


Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190


Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205
```

```
Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly
    210                 215                 220


Val Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gly
225                 230                 235                 240


Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 33
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 33

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


His Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125
```

```
Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 34
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 34

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

His Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45
```

```
Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Lys Ala Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Val Lys
                245
```

<210> 35

<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 35

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

His Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Asp Val Gln Met Thr Gln Ser Pro Ser
130 135 140

Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Ser
145 150 155 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Met Glu Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Val Ser

```
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys His Gln Gly Ser His Val Pro Arg Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Val Lys
                245
```

<210> 36
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 36

```
Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

His Ile Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Trp Ile Tyr Pro Gly Asp Gly Ser Thr Gln Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Lys Thr Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Leu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Ile Tyr Phe Cys
                85                  90                  95

Ala Arg Glu Gly Thr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
```

```
            100                 105                 110

Ser Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Val Leu Met Thr Gln Thr Pro Leu
    130                 135                 140

Ser Leu Pro Val Ser Leu Gly Asp Gln Val Ser Ile Ser Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175

Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly
    210                 215                 220

Val Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Leu Glu Ile Lys
                245
```

<210> 37
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 37

```
Gln Leu 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 Gly Tyr Thr Phe Thr Ser Tyr
```

```
            20                  25                  30

His Ile Gln Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Trp Ile Tyr Pro Gly Asp Gly Ser Thr Gln Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Arg Ala Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Asn Leu Asp Ser Val Ser Ala Ala Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Gly Thr Tyr Tyr Ala Met Asp Tyr Trp Gly Lys Gly Ser
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
    210                 215                 220

Thr Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Pro
225                 230                 235                 240
```

Gly Thr Lys Val Asp Ile Lys
245

<210> 38
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 38

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

His Ile Gln Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Trp Ile Tyr Pro Gly Asp Gly Ser Thr Gln Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Thr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
130 135 140

Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser
145 150 155 160

```
Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Val Lys
                245
```

<210> 39
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 39

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

His Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Tyr Pro Gly Asp Gly Ser Thr Gln Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Gly Thr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Glu Ile Val Leu Thr Gln Ser Pro Gly
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala
    210                 215                 220

Val Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 40
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 40

```
Gln Val Thr Leu Lys Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

His Val Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Leu
        35                  40                  45

Gly Arg Ile Tyr Pro Gly Asp Gly Ser Thr Gln Tyr Asn Glu Lys Phe
    50                  55                  60

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

Met Glu Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Gly Thr Tyr Tyr Ala Met Asp Leu Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Glu Ile Val Leu Thr Gln Ser Pro Gly
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Ser Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala
```

```
    210                 215                 220

Val Tyr Tyr Cys Gln Gln Gly Ser His Val Pro Arg Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 41
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 41

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

His Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Tyr Pro Gly Asp Gly Ser Thr Gln Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Lys Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Gly Thr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Val Met Thr Gln Thr Pro Leu
```

```
    130                 135                 140

Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Asp Trp Tyr
                165                 170                 175

Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly
    210                 215                 220

Val Tyr Tyr Cys Met Gln Gly Ser His Val Pro Arg Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 42
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-L1

<400> 42

```
Arg Ser Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu
1               5                   10                  15
```

<210> 43
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-L2

<400> 43

Lys Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg
1 5 10

<210> 44
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-L3

<400> 44

Phe Gln Gly Ser His Val Pro Arg Thr
1 5

<210> 45
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-H1

<400> 45

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr His Ile His
1 5 10

<210> 46
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-H2

<400> 46

Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe Lys
1 5 10 15

Gly Lys

<210> 47
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-H3

<400> 47

Glu Glu Ile Thr Tyr Ala Met Asp Tyr
1 5

<210> 48
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-L1

<400> 48

Arg Ser Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Asp
1 5 10 15

<210> 49
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-L2

<400> 49

Lys Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg
1 5 10

<210> 50
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-L3

<400> 50

Met Gln Gly Ser His Val Pro Arg Thr
1 5

<210> 51

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-H1

<400> 51

Ser Gly Tyr Thr Phe Thr Ser Tyr His Met His
1 5 10

<210> 52
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-H2

<400> 52

Trp Ile Tyr Pro Gly Asp Gly Ser Thr Gln Tyr Asn Glu Lys Phe Lys
1 5 10 15

Gly

<210> 53
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA antigen binding domain CDR-H3

<400> 53

Glu Gly Thr Tyr Tyr Ala Met Asp Tyr
1 5

<210> 54
<211> 670
<212> PRT
<213> Unknown

<220>
<223> LILRB1

<400> 54

```
Met Thr Pro Ile Leu Thr Val Leu Ile Cys Leu Gly Leu Ser Leu Gly
1               5                  10                  15

Pro Arg Thr His Val Gln Ala Gly His Leu Pro Lys Pro Thr Leu Trp
            20                  25                  30

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

Cys Gln Gly Gly Gln Glu Thr Gln Glu Tyr Arg Leu Tyr Arg Glu Lys
    50                  55                  60

Lys Thr Ala Leu Trp Ile Thr Arg Ile Pro Gln Glu Leu Val Lys Lys
65                  70                  75                  80

Gly Gln Phe Pro Ile Pro Ser Ile Thr Trp Glu His Ala Gly Arg Tyr
                85                  90                  95

Arg Cys Tyr Tyr Gly Ser Asp Thr Ala Gly Arg Ser Glu Ser Ser Asp
            100                 105                 110

Pro Leu Glu Leu Val Val Thr Gly Ala Tyr Ile Lys Pro Thr Leu Ser
        115                 120                 125

Ala Gln Pro Ser Pro Val Val Asn Ser Gly Gly Asn Val Ile Leu Gln
    130                 135                 140

Cys Asp Ser Gln Val Ala Phe Asp Gly Phe Ser Leu Cys Lys Glu Gly
145                 150                 155                 160

Glu Asp Glu His Pro Gln Cys Leu Asn Ser Gln Pro His Ala Arg Gly
                165                 170                 175

Ser Ser Arg Ala Ile Phe Ser Val Gly Pro Val Ser Pro Ser Arg Arg
            180                 185                 190

Trp Trp Tyr Arg Cys Tyr Ala Tyr Asp Ser Asn Ser Pro Tyr Glu Trp
        195                 200                 205

Ser Leu Pro Ser Asp Leu Leu Glu Leu Leu Val Leu Gly Val Ser Lys
```

```
    210                 215                 220

Lys Pro Ser Leu Ser Val Gln Pro Gly Pro Ile Val Ala Pro Glu Glu
225                 230                 235                 240

Thr Leu Thr Leu Gln Cys Gly Ser Asp Ala Gly Tyr Asn Arg Phe Val
                245                 250                 255

Leu Tyr Lys Asp Gly Glu Arg Asp Phe Leu Gln Leu Ala Gly Ala Gln
            260                 265                 270

Pro Gln Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Gly Pro Val Ser
        275                 280                 285

Arg Ser Tyr Gly Gly Gln Tyr Arg Cys Tyr Gly Ala His Asn Leu Ser
    290                 295                 300

Ser Glu Trp Ser Ala Pro Ser Asp Pro Leu Asp Ile Leu Ile Ala Gly
305                 310                 315                 320

Gln Phe Tyr Asp Arg Val Ser Leu Ser Val Gln Pro Gly Pro Thr Val
                325                 330                 335

Ala Ser Gly Glu Asn Val Thr Leu Leu Cys Gln Ser Gln Gly Trp Met
            340                 345                 350

Gln Thr Phe Leu Leu Thr Lys Glu Gly Ala Ala Asp Asp Pro Trp Arg
        355                 360                 365

Leu Arg Ser Thr Tyr Gln Ser Gln Lys Tyr Gln Ala Glu Phe Pro Met
    370                 375                 380

Gly Pro Val Thr Ser Ala His Ala Gly Thr Tyr Arg Cys Tyr Gly Ser
385                 390                 395                 400

Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp Pro Leu Glu
                405                 410                 415

Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly
            420                 425                 430
```

```
Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly
        435                 440                 445

Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val Val Ile Gly
    450                 455                 460

Ile Leu Val Ala Val Ile Leu Leu Leu Leu Leu Leu Leu Leu Leu Phe
465                 470                 475                 480

Leu Ile Leu Arg His Arg Arg Gln Gly Lys His Trp Thr Ser Thr Gln
                485                 490                 495

Arg Lys Ala Asp Phe Gln His Pro Ala Gly Ala Val Gly Pro Glu Pro
            500                 505                 510

Thr Asp Arg Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln
        515                 520                 525

Glu Glu Asn Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly
    530                 535                 540

Val Glu Met Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val
545                 550                 555                 560

Thr Tyr Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser
                565                 570                 575

Pro Pro Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln
            580                 585                 590

Ala Glu Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala
        595                 600                 605

Pro Gln Asp Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg
    610                 615                 620

Glu Ala Thr Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser Pro Ala Val
625                 630                 635                 640

Pro Ser Ile Tyr Ala Thr Leu Ala Ile His Pro Ser Gln Glu Gly Pro
```

645 650 655

Ser Pro Ala Val Pro Ser Ile Tyr Ala Thr Leu Ala Ile His
660 665 670

<210> 55
<211> 3229
<212> DNA
<213> Unknown

<220>
<223> LILRB1

<400> 55
aaatgagttt taaaaaggct tgtccaggaa gcacatatgg gagctggtca ctctgcattt 60

tgggccctcc tggaggtgtt tagaccttcc gagagagaaa ctgagacaca tgagagggaa 120

gaaatgactc agtggtgaga ccctgtggag tcccacccac aaccagcaca ctgtgaccca 180

ctgcacaaac ctctagccca cagctcactt cctcctttaa gaagagaaga gaaaagagga 240

gaggagagga ggaacagaaa agaaaagaaa agaaaaagtg ggaaacaaat aatctaagaa 300

tgaggagaaa gcaagaagag tgacccccct gtgggcactc cattggtttt atggcgcctc 360

tactttctgg agtttgtgta aaacaaaaat attatggtct ttgtgcacat ttacatcaag 420

ctcagcctgg gcggcacagc cagatgcgag atgcgtctct gctgatctga gtctgcctgc 480

agcatggacc tgggtcttcc ctgaagcatc tccagggctg gagggacgac tgccatgcac 540

cgagggctca tccatccaca gagcagggca gtgggaggag acgccatgac ccccatcctc 600

acggtcctga tctgtctcgg gctgagtctg ggcccccgga cccacgtgca ggcagggcac 660

ctccccaagc ccaccctctg ggctgaacca ggctctgtga tcacccaggg gagtcctgtg 720

accctcaggt gtcaggggg ccaggagacc caggagtacc gtctatatag agaaaagaaa 780

acagcaccct ggattacacg gatcccacag gagcttgtga agaagggcca gttccccatc 840

ccatccatca cctgggaaca cacagggcgg tatcgctgtt actatggtag cgacactgca 900

ggccgctcag agagcagtga ccccctggag ctggtggtga caggagccta catcaaaccc 960

accctctcag cccagcccag ccccgtggtg aactcaggag ggaatgtaac cctccagtgt 1020

gactcacagg tggcatttga tggcttcatt ctgtgtaagg aaggagaaga tgaacaccca 1080

caatgcctga actcccagcc ccatgcccgt gggtcgtccc gcgccatctt ctccgtgggc 1140

cccgtgagcc cgagtcgcag gtggtggtac aggtgctatg cttatgactc gaactctccc 1200

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gagtggtcgg cccccagcga ccccctggac atcctgatcg caggacagtt ctatgacaga 1560

gtctccctct cggtgcagcc gggccccacg gtggcctcag gagagaacgt gaccctgctg 1620

tgtcagtcac agggatggat gcaaactttc cttctgacca aggagggggc agctgatgac 1680

ccatggcgtc taagatcaac gtaccaatct caaaaatacc aggctgaatt ccccatgggt 1740

cctgtgacct cagcccatgc ggggacctac aggtgctacg gctcacagag ctccaaaccc 1800

tacctgctga ctcaccccag tgacccctg gagctcgtgg tctcaggacc gtctgggggc 1860

cccagctccc cgacaacagg ccccacctcc acatctggcc ctgaggacca gcccctcacc 1920

cccaccgggt cggatcccca gagtggtctg ggaaggcacc tgggggttgt gatcggcatc 1980

ttggtggccg tcatcctact gctcctcctc ctcctcctcc tcttcctcat cctccgacat 2040

cgacgtcagg gcaaacactg gacatcgacc cagagaaagg ctgatttcca acatcctgca 2100

ggggctgtgg ggccagagcc cacagacaga ggcctgcagt ggaggtccag cccagctgcc 2160

gatgcccagg aagaaaacct ctatgctgcc gtgaagcaca cacagcctga ggatggggtg 2220

gagatggaca ctcggagccc acacgatgaa gacccccagg cagtgacgta tgccgaggtg 2280

aaacactcca gacctaggag agaaatggcc tctcctcctt ccccactgtc tggggaattc 2340

ctggacacaa aggacagaca ggcggaagag gacaggcaga tggacactga ggctgctgca 2400

tctgaagccc cccaggatgt gacctacgcc cagctgcaca gcttgaccct cagacgggag 2460

gcaactgagc ctcctccatc ccaggaaggg ccctctccag ctgtgcccag catctacgcc 2520

actctggcca tccactagcc cagggggga cgcagacccc acactccatg gagtctggaa 2580

tgcatgggag ctgccccccc agtggacacc attggacccc acccagcctg gatctacccc 2640

aggagactct gggaactttt aggggtcact caattctgca gtataaataa ctaatgtctc 2700

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ggaaaactac aagccacgaa tgaatgaatt aggaaagaaa aaaagtagga aatgaatgat 2880

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catggtgaaa ccctgtctct cctaaaaata caaaaattag ctggatgtgg tggcagtgcc 3060

tgtaatccca gctatttggg aggctgaggc aggagaatcg cttgaaccag ggagtcagag 3120

gtttcagtga gccaagatcg caccactgct ctccagcctg gcgacagagg gagactccat 3180

ctcaaattaa aaaaaaaaaa aaaaaagaaa gaaaaaaaaa aaaaaaaaa 3229

<210> 56
<211> 6
<212> PRT
<213> Unknown

<220>
<223> immunoreceptor tyrosine-based inhibitory motif

<400> 56

Asn Leu Tyr Ala Ala Val
1 5

<210> 57
<211> 6
<212> PRT
<213> Unknown

<220>
<223> immunoreceptor tyrosine-based inhibitory motif

<400> 57

Val Thr Tyr Ala Glu Val
1 5

<210> 58
<211> 6
<212> PRT
<213> Unknown

<220>
<223> immunoreceptor tyrosine-based inhibitory motif

<400> 58

Val Thr Tyr Ala Gln Leu
1 5

<210> 59
<211> 6
<212> PRT
<213> Unknown

<220>
<223> immunoreceptor tyrosine-based inhibitory motif

<400> 59

Ser Ile Tyr Ala Thr Leu
1 5

<210> 60
<211> 35
<212> PRT
<213> Unknown

<220>
<223> ITIM1-2

<400> 60

Asn Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu
1 5 10 15

Met Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr
20 25 30

Ala Glu Val
35

<210> 61
<211> 58
<212> PRT
<213> Unknown

<220>
<223> ITIM2-3

<400> 61

Val Thr Tyr Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala
1 5 10 15

Ser Pro Pro Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg
            20   25   30

Gln Ala Glu Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu
        35   40   45

Ala Pro Gln Asp Val Thr Tyr Ala Gln Leu
    50   55

<210> 62
<211> 36
<212> PRT
<213> Unknown

<220>
<223> ITIM3-4

<400> 62

Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala Thr
1   5   10   15

Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro Ser Ile
            20   25   30

Tyr Ala Thr Leu
        35

<210> 63
<211> 87
<212> PRT
<213> Unknown

<220>
<223> ITIM1-3

<400> 63

Asn Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu
1   5   10   15

Met Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr
            20   25   30

Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro

```
        35                  40                  45

Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu
    50                  55                  60

Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln
65                  70                  75                  80

Asp Val Thr Tyr Ala Gln Leu
                85
```

<210> 64
<211> 88
<212> PRT
<213> Unknown

<220>
<223> ITIM2-4

<400> 64

```
Val Thr Tyr Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala
1               5                   10                  15

Ser Pro Pro Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg
            20                  25                  30

Gln Ala Glu Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu
        35                  40                  45

Ala Pro Gln Asp Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg
    50                  55                  60

Arg Glu Ala Thr Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser Pro Ala
65                  70                  75                  80

Val Pro Ser Ile Tyr Ala Thr Leu
                85
```

<210> 65
<211> 117
<212> PRT
<213> Unknown

<220>
<223> ITIM1-4

<400> 65

Asn Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu
1   5   10   15

Met Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr
            20   25   30

Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro
        35   40   45

Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu
    50   55   60

Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln
65   70   75   80

Asp Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala
                85   90   95

Thr Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro Ser
            100   105   110

Ile Tyr Ala Thr Leu
        115

<210> 66
<211> 20
<212> PRT
<213> Unknown

<220>
<223> D3D4 domain

<400> 66

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp
1   5   10   15

Pro Leu Glu Leu
            20

<210> 67
<211> 43
<212> PRT
<213> Unknown

<220>
<223> Short hinge

<400> 67

Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro
1   5   10   15

Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser
            20   25   30

Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly
        35   40

<210> 68
<211> 86
<212> PRT
<213> Unknown

<220>
<223> Hinge-transmembrane

<400> 68

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp
1   5   10   15

Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro
            20   25   30

Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
        35   40   45

Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
    50   55   60

Val Ile Gly Ile Leu Val Ala Val Ile Leu Leu Leu Leu Leu Leu Leu
65   70   75   80

Leu Leu Phe Leu Ile Leu

85

<210> 69
<211> 190
<212> PRT
<213> Unknown

<220>
<223> Transmembrane-intracellular domain.

<400> 69

Val Val Ile Gly Ile Leu Val Ala Val Ile Leu Leu Leu Leu Leu
1 5 10 15

Leu Leu Leu Phe Leu Ile Leu Arg His Arg Arg Gln Gly Lys His Trp
20 25 30

Thr Ser Thr Gln Arg Lys Ala Asp Phe Gln His Pro Ala Gly Ala Val
35 40 45

Gly Pro Glu Pro Thr Asp Arg Gly Leu Gln Trp Arg Ser Ser Pro Ala
50 55 60

Ala Asp Ala Gln Glu Glu Asn Leu Tyr Ala Ala Val Lys His Thr Gln
65 70 75 80

Pro Glu Asp Gly Val Glu Met Asp Thr Arg Ser Pro His Asp Glu Asp
85 90 95

Pro Gln Ala Val Thr Tyr Ala Glu Val Lys His Ser Arg Pro Arg Arg
100 105 110

Glu Met Ala Ser Pro Pro Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr
115 120 125

Lys Asp Arg Gln Ala Glu Glu Asp Arg Gln Met Asp Thr Glu Ala Ala
130 135 140

Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr Ala Gln Leu His Ser Leu
145 150 155 160

Thr Leu Arg Arg Glu Ala Thr Glu Pro Pro Pro Ser Gln Glu Gly Pro

```
                165                 170                 175

Ser Pro Ala Val Pro Ser Ile Tyr Ala Thr Leu Ala Ile His
            180                 185                 190


<210>  70
<211>  167
<212>  PRT
<213>  Unknown

<220>
<223>  LILRB1 intracellular domain

<400>  70

Arg His Arg Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg Lys Ala
1               5                   10                  15


Asp Phe Gln His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr Asp Arg
            20                  25                  30


Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu Glu Asn
        35                  40                  45


Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu Met
    50                  55                  60


Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr Ala
65                  70                  75                  80


Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro Ser
                85                  90                  95


Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu Glu
            100                 105                 110


Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln Asp
        115                 120                 125


Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala Thr
    130                 135                 140


Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro Ser Ile
```

145 150 155 160

Tyr Ala Thr Leu Ala Ile His
165

<210> 71
<211> 253
<212> PRT
<213> Unknown

<220>
<223> LILRB1 hinge-transmembrane-intracellular domain

<400> 71

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp
1 5 10 15

Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro
20 25 30

Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
35 40 45

Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
50 55 60

Val Ile Gly Ile Leu Val Ala Val Ile Leu Leu Leu Leu Leu Leu Leu
65 70 75 80

Leu Leu Phe Leu Ile Leu Arg His Arg Arg Gln Gly Lys His Trp Thr
85 90 95

Ser Thr Gln Arg Lys Ala Asp Phe Gln His Pro Ala Gly Ala Val Gly
100 105 110

Pro Glu Pro Thr Asp Arg Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala
115 120 125

Asp Ala Gln Glu Glu Asn Leu Tyr Ala Ala Val Lys His Thr Gln Pro
130 135 140

Glu Asp Gly Val Glu Met Asp Thr Arg Ser Pro His Asp Glu Asp Pro

```
145                 150                 155                 160

Gln Ala Val Thr Tyr Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu
                165                 170                 175

Met Ala Ser Pro Pro Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys
            180                 185                 190

Asp Arg Gln Ala Glu Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala
        195                 200                 205

Ser Glu Ala Pro Gln Asp Val Thr Tyr Ala Gln Leu His Ser Leu Thr
    210                 215                 220

Leu Arg Arg Glu Ala Thr Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser
225                 230                 235                 240

Pro Ala Val Pro Ser Ile Tyr Ala Thr Leu Ala Ile His
                245                 250
```

<210> 72
<211> 233
<212> PRT
<213> Unknown

<220>
<223> LILRB1 hinge-transmembrane-intracellular domain

<400> 72

```
Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro
1               5                   10                  15

Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser
            20                  25                  30

Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val Val Ile Gly Ile
        35                  40                  45

Leu Val Ala Val Ile Leu Leu Leu Leu Leu Leu Leu Leu Leu Phe Leu
    50                  55                  60

Ile Leu Arg His Arg Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg
```

65 70 75 80

Lys Ala Asp Phe Gln His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr
85 90 95

Asp Arg Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu
100 105 110

Glu Asn Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly Val
115 120 125

Glu Met Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr
130 135 140

Tyr Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro
145 150 155 160

Pro Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala
165 170 175

Glu Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro
180 185 190

Gln Asp Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu
195 200 205

Ala Thr Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro
210 215 220

Ser Ile Tyr Ala Thr Leu Ala Ile His
225 230

<210> 73
<211> 63
<212> PRT
<213> Unknown

<220>
<223> LILRB1 hinge domain

<400> 73

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp

1 5 10 15

Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro
20 25 30

Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
35 40 45

Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly
50 55 60

<210> 74
<211> 23
<212> PRT
<213> Unknown

<220>
<223> LILRB1 transmembrane domain

<400> 74

Val Val Ile Gly Ile Leu Val Ala Val Ile Leu Leu Leu Leu Leu Leu
1 5 10 15

Leu Leu Leu Phe Leu Ile Leu
20

<210> 75
<211> 740
<212> PRT
<213> Homo sapiens

<400> 75

Met Arg Gln Thr Leu Pro Leu Leu Leu Leu Thr Val Leu Arg Pro Ser
1 5 10 15

Trp Ala Asp Pro Pro Gln Glu Lys Val Pro Leu Phe Arg Val Thr Gln
20 25 30

Gln Gly Pro Trp Gly Ser Ser Gly Ser Asn Ala Thr Asp Ser Pro Cys
35 40 45

Glu Gly Leu Pro Ala Ala Asp Ala Thr Ala Leu Thr Leu Ala Asn Arg
50 55 60

```
Asn Leu Glu Arg Leu Pro Gly Cys Leu Pro Arg Thr Leu Arg Ser Leu
65                  70                  75                  80

Asp Ala Ser His Asn Leu Leu Arg Ala Leu Ser Thr Ser Glu Leu Gly
                85                  90                  95

His Leu Glu Gln Leu Gln Val Leu Thr Leu Arg His Asn Arg Ile Ala
            100                 105                 110

Ala Leu Arg Trp Gly Pro Gly Gly Pro Ala Gly Leu His Thr Leu Asp
        115                 120                 125

Leu Ser Tyr Asn Gln Leu Ala Ala Leu Pro Pro Cys Thr Gly Pro Ala
    130                 135                 140

Leu Ser Ser Leu Arg Ala Leu Ala Leu Ala Gly Asn Pro Leu Arg Ala
145                 150                 155                 160

Leu Gln Pro Arg Ala Phe Ala Cys Phe Pro Ala Leu Gln Leu Leu Asn
                165                 170                 175

Leu Ser Cys Thr Ala Leu Gly Arg Gly Ala Gln Gly Gly Ile Ala Glu
            180                 185                 190

Ala Ala Phe Ala Gly Glu Asp Gly Ala Pro Leu Val Thr Leu Glu Val
        195                 200                 205

Leu Asp Leu Ser Gly Thr Phe Leu Glu Arg Val Glu Ser Gly Trp Ile
    210                 215                 220

Arg Asp Leu Pro Lys Leu Thr Ser Leu Tyr Leu Arg Lys Met Pro Arg
225                 230                 235                 240

Leu Thr Thr Leu Glu Gly Asp Ile Phe Lys Met Thr Pro Asn Leu Gln
                245                 250                 255

Gln Leu Asp Cys Gln Asp Ser Pro Ala Leu Ala Ser Val Ala Thr His
            260                 265                 270
```

```
Ile Phe Gln Asp Thr Pro His Leu Gln Val Leu Leu Phe Gln Asn Cys
        275                 280                 285

Asn Leu Ser Ser Phe Pro Pro Trp Thr Leu Asp Ser Ser Gln Val Leu
    290                 295                 300

Ser Ile Asn Leu Phe Gly Asn Pro Leu Thr Cys Ser Cys Asp Leu Ser
305                 310                 315                 320

Trp Leu Leu Thr Asp Ala Lys Arg Thr Val Leu Ser Arg Ala Ala Asp
                325                 330                 335

Thr Met Cys Ala Pro Ala Ala Gly Ser Ser Gly Pro Phe Ser Ala Ser
            340                 345                 350

Leu Ser Leu Ser Gln Leu Pro Gly Val Cys Gln Ser Asp Gln Ser Thr
        355                 360                 365

Thr Leu Gly Ala Ser His Pro Pro Cys Phe Asn Arg Ser Thr Tyr Ala
    370                 375                 380

Gln Gly Thr Thr Val Ala Pro Ser Ala Ala Pro Ala Thr Arg Pro Ala
385                 390                 395                 400

Gly Asp Gln Gln Ser Val Ser Lys Ala Pro Asn Val Gly Ser Arg Thr
                405                 410                 415

Ile Ala Ala Trp Pro His Ser Asp Ala Arg Glu Gly Thr Ala Pro Ser
            420                 425                 430

Thr Thr Asn Ser Val Ala Gly His Ser Asn Ser Ser Val Phe Pro Arg
        435                 440                 445

Ala Ala Ser Thr Thr Arg Thr Gln His Arg Gly Glu His Ala Pro Glu
    450                 455                 460

Leu Val Leu Glu Pro Asp Ile Ser Ala Ala Ser Thr Pro Leu Ala Ser
465                 470                 475                 480

Lys Leu Leu Gly Pro Phe Pro Thr Ser Trp Asp Arg Ser Ile Ser Ser
                485                 490                 495
```

```
Pro Gln Pro Gly Gln Arg Thr His Ala Thr Pro Gln Ala Pro Asn Pro
            500                 505                 510

Ser Leu Ser Glu Gly Glu Ile Pro Val Leu Leu Leu Asp Asp Tyr Ser
        515                 520                 525

Glu Glu Glu Glu Gly Arg Lys Glu Glu Val Gly Thr Pro His Gln Asp
    530                 535                 540

Val Pro Cys Asp Tyr His Pro Cys Lys His Leu Gln Thr Pro Cys Ala
545                 550                 555                 560

Glu Leu Gln Arg Arg Trp Arg Cys Arg Cys Pro Gly Leu Ser Gly Glu
                565                 570                 575

Asp Thr Ile Pro Asp Pro Pro Arg Leu Gln Gly Val Thr Glu Thr Thr
            580                 585                 590

Asp Thr Ser Ala Leu Val His Trp Cys Ala Pro Asn Ser Val Val His
        595                 600                 605

Gly Tyr Gln Ile Arg Tyr Ser Ala Glu Gly Trp Ala Gly Asn Gln Ser
    610                 615                 620

Val Val Gly Val Ile Tyr Ala Thr Ala Arg Gln His Pro Leu Tyr Gly
625                 630                 635                 640

Leu Ser Pro Gly Thr Thr Tyr Arg Val Cys Val Leu Ala Ala Asn Arg
                645                 650                 655

Ala Gly Leu Ser Gln Pro Arg Ser Ser Gly Trp Arg Ser Pro Cys Ala
            660                 665                 670

Ala Phe Thr Thr Lys Pro Ser Phe Ala Leu Leu Leu Ser Gly Leu Cys
        675                 680                 685

Ala Ala Ser Gly Leu Leu Leu Ala Ser Thr Val Val Leu Ser Ala Cys
    690                 695                 700
```

```
Leu Cys Arg Arg Gly Gln Thr Leu Gly Leu Gln Arg Cys Asp Thr His
705                 710                 715                 720


Leu Val Ala Tyr Lys Asn Pro Ala Phe Asp Asp Tyr Pro Leu Gly Leu
                725                 730                 735


Gln Thr Val Ser
            740


<210>  76
<211>  320
<212>  PRT
<213>  Homo sapiens

<400>  76

Met Gly Leu Pro Trp Gly Gln Pro His Leu Gly Leu Gln Met Leu Leu
1               5                   10                  15


Leu Ala Leu Asn Cys Leu Arg Pro Ser Leu Ser Leu Gly Glu Trp Gly
            20                  25                  30


Ser Trp Met Asp Ala Ser Ser Gln Thr Gln Gly Ala Gly Gly Pro Ala
        35                  40                  45


Gly Val Ile Gly Pro Trp Ala Pro Ala Pro Leu Arg Leu Gly Glu Ala
    50                  55                  60


Ala Pro Gly Thr Pro Thr Pro Val Ser Val Ala His Leu Leu Ser Pro
65                  70                  75                  80


Val Ala Thr Glu Leu Val Pro Tyr Thr Pro Gln Ile Thr Ala Trp Asp
                85                  90                  95


Leu Glu Gly Lys Val Thr Ala Thr Thr Phe Ser Leu Glu Gln Pro Arg
            100                 105                 110


Cys Val Phe Asp Gly Leu Ala Ser Ala Ser Asp Thr Val Trp Leu Val
        115                 120                 125


Val Ala Phe Ser Asn Ala Ser Arg Gly Phe Gln Asn Pro Glu Thr Leu
    130                 135                 140
```

```
Ala Asp Ile Pro Ala Ser Pro Gln Leu Leu Thr Asp Gly His Tyr Met
145                 150                 155                 160


Thr Leu Pro Leu Ser Pro Asp Gln Leu Pro Cys Gly Asp Pro Met Ala
                165                 170                 175


Gly Ser Gly Gly Ala Pro Val Leu Arg Val Gly His Asp His Gly Cys
            180                 185                 190


His Gln Gln Pro Phe Cys Asn Ala Pro Leu Pro Gly Pro Gly Pro Tyr
        195                 200                 205


Arg Glu Asp Pro Arg Ile His Arg His Leu Ala Arg Ala Ala Lys Trp
    210                 215                 220


Gln His Asp Arg His Tyr Leu His Pro Leu Phe Ser Gly Arg Pro Pro
225                 230                 235                 240


Thr Leu Gly Leu Leu Gly Ser Leu Tyr His Ala Leu Leu Gln Pro Val
                245                 250                 255


Val Ala Gly Gly Gly Pro Gly Ala Ala Ala Asp Arg Leu Leu His Gly
            260                 265                 270


Gln Ala Leu His Asp Pro Pro His Pro Thr Gln Arg Gly Arg His Thr
        275                 280                 285


Ala Gly Gly Leu Gln Ala Trp Pro Gly Pro Pro Pro Gln Pro Gln Pro
    290                 295                 300


Leu Ala Trp Pro Leu Cys Met Gly Leu Gly Glu Met Gly Arg Arg Glu
305                 310                 315                 320


<210>  77
<211>  276
<212>  PRT
<213>  Homo sapiens

<400>  77

Met Gly Leu Pro Trp Gly Gln Pro His Leu Gly Leu Gln Met Leu Leu
1               5                   10                  15
```

```
Leu Ala Leu Asn Cys Leu Arg Pro Ser Leu Ser Leu Glu Leu Val Pro
            20                  25                  30

Tyr Thr Pro Gln Ile Thr Ala Trp Asp Leu Glu Gly Lys Val Thr Ala
        35                  40                  45

Thr Thr Phe Ser Leu Glu Gln Pro Arg Cys Val Phe Asp Gly Leu Ala
    50                  55                  60

Ser Ala Ser Asp Thr Val Trp Leu Val Val Ala Phe Ser Asn Ala Ser
65                  70                  75                  80

Arg Gly Phe Gln Asn Pro Glu Thr Leu Ala Asp Ile Pro Ala Ser Pro
                85                  90                  95

Gln Leu Leu Thr Asp Gly His Tyr Met Thr Leu Pro Leu Ser Pro Asp
            100                 105                 110

Gln Leu Pro Cys Gly Asp Pro Met Ala Gly Ser Gly Gly Ala Pro Val
        115                 120                 125

Leu Arg Val Gly His Asp His Gly Cys His Gln Gln Pro Phe Cys Asn
    130                 135                 140

Ala Pro Leu Pro Gly Pro Gly Pro Tyr Arg Val Lys Phe Leu Leu Met
145                 150                 155                 160

Asp Thr Arg Gly Ser Pro Arg Ala Glu Thr Lys Trp Ser Asp Pro Ile
                165                 170                 175

Thr Leu His Gln Gly Lys Thr Pro Gly Ser Ile Asp Thr Trp Pro Gly
            180                 185                 190

Arg Arg Ser Gly Ser Met Ile Val Ile Thr Ser Ile Leu Ser Ser Leu
        195                 200                 205

Ala Gly Leu Leu Leu Leu Ala Phe Leu Ala Ala Ser Thr Met Arg Phe
    210                 215                 220
```

```
Ser Ser Leu Trp Trp Pro Glu Glu Ala Pro Glu Gln Leu Arg Ile Gly
225                 230                 235                 240


Ser Phe Met Gly Lys Arg Tyr Met Thr His His Ile Pro Pro Ser Glu
                245                 250                 255


Ala Ala Thr Leu Pro Val Gly Cys Lys Pro Gly Leu Asp Pro Leu Pro
            260                 265                 270


Ser Leu Ser Pro
        275
```

<210> 78
<211> 265
<212> PRT
<213> Homo sapiens

<400> 78

```
Met Gly Leu Pro Trp Gly Gln Pro His Leu Gly Leu Gln Met Leu Leu
1               5                   10                  15


Leu Ala Leu Asn Cys Leu Arg Pro Ser Leu Ser Leu Glu Leu Val Pro
            20                  25                  30


Tyr Thr Pro Gln Ile Thr Ala Trp Asp Leu Glu Gly Lys Val Thr Ala
        35                  40                  45


Thr Thr Phe Ser Leu Glu Gln Pro Arg Cys Val Phe Asp Gly Leu Ala
    50                  55                  60


Ser Ala Ser Asp Thr Val Trp Leu Val Val Ala Phe Ser Asn Ala Ser
65                  70                  75                  80


Arg Gly Phe Gln Asn Pro Glu Thr Leu Ala Asp Ile Pro Ala Ser Pro
                85                  90                  95


Gln Leu Leu Thr Asp Gly His Tyr Met Thr Leu Pro Leu Ser Pro Asp
            100                 105                 110


Gln Leu Pro Cys Gly Asp Pro Met Ala Gly Ser Gly Gly Ala Pro Val
        115                 120                 125
```

```
Leu Arg Val Gly His Asp His Gly Cys His Gln Gln Pro Phe Cys Asn
    130                 135                 140

Ala Pro Leu Pro Gly Pro Gly Pro Tyr Arg Glu Asp Pro Arg Ile His
145                 150                 155                 160

Arg His Leu Ala Arg Ala Ala Lys Trp Gln His Asp Arg His Tyr Leu
                165                 170                 175

His Pro Leu Phe Ser Gly Arg Pro Pro Thr Leu Gly Leu Leu Gly Ser
            180                 185                 190

Leu Tyr His Ala Leu Leu Gln Pro Val Val Ala Gly Gly Gly Pro Gly
        195                 200                 205

Ala Ala Ala Asp Arg Leu Leu His Gly Gln Ala Leu His Asp Pro Pro
    210                 215                 220

His Pro Thr Gln Arg Gly Arg His Thr Ala Gly Gly Leu Gln Ala Trp
225                 230                 235                 240

Pro Gly Pro Pro Pro Gln Pro Gln Pro Leu Ala Trp Pro Leu Cys Met
                245                 250                 255

Gly Leu Gly Glu Met Gly Arg Arg Glu
            260                 265
```

<210> 79
<211> 276
<212> PRT
<213> Homo sapiens

<400> 79

```
Met Gly Leu Pro Trp Gly Gln Pro His Leu Gly Leu Gln Met Leu Leu
1               5                   10                  15

Leu Ala Leu Asn Cys Leu Arg Pro Ser Leu Ser Leu Glu Leu Val Pro
            20                  25                  30

Tyr Thr Pro Gln Ile Thr Ala Trp Asp Leu Glu Gly Lys Val Thr Ala
        35                  40                  45
```

```
Thr Thr Phe Ser Leu Glu Gln Pro Arg Cys Val Phe Asp Gly Leu Ala
    50                  55                  60

Ser Ala Ser Asp Thr Val Trp Leu Val Val Ala Phe Ser Asn Ala Ser
65                  70                  75                  80

Arg Gly Phe Gln Asn Pro Glu Thr Leu Ala Asp Ile Pro Ala Ser Pro
                85                  90                  95

Gln Leu Leu Thr Asp Gly His Tyr Met Thr Leu Pro Leu Ser Pro Asp
            100                 105                 110

Gln Leu Pro Cys Gly Asp Pro Met Ala Gly Ser Gly Gly Ala Pro Val
        115                 120                 125

Leu Arg Val Gly His Asp His Gly Cys His Gln Gln Pro Phe Cys Asn
    130                 135                 140

Ala Pro Leu Pro Gly Pro Gly Pro Tyr Arg Val Lys Phe Leu Leu Met
145                 150                 155                 160

Asp Thr Arg Gly Ser Pro Arg Ala Glu Thr Lys Trp Ser Asp Pro Ile
                165                 170                 175

Thr Leu His Gln Gly Lys Thr Pro Gly Ser Ile Asp Thr Trp Pro Gly
            180                 185                 190

Arg Arg Ser Gly Ser Met Ile Val Ile Thr Ser Ile Leu Ser Ser Leu
        195                 200                 205

Ala Gly Leu Leu Leu Leu Ala Phe Leu Ala Ala Ser Thr Met Arg Phe
    210                 215                 220

Ser Ser Leu Trp Trp Pro Glu Glu Ala Pro Glu Gln Leu Arg Ile Gly
225                 230                 235                 240

Ser Phe Met Gly Lys Arg Tyr Met Thr His His Ile Pro Pro Arg Glu
                245                 250                 255
```

Ala Ala Thr Leu Pro Val Gly Cys Lys Pro Gly Leu Asp Pro Leu Pro
            260   265   270

Ser Leu Ser Pro
        275

<210> 80
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 80

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
            20   25   30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35   40   45

Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys Phe
    50   55   60

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

Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95

Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115   120   125

Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile
    130   135   140

```
Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Ser Ala Ser
145                 150                 155                 160


Ser Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Ser Gly Thr Ser
                165                 170                 175


Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro
            180                 185                 190


Gly Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile
        195                 200                 205


Ser Ser Val Glu Ala Glu Asp Asp Ala Thr Tyr Tyr Cys Gln Gln Trp
    210                 215                 220


Ser Gly Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
225                 230                 235


<210>  81
<211>  64
<212>  PRT
<213>  Unknown

<220>
<223>  Hinge (iTIM hinge)

<400>  81

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp
1               5                   10                  15


Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro
            20                  25                  30


Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
        35                  40                  45


Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
    50                  55                  60


<210>  82
<211>  44
<212>  PRT
<213>  Unknown
```

<220>
<223> Short hinge 2

<400> 82

Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro
1   5   10   15

Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser
            20   25   30

Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
        35   40

<210> 83
<211> 67
<212> PRT
<213> Unknown

<220>
<223> Long hinge 1

<400> 83

Ala Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Pro Val Pro Ser
1   5   10   15

Thr Pro Pro Thr Pro Ser Pro Ser Thr Pro Pro Thr Pro Ser Pro Ser
            20   25   30

Gly Gly Ser Gly Asn Ser Ser Gly Ser Gly Gly Ser Pro Val Pro Ser
        35   40   45

Thr Pro Pro Thr Pro Ser Pro Ser Thr Pro Pro Thr Pro Ser Pro Ser
    50   55   60

Ala Ser Val
65

<210> 84
<211> 75
<212> PRT
<213> Unknown

<220>

<223> Long hinge 2

<400> 84

```
Ala Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Pro Val Pro Ser
1               5                   10                  15


Thr Pro Pro Thr Asn Ser Ser Ser Thr Pro Pro Thr Pro Ser Pro Ser
            20                  25                  30


Pro Val Pro Ser Thr Pro Pro Thr Asn Ser Ser Ser Thr Pro Pro Thr
        35                  40                  45


Pro Ser Pro Ser Pro Val Pro Ser Thr Pro Pro Thr Asn Ser Ser Ser
    50                  55                  60


Thr Pro Pro Thr Pro Ser Pro Ser Ala Ser Val
65                  70                  75
```

<210> 85
<211> 407
<212> PRT
<213> Artificial Sequence

<220>
<223> PA2.1.14 (VL:VH) scFv LIR1 sHTICD

<400> 85

```
Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
1               5                   10                  15


Thr Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gln
            20                  25                  30


Gly Thr Lys Val Glu Val Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
        35                  40                  45


Ser Gly Gly Gly Gly Ser Gly Gly Gln Val Gln Leu Val Gln Ser Gly
    50                  55                  60


Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala
65                  70                  75                  80
```

```
Ser Gly Tyr Thr Phe Thr Ser Tyr His Ile His Trp Val Arg Gln Ala
                85                  90                  95

Pro Gly Gln Gly Leu Glu Trp Ile Gly Trp Ile Tyr Pro Gly Asn Val
            100                 105                 110

Asn Thr Glu Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Ile Thr Ala
        115                 120                 125

Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
    130                 135                 140

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Glu Ile Thr Tyr Ala
145                 150                 155                 160

Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Val Val
                165                 170                 175

Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro Thr Ser
            180                 185                 190

Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser Asp Pro
        195                 200                 205

Gln Ser Gly Leu Gly Arg His Leu Gly Val Val Ile Gly Ile Leu Val
    210                 215                 220

Ala Val Ile Leu Leu Leu Leu Leu Leu Leu Leu Leu Phe Leu Ile Leu
225                 230                 235                 240

Arg His Arg Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg Lys Ala
                245                 250                 255

Asp Phe Gln His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr Asp Arg
            260                 265                 270

Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu Glu Asn
        275                 280                 285

Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu Met
    290                 295                 300
```

```
Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr Ala
305                 310                 315                 320


Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro Ser
                325                 330                 335


Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu Glu
            340                 345                 350


Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln Asp
        355                 360                 365


Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala Thr
    370                 375                 380


Glu Pro Pro Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro Ser Ile
385                 390                 395                 400


Tyr Ala Thr Leu Ala Ile His
                405


<210>  86
<211>  500
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  PA2.1.14 (VL:VH) scFv LIR1 HTICD

<400>  86

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser Ile Val His Ser
            20                  25                  30


Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        35                  40                  45


Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60
```

```
Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
65                  70                  75                  80

Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly
                85                  90                  95

Ser His Val Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly
    130                 135                 140

Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser
145                 150                 155                 160

Tyr His Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp
                165                 170                 175

Ile Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys
            180                 185                 190

Phe Lys Gly Lys Ala Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala
        195                 200                 205

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr
    210                 215                 220

Cys Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240

Thr Leu Val Thr Val Ser Ser Tyr Gly Ser Gln Ser Ser Lys Pro Tyr
                245                 250                 255

Leu Leu Thr His Pro Ser Asp Pro Leu Glu Leu Val Val Ser Gly Pro
            260                 265                 270
```

```
Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro Thr Ser Thr Ser Gly
        275                 280                 285

Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly
    290                 295                 300

Leu Gly Arg His Leu Gly Val Val Ile Gly Ile Leu Val Ala Val Ile
305                 310                 315                 320

Leu Leu Leu Leu Leu Leu Leu Leu Leu Phe Leu Ile Leu Arg His Arg
                325                 330                 335

Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg Lys Ala Asp Phe Gln
            340                 345                 350

His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr Asp Arg Gly Leu Gln
        355                 360                 365

Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu Glu Asn Leu Tyr Ala
    370                 375                 380

Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu Met Asp Thr Arg
385                 390                 395                 400

Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr Ala Glu Val Lys
                405                 410                 415

His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro Ser Pro Leu Ser
            420                 425                 430

Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu Glu Asp Arg Gln
        435                 440                 445

Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr
    450                 455                 460

Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala Thr Glu Pro Pro
465                 470                 475                 480

Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro Ser Ile Tyr Ala Thr
                485                 490                 495
```

Leu Ala Ile His
            500

<210> 87
<211> 462
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN_SsI CD8_HT 41BB CD3z

<400> 87

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
            20   25   30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35   40   45

Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys Phe
    50   55   60

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

Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95

Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115   120   125

Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile
    130   135   140

Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Ser Ala Ser
145   150   155   160

```
Ser Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Ser Gly Thr Ser
                165                 170                 175

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro
            180                 185                 190

Gly Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile
        195                 200                 205

Ser Ser Val Glu Ala Glu Asp Asp Ala Thr Tyr Tyr Cys Gln Gln Trp
    210                 215                 220

Ser Gly Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile Thr
225                 230                 235                 240

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                245                 250                 255

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            260                 265                 270

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        275                 280                 285

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    290                 295                 300

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
305                 310                 315                 320

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
                325                 330                 335

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
            340                 345                 350

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
        355                 360                 365
```

```
Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
    370                 375                 380

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
385                 390                 395                 400

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
                405                 410                 415

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
            420                 425                 430

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
        435                 440                 445

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
    450                 455                 460
```

<210> 88
<211> 480
<212> PRT
<213> Artificial Sequence

<220>
<223> PA2.1.14 scFv LIR1 sHTICD

<400> 88

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

His Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Lys Ala Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190

Asn Arg Phe Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Val Lys Val Val Ser Gly Pro Ser Gly Gly Pro
                245                 250                 255

Ser Ser Pro Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln
            260                 265                 270

Pro Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His
        275                 280                 285

Leu Gly Val Val Ile Gly Ile Leu Val Ala Val Ile Leu Leu Leu Leu
    290                 295                 300
```

```
Leu Leu Leu Leu Leu Phe Leu Ile Leu Arg His Arg Arg Gln Gly Lys
305                 310                 315                 320

His Trp Thr Ser Thr Gln Arg Lys Ala Asp Phe Gln His Pro Ala Gly
                325                 330                 335

Ala Val Gly Pro Glu Pro Thr Asp Arg Gly Leu Gln Trp Arg Ser Ser
            340                 345                 350

Pro Ala Ala Asp Ala Gln Glu Glu Asn Leu Tyr Ala Ala Val Lys His
        355                 360                 365

Thr Gln Pro Glu Asp Gly Val Glu Met Asp Thr Arg Ser Pro His Asp
    370                 375                 380

Glu Asp Pro Gln Ala Val Thr Tyr Ala Glu Val Lys His Ser Arg Pro
385                 390                 395                 400

Arg Arg Glu Met Ala Ser Pro Pro Ser Pro Leu Ser Gly Glu Phe Leu
                405                 410                 415

Asp Thr Lys Asp Arg Gln Ala Glu Glu Asp Arg Gln Met Asp Thr Glu
            420                 425                 430

Ala Ala Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr Ala Gln Leu His
        435                 440                 445

Ser Leu Thr Leu Arg Arg Glu Ala Thr Glu Pro Pro Pro Ser Gln Glu
    450                 455                 460

Gly Pro Ser Pro Ala Val Pro Ser Ile Tyr Ala Thr Leu Ala Ile His
465                 470                 475                 480
```

<210> 89
<211> 500
<212> PRT
<213> Artificial Sequence

<220>
<223> PA2.1.14 scFv LIR1 HTICD

<400> 89

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


His Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
    50                  55                  60


Lys Gly Lys Ala Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140


Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser
145                 150                 155                 160


Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp Tyr
                165                 170                 175


Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Val Ser
            180                 185                 190


Asn Arg Phe Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205
```

```
Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Arg Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Val Lys Tyr Gly Ser Gln Ser Ser Lys Pro Tyr
                245                 250                 255

Leu Leu Thr His Pro Ser Asp Pro Leu Glu Leu Val Val Ser Gly Pro
            260                 265                 270

Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro Thr Ser Thr Ser Gly
        275                 280                 285

Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly
    290                 295                 300

Leu Gly Arg His Leu Gly Val Val Ile Gly Ile Leu Val Ala Val Ile
305                 310                 315                 320

Leu Leu Leu Leu Leu Leu Leu Leu Leu Phe Leu Ile Leu Arg His Arg
                325                 330                 335

Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg Lys Ala Asp Phe Gln
            340                 345                 350

His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr Asp Arg Gly Leu Gln
        355                 360                 365

Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu Glu Asn Leu Tyr Ala
    370                 375                 380

Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu Met Asp Thr Arg
385                 390                 395                 400

Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr Ala Glu Val Lys
                405                 410                 415

His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro Ser Pro Leu Ser
            420                 425                 430
```

```
Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu Glu Asp Arg Gln
        435                 440                 445


Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr
    450                 455                 460


Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala Thr Glu Pro Pro
465                 470                 475                 480


Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro Ser Ile Tyr Ala Thr
                485                 490                 495


Leu Ala Ile His
            500
```

<210> 90
<211> 32
<212> PRT
<213> Unknown

<220>
<223> Hinge (truncated)

<400> 90

```
Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
1               5                   10                  15


Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
            20                  25                  30
```

<210> 91
<211> 85
<212> PRT
<213> Unknown

<220>
<223> 2X short hinge

<400> 91

```
Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro
1               5                   10                  15
```

Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser
            20   25   30

Asp Pro Gln Ser Gly Leu Gly Arg His Val Val Ser Gly Pro Ser Gly
        35   40   45

Gly Pro Ser Ser Pro Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu
    50   55   60

Asp Gln Pro Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly
65   70   75   80

Arg His Leu Gly Val
                85

<210> 92
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H1

<400> 92

Ser Gly Gly Tyr Tyr Trp Ser
1   5

<210> 93
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H1

<400> 93

Thr Ser Gly Val Gly Val Gly
1   5

<210> 94
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> anti-HLA-A*11 CDR-H1

<400> 94

Ser Tyr Ala Met His
1   5

<210> 95
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H1

<400> 95

Ser Tyr Asp Met His
1   5

<210> 96
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H1

<400> 96

Ser Tyr Trp Met His
1   5

<210> 97
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H2

<400> 97

Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1   5   10   15

<210> 98
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H2

<400> 98

Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser Leu Lys Ser
1   5   10   15

<210> 99
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H2

<400> 99

Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe Gln
1   5   10   15

Gly

<210> 100
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H2

<400> 100

Ala Ile Gly Thr Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys Gly
1   5   10   15

<210> 101
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H2

<400> 101

Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 102
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 102

His Tyr Tyr Tyr Tyr Ser Met Asp Val
1   5

<210> 103
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 103

His Tyr Tyr Tyr Tyr Tyr Leu Asp Val
1   5

<210> 104
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 104

His Tyr Tyr Tyr Tyr Met Asp Val
1   5

<210> 105
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> anti-HLA-A*11 CDR-H3

<400> 105

His Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5

<210> 106
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 106

Lys Thr Thr Ser Phe Tyr Phe Asp Tyr
1 5

<210> 107
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 107

Arg His Met Arg Leu Ser Cys Phe Asp Tyr
1 5 10

<210> 108
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 108

Glu Gly Asn Gly Ala Asn Pro Asp Ala Phe Asp Ile
1 5 10

<210> 109
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 109

Asp Leu Pro Gly Ser Tyr Trp Tyr Phe Asp Leu
1   5   10

<210> 110
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR-H3

<400> 110

Gly Val Leu Leu Tyr Asn Trp Phe Asp Pro
1   5   10

<210> 111
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR1 LC

<400> 111

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1   5   10

<210> 112
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR2 LC

<400> 112

Ala Ala Ser Ser Leu Gln Ser
1   5

<210> 113
<211> 9

<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 CDR3 LC

<400> 113

Gln Gln Ser Tyr Ser Thr Pro Leu Thr
1   5

<210> 114
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 114

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1   5   10   15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20   25   30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35   40   45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50   55   60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65   70   75   80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85   90   95

Cys Ala Arg His Tyr Tyr Tyr Tyr Ser Met Asp Val Trp Gly Lys Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115   120   125

```
Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 115
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 115

```
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1               5                   10                  15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
            20                  25                  30

Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
        35                  40                  45
```

```
Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser
    50                  55                  60

Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65                  70                  75                  80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
                85                  90                  95

Cys Ala His Arg His Met Arg Leu Ser Cys Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 116
<211> 245

<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 116

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Asn Gly Ala Asn Pro Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145 150 155 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
180 185 190

```
Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205


Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240


Lys Val Glu Ile Lys
                245


<210>  117
<211>  243
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*11 antigen binding domain

<400>  117

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Gly Thr Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
    50                  55                  60


Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
65                  70                  75                  80


Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Arg Asp Leu Pro Gly Ser Tyr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110
```

```
Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140


Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190


Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205


Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220


Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240


Glu Ile Lys
```

<210> 118
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 118

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30
```

```
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg His Tyr Tyr Tyr Tyr Tyr Leu Asp Val Trp Gly Lys Gly
            100                 105                 110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240
```

Glu Ile Lys

<210> 119
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 119

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45

Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Cys Leu Gly Val Leu Leu Tyr Asn Trp Phe Asp Pro Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160
```

```
Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 120
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 120

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
```

```
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg His Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 121
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 121

```
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1               5                  10                  15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
            20                  25                  30

Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
        35                  40                  45

Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser
    50                  55                  60

Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65                  70                  75                  80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
                85                  90                  95

Cys Ala His Lys Thr Thr Ser Phe Tyr Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220
```

```
Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240


Glu Ile Lys



<210>  122
<211>  243
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*11 antigen binding domain

<400>  122

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg His Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly
            100                 105                 110


Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140
```

```
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190


Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205


Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220


Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240


Glu Ile Lys
```

<210> 123
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 123

```
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg       60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga      120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac      180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc      240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac      300

tactactact actccatgga cgtctggggc aaagggacca cggtcaccgt gtcctcaggc      360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg      420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg      480
```

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagcccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 124
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 124
cagatcaccc tgaaagagtc cggccccacc ctggtgaaac ccacccagac cctgaccctg 60

acatgcacct tcagcggctt cagcctgagc acctctggcg tgggcgtggg ctggatcaga 120

cagcctcccg gcaaggccct ggaatggctg gccctgatct actggaacga cgacaagcgg 180

tacagcccca gcctgaagtc ccggctgacc atcaccaagg acacctcgaa gaaccaggtg 240

gtgctgacca tgacaaacat ggaccccgtg gacaccgcca catattactg tgcacacaga 300

cacatgcgtt taagctgttt tgactactgg ggccagggaa ccctggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgacatccag 420

atgacccagt ctccatcctc cctgtctgca tctgtaggag acagagtcac catcacttgc 480

cgggcaagtc agagcattag cagctattta aattggtatc agcagaaacc agggaaagcc 540

cctaagctcc tgatctatgc tgcatccagt ttgcaaagtg gggtcccatc aaggttcagt 600

ggcagtggat ctgggacaga tttcactctc accatcagca gtctgcaacc tgaagatttt 660

gcaacttact actgtcaaca gagttacagt acccctctca ctttcggcgg cggaacaaag 720

gtggagatca ag 732

<210> 125
<211> 735
<212> DNA
<213> Artificial Sequence

<220>

<223> HLA-A*11 antigen binding domain

<400> 125
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg ccagcggcta caccttcacc agctacgcca tgcactgggt tcgacaggcc 120

cctggccaga gactggaatg gatgggctgg atcaacgccg gcaacggcaa caccaagtac 180

agccagaaat tccagggcag agtgaccatc acccgggaca ccagcgccag caccgcctac 240

atggaactga gcagcctgcg gagcgaggac accgctgtgt attactgtgc gagagaagga 300

aatggtgcca accctgatgc ttttgatatc tggggccaag ggacaatggt caccgtgtcc 360

tcaggcggag gtggaagcgg agggggagga tctggcggcg gaggaagcgg aggcgacatc 420

cagatgaccc agtctccatc ctccctgtct gcatctgtag gagacagagt caccatcact 480

tgccgggcaa gtcagagcat tagcagctat ttaaattggt atcagcagaa accagggaaa 540

gcccctaagc tcctgatcta tgctgcatcc agtttgcaaa gtggggtccc atcaaggttc 600

agtggcagtg gatctgggac agatttcact ctcaccatca gcagtctgca acctgaagat 660

tttgcaactt actactgtca acagagttac agtacccctc tcactttcgg cggcggaaca 720

aaggtggaga tcaag 735

<210> 126
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 126
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctacgaca tgcactgggt ccgccaggcc 120

accggcaagg gactggaatg ggtgtccgcc atcggcacag ccggcgacac ttactacccc 180

ggcagcgtga agggccggtt caccatcagc agagagaacg ccaagaacag cctgtacctg 240

cagatgaaca gccttcgagc cggcgatacc gccgtgtatt actgtgcaag agatctccct 300

ggtagctact ggtacttcga tctctggggc cgtggcaccc tggtcactgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagcccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 127
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 127
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac 300

tactactact actacctgga cgtctggggc aaagggacca cggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagcccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 128
<211> 729
<212> DNA
<213> Artificial Sequence

<220>

<223> HLA-A*11 antigen binding domain

<400> 128
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctactgga tgcactgggt ccgccaggcc 120

cctggcaagg gactggtctg ggtgtctcga atcaacagcg acggcagcag caccagctac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgttg tttgggtgtt 300

ttattataca actggttcga cccctggggc cagggaaccc tggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 129
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 129
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac 300

tactactact acatggacgt ctggggcaaa gggaccacgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgacat ccagatgacc 420

cagtctccat cctccctgtc tgcatctgta ggagacagag tcaccatcac ttgccgggca 480

agtcagagca ttagcagcta tttaaattgg tatcagcaga aaccagggaa agcccctaag 540

ctcctgatct atgctgcatc cagtttgcaa agtggggtcc catcaaggtt cagtggcagt 600

ggatctggga cagatttcac tctcaccatc agcagtctgc aacctgaaga ttttgcaact 660

tactactgtc aacagagtta cagtacccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 130
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA-A*11 antigen binding domain

<400> 130
cagatcaccc tgaaagagtc cggccccacc ctggtgaaac ccacccagac cctgaccctg 60

acatgcacct tcagcggctt cagcctgagc acctctggcg tgggcgtggg ctggatcaga 120

cagcctcccg gcaaggccct ggaatggctg gccctgatct actggaacga cgacaagcgg 180

tacagcccca gcctgaagtc ccggctgacc atcaccaagg acacctcgaa gaaccaggtg 240

gtgctgacca tgacaaacat ggaccccgtg gacaccgcca catattactg tgcacacaaa 300

acgacgtcgt tttactttga ctactggggc cagggaaccc tggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagccccт 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 131
<211> 729
<212> DNA
<213> Artificial Sequence

<220>

<223> HLA-A*11 antigen binding domain

<400> 131
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac 300

tactactact actacatgga cgtctggggc aaagggacca cggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 132
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 132

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

```
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg His Tyr Tyr Tyr Tyr Ser Met Asp Val Trp Gly Lys Gly
            100                 105                 110


Thr Thr Val Thr Val Ser Ser
        115


<210>  133
<211>  120
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  anti-HLA-A*11 heavy chain

<400>  133

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1               5                   10                  15


Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
            20                  25                  30


Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
        35                  40                  45


Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser
    50                  55                  60


Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65                  70                  75                  80


Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
                85                  90                  95


Cys Ala His Arg His Met Arg Leu Ser Cys Phe Asp Tyr Trp Gly Gln
            100                 105                 110
```

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 134
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 134

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
        35   40   45

Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
    50   55   60

Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Glu Gly Asn Gly Ala Asn Pro Asp Ala Phe Asp Ile Trp Gly
            100   105   110

Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 135
<211> 119
<212> PRT
<213> Artificial Sequence

<220>

<223> anti-HLA-A*11 heavy chain

<400> 135

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Gly Thr Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
    50                  55                  60


Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
65                  70                  75                  80


Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Arg Asp Leu Pro Gly Ser Tyr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser
        115
```

<210> 136
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 136

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30
```

```
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg His Tyr Tyr Tyr Tyr Tyr Leu Asp Val Trp Gly Lys Gly
            100                 105                 110


Thr Thr Val Thr Val Ser Ser
        115


<210>  137
<211>  119
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  anti-HLA-A*11 heavy chain

<400>  137

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45


Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Cys Leu Gly Val Leu Leu Tyr Asn Trp Phe Asp Pro Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser
        115


<210>  138
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  anti-HLA-A*11 heavy chain

<400>  138

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg His Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
            100                 105                 110


Thr Val Thr Val Ser Ser
        115
```

<210> 139
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 139

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45

Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala His Lys Thr Thr Ser Phe Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 140
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 140

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg His Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly
            100                 105                 110

Thr Thr Val Thr Val Ser Ser
        115


<210>  141
<211>  107
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  anti-HLA-A*11 light chain

<400>  141

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
```

```
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210>  142
<211>  357
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  anti-HLA-A*11 heavy chain

<400>  142
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg       60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga      120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac      180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc      240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac      300

tactactact actccatgga cgtctggggc aaagggacca cggtcaccgt gtcctca         357


<210>  143
<211>  360
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  anti-HLA-A*11 heavy chain

<400>  143
cagatcaccc tgaaagagtc cggccccacc ctggtgaaac ccacccagac cctgaccctg       60

acatgcacct tcagcggctt cagcctgagc acctctggcg tgggcgtggg ctggatcaga      120

cagcctcccg gcaaggccct ggaatggctg gccctgatct actggaacga cgacaagcgg      180

tacagcccca gcctgaagtc ccggctgacc atcaccaagg acacctcgaa gaaccaggtg      240

gtgctgacca tgacaaacat ggaccccgtg gacaccgcca catattactg tgcacacaga      300
```

cacatgcgtt taagctgttt tgactactgg ggccagggaa ccctggtcac cgtgtcctca 360

<210> 144
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 144
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg ccagcggcta caccttcacc agctacgcca tgcactgggt tcgacaggcc 120

cctggccaga gactggaatg gatgggctgg atcaacgccg gcaacggcaa caccaagtac 180

agccagaaat tccagggcag agtgaccatc acccgggaca ccagcgccag caccgcctac 240

atggaactga gcagcctgcg gagcgaggac accgctgtgt attactgtgc gagagaagga 300

aatggtgcca accctgatgc ttttgatatc tggggccaag ggacaatggt caccgtgtcc 360

tca 363

<210> 145
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 145
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctacgaca tgcactgggt ccgccaggcc 120

accggcaagg gactggaatg ggtgtccgcc atcggcacag ccggcgacac ttactacccc 180

ggcagcgtga agggccggtt caccatcagc agagagaacg ccaagaacag cctgtacctg 240

cagatgaaca gccttcgagc cggcgatacc gccgtgtatt actgtgcaag agatctccct 300

ggtagctact ggtacttcga tctctggggc cgtggcaccc tggtcactgt gtcctca 357

<210> 146
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 146
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac 300

tactactact actacctgga cgtctggggc aaagggacca cggtcaccgt gtcctca 357

<210> 147
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 147
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctactgga tgcactgggt ccgccaggcc 120

cctggcaagg gactggtctg ggtgtctcga atcaacagcg acggcagcag caccagctac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgttg tttgggtgtt 300

ttattataca actggttcga cccctggggc cagggaaccc tggtcaccgt gtcctca 357

<210> 148
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 148
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac 300

tactactact acatggacgt ctggggcaaa gggaccacgg tcaccgtgtc ctca 354

<210> 149
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 149
cagatcaccc tgaaagagtc cggccccacc ctggtgaaac ccacccagac cctgaccctg 60

acatgcacct tcagcggctt cagcctgagc acctctggcg tgggcgtggg ctggatcaga 120

cagcctcccg gcaaggccct ggaatggctg gccctgatct actggaacga cgacaagcgg 180

tacagcccca gcctgaagtc ccggctgacc atcaccaagg acacctcgaa gaaccaggtg 240

gtgctgacca tgacaaacat ggaccccgtg gacaccgcca catattactg tgcacacaaa 300

acgacgtcgt tttactttga ctactggggc cagggaaccc tggtcaccgt gtcctca 357

<210> 150
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 heavy chain

<400> 150
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagcccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagacac 300

tactactact actacatgga cgtctggggc aaagggacca cggtcaccgt gtcctca 357

<210> 151
<211> 321

<212> DNA
<213> Artificial Sequence

<220>
<223> anti-HLA-A*11 light chain

<400> 151
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacagta cccctctcac tttcggcggc 300

ggaacaaagg tggagatcaa g 321

<210> 152
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 152

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly

<210> 153
<211> 66
<212> PRT
<213> Unknown

<220>
<223> encodes signal sequence

<400> 153

Ala Thr Gly Gly Ala Cys Ala Thr Gly Ala Gly Gly Gly Thr Cys Cys
1 5 10 15

Cys Cys Gly Cys Thr Cys Ala Gly Cys Thr Cys Cys Thr Gly Gly Gly
20 25 30

Gly Cys Thr Cys Cys Thr Gly Cys Thr Ala Cys Thr Cys Thr Gly Gly
        35   40   45

Cys Thr Cys Cys Gly Ala Gly Gly Thr Gly Cys Cys Ala Gly Ala Thr
    50   55   60

Gly Thr
65

<210> 154
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 154

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20   25   30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
    50   55   60

Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65   70   75   80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85   90   95

Tyr Cys Thr Thr Asp Leu Pro Lys Leu Arg Asn Phe His Ile Trp Gly
            100   105   110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115   120   125

```
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys
                245
```

<210> 155
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 155

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Tyr Val
        35                  40                  45
```

```
Ser Ala Ile Ser Ser Asn Gly Gly Ser Thr Tyr Tyr Ala Asn Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Gly Ser Leu Arg Ala Glu Asp Met Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Leu Glu Tyr His Gly Phe Arg Gln Tyr Gly Leu Arg Tyr Trp
            100                 105                 110

His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 156
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 156

Gln Leu Gln Leu Gln Glu Ser Gly Ser Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Ser Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Arg Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Ser Ile Lys Phe Trp Phe Ala Gly Ile Asn Tyr Phe Phe Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
165 170 175

```
Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190


Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220


Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240


Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 157
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 157

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45


Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Ser Gly Phe Leu Gly Met Gly Ser Asn Phe Ile Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 158
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 158

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Leu Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Ser Gly Asp Arg Ala Arg Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240
```

Glu Ile Lys

<210> 159
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 159

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Pro Arg Gly Tyr His Gln Met Val Asp Ala Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

```
Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 160
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 160

```
Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
```

```
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Val Arg Phe Leu Ala Ala Arg Thr Thr Ile Pro Glu Ala
            100                 105                 110

Asn Phe Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp
    130                 135                 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250
```

<210> 161
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 161

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Leu Ser Arg Ala Arg Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205
```

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 162
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 162

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Arg Gly Arg Val Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

```
Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys
```

<210> 163
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 163

```
Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45
```

```
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Ile Lys Phe Thr Ser Phe Leu Tyr Val His Gly Phe Leu
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 164
<211> 246

<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 164

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gln Arg Trp Leu Tyr Leu Gly Gly Ile Arg Arg His Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
165 170 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
180 185 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 165
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 165

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 Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Glu Trp Ile Pro Ser Arg Pro Tyr Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

```
Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 166
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 166

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30
```

```
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Ser Thr Gly Thr Gly Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240
```

Val Glu Ile Lys

<210> 167
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 167

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Arg Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Asn Trp Asn Gly Gly Ser Thr Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr His Cys
85 90 95

Ala Arg Glu Arg Tyr Arg Arg Val Leu His Trp Tyr Phe Asp Leu Trp
100 105 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

```
Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 168
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 168

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Pro Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val
            100                 105                 110

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
    130                 135                 140

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
145                 150                 155                 160

Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
                165                 170                 175

Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro
            180                 185                 190

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser
    210                 215                 220

Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225                 230                 235                 240


<210>  169
<211>  246
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  MSLN scFv domain

<400>  169

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu His Met Gly Thr Ile Pro Tyr Tyr Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240
```

Thr Lys Val Glu Ile Lys
245

<210> 170
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 170

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Glu Phe Gly Tyr Gly Asp Val Leu Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

```
Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 171
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 171

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Asp Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
```

```
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Asp Val Val Lys Gly Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 172
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 172

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Asp Phe Ser His Lys Leu Gly Tyr Phe Gln His Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205
```

```
Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240


Lys Val Glu Ile Lys
                245


<210>  173
<211>  238
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  MSLN scFv domain

<400>  173

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


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

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
145                 150                 155                 160

Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                165                 170                 175

Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg
            180                 185                 190

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
        195                 200                 205

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser
    210                 215                 220

Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225                 230                 235


<210>  174
<211>  244
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  MSLN scFv domain

<400>  174

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Asp Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60
```

```
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Arg Arg Asp Trp Asp Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 175
<211> 243
<212> PRT
<213> Artificial Sequence

<220>

<223> MSLN scFv domain

<400> 175

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gly
1               5                  10                  15


Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30


Asn Trp Trp Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45


Ile Gly Glu Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu
    50                  55                  60


Lys Ser Arg Val Thr Ile Ser Val Asp Lys Ser Lys Asn Gln Phe Ser
65                  70                  75                  80


Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asp Gln Gln Ala Leu Lys Tyr Arg Val Asp Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140


Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190


Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205
```

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 176
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 176

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Thr Leu Gly Cys Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

```
Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 177
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 177

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
            20                  25                  30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Asp Gly Ser Asn Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 178
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 178

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ala Phe Leu Phe Leu Ser Phe Ser Val Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140


Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175
```

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
180 185 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 179
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 179

Glu Val Gln Leu Val Glu Ser Gly Gly Val Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Leu Ile Ser Trp Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

```
Ala Lys Gly Ile Phe Tyr Ser Ser Lys Glu Asp Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys
                245
```

<210> 180
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 180

```
Glu Val Gln Leu Val Glu Ser Gly Gly Val Val Val Gln Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Leu Ile Ser Trp Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Ile Trp Ile Phe Tyr Ser Ser Asn Pro Lys Pro Thr Val
            100                 105                 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240
```

Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 181
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 181

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe
50 55 60

Thr Gly Arg Phe Val Phe Ser Phe Asp Thr Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Cys Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Lys Asp Gln Thr Leu Thr Tyr Gly Asn Trp Phe Asp Pro Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

```
Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175


Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190


Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205


Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220


Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240


Thr Lys Val Glu Ile Lys
                245


<210>  182
<211>  242
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  MSLN scFv domain

<400>  182

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 Gly Gly Ser Val Ser Ser Gly
            20                  25                  30


Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
```

```
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp His Tyr Glu Arg Gly Leu Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 183
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 183

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Met Tyr Asn Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205
```

```
Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ala Asn Ser Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 184
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 184

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Arg Arg Pro Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125
```

```
Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Gly Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Ala Asn Ser Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys
```

<210> 185
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 185

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Val His Leu Lys Arg Arg Pro Tyr Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 186
<211> 242

<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 186

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Val His Lys Lys Pro Ile Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
130 135 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
180 185 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 187
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 187

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Thr Ser Arg Arg Cys Thr Phe Gln His Trp Gly Gln Gly Thr
100 105 110

```
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 188
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 188

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30
```

```
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Thr Ser Pro Arg Pro Leu Phe Gln His Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240
```

Ile Lys

<210> 189
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 189

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Pro Tyr Gln Val Arg Gly Val Tyr Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160
```

```
Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 190
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 190

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Pro Tyr Lys Lys Arg Arg Thr Val Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 191
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 191

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Leu Gln Arg Gly Leu Ala Leu Phe Gln His Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220
```

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 192
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 192

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Ile Leu Ser Val Pro Tyr Phe Asp Leu Trp Gly Arg Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
130 135 140

```
Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175


Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190


Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205


Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220


Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240


Ile Lys
```

<210> 193
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 193

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Gly Trp Ile Arg Val Pro Leu Arg Leu Pro Leu Phe Gln His
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser
            180                 185                 190

Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 194
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 194

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Val Thr Ile Phe Ala Ile 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 Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140


Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175


Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190
```

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 195
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 195

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Arg Gly Phe Val His Phe Asp Leu Trp Gly Arg Gly
100 105 110

```
Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140


Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190


Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205


Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220


Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240


Glu Ile Lys
```

<210> 196
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 196

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30
```

```
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Thr Ser Arg Gly Leu Cys Val Leu Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 197
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 197

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Gly Pro Ser Ser Tyr Trp Tyr Phe Asp Leu Trp Gly Arg
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140


Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160


Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175
```

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
180 185 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
210 215 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 198
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 198

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Asn Ile Tyr Met Gly Gly Ile Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 199
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 199

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Leu Thr Val Arg Thr Gly Ala Phe Asp Ile Trp Gly Gln Gly
            100                 105                 110

Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220
```

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 200
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 200

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Arg Thr Ala His Leu Asp Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
130 135 140

```
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190


Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205


Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220


Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240


Glu Ile Lys
```

<210> 201
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 201

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Leu Ile Phe Pro Val Val Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 202
<211> 246
<212> PRT
<213> Artificial Sequence

<220>

<223> MSLN scFv domain

<400> 202

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asp Gly Tyr Arg Lys Tyr Gly Tyr Val Phe Phe Asp Ile Trp
            100                 105                 110


Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
    130                 135                 140


Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160


Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
                165                 170                 175


Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
            180                 185                 190


Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205
```

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 203
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 203

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Gly Arg Tyr Arg Arg Phe Trp His Ala Phe Asp Ile Trp
100 105 110

Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
            180                 185                 190

Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 204
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 204

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala His Ile Arg Gly Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 205
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 205

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Thr Trp Met Gly Gly Gly Gly Arg Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110


Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln
    130                 135                 140


Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln
                165                 170                 175
```

```
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys
                245
```

<210> 206
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 206

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Thr Ser Arg Thr Thr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 207
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 207

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Trp Met Gly Gly Gly Gly Arg Leu Tyr Phe Asp Leu Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240
```

Lys Val Glu Ile Lys
245

<210> 208
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 208

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Trp Gly Gly Arg Leu Tyr Trp Tyr Phe Asp Leu Trp Gly Arg
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

```
Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 209
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 209

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Ile Arg Gln Leu Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 210
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 210

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Phe Ala Asn Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205
```

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 211
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 211

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Asp Arg Thr Thr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

```
Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 212
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 212

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Arg Trp Gly Lys Asp Gly Pro Tyr Trp Tyr Phe Asp Leu Trp
            100                 105                 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
            180                 185                 190

Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 213
<211> 246

<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 213

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Arg Arg Asp Ser Tyr Gly Pro Tyr Trp Tyr Phe Asp Leu Trp
100 105 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
165 170 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
180 185 190

Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 214
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 214

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asn Arg Pro Pro Pro Gly Tyr Trp Tyr Phe Asp Leu Trp Gly
100 105 110

```
Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln
    130                 135                 140


Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu
            180                 185                 190


Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205


Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240


Lys Val Glu Ile Lys
                245
```

<210> 215
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 215

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Arg Arg Phe Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240
```

Glu Ile Lys

<210> 216
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 216

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30


Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
    50                  55                  60


Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80


Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95


Tyr Cys Thr Thr Asp Leu Pro Lys Leu Arg Asn Phe His Ile Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 217
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 217

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Tyr Val
35 40 45

Ser Ala Ile Ser Ser Asn Gly Gly Ser Thr Tyr Tyr Ala Asn Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Gly Ser Leu Arg Ala Glu Asp Met Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Leu Glu Tyr His Gly Phe Arg Gln Tyr Gly Leu Arg Tyr Trp
100 105 110

His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 218
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 218

Gln Leu Gln Leu Gln Glu Ser Gly Ser Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Ser Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

```
Trp Ile Gly Tyr Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Arg Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Ser Ile Lys Phe Trp Phe Ala Gly Ile Asn Tyr Phe Phe Pro
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 219
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 219

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45

Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

Ala Ser Gly Phe Leu Gly Met Gly Ser Asn Phe Ile Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 220
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 220

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Leu Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Ser Gly Asp Arg Ala Arg Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 221
<211> 123

<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 221

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35   40   45

Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Tyr Pro Arg Gly Tyr His Gln Met Val Asp Ala Phe Asp Ile
            100   105   110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 222
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 222

Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Val Arg Phe Leu Ala Ala Arg Thr Thr Ile Pro Glu Ala
            100                 105                 110

Asn Phe Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 223
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 223

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Leu Ser Arg Ala Arg Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 224
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 224

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Arg Gly Arg Val Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
        115

<210> 225
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 225

Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
            20   25   30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35   40   45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50   55   60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65   70   75   80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85   90   95

Cys Ala Arg Ile Lys Phe Thr Ser Phe Leu Tyr Val His Gly Phe Leu
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 226
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 226

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gln Arg Trp Leu Tyr Leu Gly Gly Ile Arg Arg His Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 227
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 227

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 Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

```
Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Glu Trp Ile Pro Ser Arg Pro Tyr Tyr Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 228
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 228

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95
```

```
Cys Ala Arg Glu Ser Thr Gly Thr Gly Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110


Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210>  229
<211>  122
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  229

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Arg Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30


Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Gly Ile Asn Trp Asn Gly Gly Ser Thr Gly Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr His Cys
                85                  90                  95


Ala Arg Glu Arg Tyr Arg Arg Val Leu His Trp Tyr Phe Asp Leu Trp
            100                 105                 110


Gly Arg Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  230
<211>  116
```

<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 230

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50   55   60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Glu Pro Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val
            100   105   110

Thr Val Ser Ser
        115

<210> 231
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 231

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1   5   10   15

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu His Met Gly Thr Ile Pro Tyr Tyr Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 232
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 232

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60
```

```
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Glu Phe Gly Tyr Gly Asp Val Leu Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 233
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 233

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Asp Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Asp Val Val Lys Gly Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110
```

Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 234
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 234

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Glu Asp Phe Ser His Lys Leu Gly Tyr Phe Gln His Trp Gly
            100   105   110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 235
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 235

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Tyr Val Trp Gly Gln Gly Thr Leu Val Thr Val
100 105 110

Ser Ser

<210> 236
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 236

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Asp Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

```
Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Arg Arg Asp Trp Asp Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 237
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 237

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gly
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Asn Trp Trp Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Glu Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Ile Ser Val Asp Lys Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Asp Gln Gln Ala Leu Lys Tyr Arg Val Asp Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser
        115


<210>  238
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  238

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asp Leu Thr Leu Gly Cys Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  239
<211>  118
```

<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 239

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
            20   25   30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
    50   55   60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65   70   75   80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85   90   95

Arg Asp Gly Ser Asn Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 240
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 240

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ala Phe Leu Phe Leu Ser Phe Ser Val Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  241
<211>  121
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  241

Glu Val Gln Leu Val Glu Ser Gly Gly Val Val Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30


Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Leu Ile Ser Trp Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95


Ala Lys Gly Ile Phe Tyr Ser Ser Lys Glu Asp Phe Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  242
<211>  124
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  242

Glu Val Gln Leu Val Glu Ser Gly Gly Val Val Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30


Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Leu Ile Ser Trp Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95


Ala Lys Asp Ile Trp Ile Phe Tyr Ser Ser Asn Pro Lys Pro Thr Val
            100                 105                 110
```

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 243
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 243

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe
50 55 60

Thr Gly Arg Phe Val Phe Ser Phe Asp Thr Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Cys Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Lys Asp Gln Thr Leu Thr Tyr Gly Asn Trp Phe Asp Pro Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 244
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 244

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 Gly Gly Ser Val Ser Ser Gly
            20   25   30

Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35   40   45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser
    50   55   60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65   70   75   80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85   90   95

Cys Ala Arg Asp His Tyr Glu Arg Gly Leu Tyr Trp Gly Gln Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 245
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 245

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

```
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Met Tyr Asn Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser
        115
```

<210> 246
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 246

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

Ala Arg Asp Arg Arg Pro Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser
115

<210> 247
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 247

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Val His Leu Lys Arg Arg Pro Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 248
<211> 118

<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 248

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Ser Val His Lys Lys Pro Ile Phe Asp Tyr Trp Gly Gln Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 249
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 249

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Thr Ser Arg Arg Cys Thr Phe Gln His Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  250
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  250

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Thr Ser Pro Arg Pro Leu Phe Gln His Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115
```

<210> 251
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 251

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Pro Tyr Gln Val Arg Gly Val Tyr Phe Asp Tyr Trp Gly Gln
            100                 105                 110
```

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 252
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 252

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Ser Pro Tyr Lys Lys Arg Arg Thr Val Phe Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 253
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 253

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Ser Leu Gln Arg Gly Leu Ala Leu Phe Gln His Trp Gly Gln Gly
            100   105   110

Thr Leu Val Thr Val Ser Ser
        115

<210> 254
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 254

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

```
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Ile Leu Ser Val Pro Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser
        115
```

<210> 255
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 255

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

Ala Ser Gly Trp Ile Arg Val Pro Leu Arg Leu Pro Leu Phe Gln His
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 256
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 256

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Thr Ile Phe Ala Ile Phe Asp Ile Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

<210> 257
<211> 119

<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 257

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Val Gly Arg Gly Phe Val His Phe Asp Leu Trp Gly Arg Gly
            100   105   110

Thr Leu Val Thr Val Ser Ser
        115

<210> 258
<211> 1503
<212> DNA
<213> Artificial Sequence

<220>
<223> PA2.1.14 scFv LIR1 HTICD

<400> 258
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tcctgcaagg cttctggata caccttcact agctatcata tacattgggt gcgccaggcc   120

cccggacaag ggcttgagtg gatcggatgg atctaccctg gcaatgttaa cacagaatat   180

aatgagaagt tcaagggcaa agccaccatt accgcggacg aatccacgaa cacagcctac 240

atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagggaggaa 300

attacctacg ctatggacta ctggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacat tcaaatgacc 420

cagagcccat ccaccctgag cgcatctgta ggtgaccggg tcaccatcac ttgtagatcc 480

agtcagagta ttgtacacag taatgggaac acctatttgg aatggtatca gcagaaacca 540

ggtaaagccc caaaattgct catctacaaa gtctctaaca gatttagtgg tgtaccagcc 600

aggttcagcg gttccggaag tggtactgaa ttcaccctca cgatctcctc tctccagcca 660

gatgatttcg ccacttatta ctgttttcaa ggttcacatg tgccgcgcac attcggtcag 720

ggtactaaag tagaagtcaa atacggctca cagagctcca aaccctacct gctgactcac 780

cccagtgacc ccctggagct cgtggtctca ggaccgtctg ggggccccag ctccccgaca 840

acaggcccca cctccacatc tggccctgag gaccagcccc tcacccccac cgggtcggat 900

ccccagagtg gtctgggaag gcacctgggg gttgtgatcg gcatcttggt ggccgtcatc 960

ctactgctcc tcctcctcct cctcctcttc ctcatcctcc gacatcgacg tcagggcaaa 1020

cactggacat cgacccagag aaaggctgat ttccaacatc ctgcaggggc tgtggggcca 1080

gagcccacag acagaggcct gcagtggagg tccagcccag ctgccgatgc ccaggaagaa 1140

aacctctatg ctgccgtgaa gcacacacag cctgaggatg gggtggagat ggacactcgg 1200

agcccacacg atgaagaccc ccaggcagtg acgtatgccg aggtgaaaca ctccagacct 1260

aggagagaaa tggcctctcc tccttcccca ctgtctgggg aattcctgga cacaaaggac 1320

agacaggcgg aagaggacag gcagatggac actgaggctg ctgcatctga agccccccag 1380

gatgtgacct acgcccagct gcacagcttg accctcagac gggaggcaac tgagcctcct 1440

ccatcccagg aagggccctc tccagctgtg cccagcatct acgccactct ggccatccac 1500

tag 1503

<210> 259
<211> 120
<212> PRT
<213> Artificial Sequence

<220>

<223> heavy chain variable fragment

<400> 259

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Thr Ser Arg Gly Leu Cys Val Leu Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 260
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 260

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30
```

```
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Gly Pro Ser Ser Tyr Trp Tyr Phe Asp Leu Trp Gly Arg
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  261
<211>  120
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  261

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asn Ile Tyr Met Gly Gly Ile Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  262
<211>  119
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  262

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Leu Thr Val Arg Thr Gly Ala Phe Asp Ile Trp Gly Gln Gly
            100                 105                 110


Thr Met Val Thr Val Ser Ser
        115
```

<210> 263
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 263

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Leu Arg Thr Ala His Leu Asp Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser
        115
```

<210> 264
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 264

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Leu Ile Phe Pro Val Val Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser
        115


<210>  265
<211>  122
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  265

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asp Gly Tyr Arg Lys Tyr Gly Tyr Val Phe Phe Asp Ile Trp
            100                 105                 110


Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210>  266
<211>  122
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  266

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asp Gly Arg Tyr Arg Arg Phe Trp His Ala Phe Asp Ile Trp
            100                 105                 110
```

Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 267
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 267

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Ala His Ile Arg Gly Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 268
<211> 121
<212> PRT
<213> Artificial Sequence

<220>

<223> heavy chain variable fragment

<400> 268

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Thr Trp Met Gly Gly Gly Gly Arg Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110


Arg Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 269
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 269

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Thr Ser Arg Thr Thr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100   105   110

Thr Leu Val Thr Val Ser Ser
        115

<210> 270
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 270

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Trp Met Gly Gly Gly Gly Arg Leu Tyr Phe Asp Leu Trp Gly
            100                 105                 110


Arg Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  271
<211>  120
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  271

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Trp Gly Gly Arg Leu Tyr Trp Tyr Phe Asp Leu Trp Gly Arg
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 272
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 272

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Ile Arg Gln Leu Trp Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 273
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 273

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Phe Ala Asn Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser
        115


<210>  274
<211>  119
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  274

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Val Asp Arg Thr Thr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser
        115


<210>  275
<211>  122
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  heavy chain variable fragment

<400>  275

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Arg Trp Gly Lys Asp Gly Pro Tyr Trp Tyr Phe Asp Leu Trp
            100                 105                 110
```

Gly Arg Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 276
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 276

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Arg Arg Asp Ser Tyr Gly Pro Tyr Trp Tyr Phe Asp Leu Trp
            100   105   110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 277
<211> 121
<212> PRT
<213> Artificial Sequence

<220>

<223> heavy chain variable fragment

<400> 277

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Asn Arg Pro Pro Pro Gly Tyr Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110


Arg Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 278
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain variable fragment

<400> 278

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Gly Arg Arg Phe Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser
        115


<210>  279
<211>  107
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  light chain variable fragment

<400>  279

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
```

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 280
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> light chain variable fragment

<400> 280

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 281
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> light chain variable fragment

<400> 281

Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 282
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> light chain variable fragment

<400> 282

Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 283
<211> 42
<212> PRT
<213> Unknown

<220>
<223> 4-1BB co-stimulatory domain

<400> 283

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> 284
<211> 126
<212> DNA
<213> Unknown

<220>
<223> encodes 4-1BB co-stimulatory domain

<400> 284
aaacggggca gaaagaaact cctgtatata ttcaaacaac catttatgag gccagtacaa 60

actactcaag aggaagatgg ctgtagctgc cgatttccag aagaagaaga aggaggatgt 120

gaactg 126

<210> 285
<211> 195

<212> PRT
<213> Artificial Sequence

<220>
<223> CAR intracellular domain

<400> 285

```
Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
1               5                  10                  15


Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
            20                  25                  30


Pro Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu
        35                  40                  45


Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
    50                  55                  60


Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
65                  70                  75                  80


Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
                85                  90                  95


Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
            100                 105                 110


Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
        115                 120                 125


Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
    130                 135                 140


Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
145                 150                 155                 160


Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
                165                 170                 175


Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
            180                 185                 190
```

Pro Pro Arg
195

<210> 286
<211> 512
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 286

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
50 55 60

Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Thr Thr Asp Leu Pro Lys Leu Arg Asn Phe His Ile Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145 150 155 160

```
Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
                245                 250                 255

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
            260                 265                 270

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
        275                 280                 285

Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
    290                 295                 300

Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys
305                 310                 315                 320

Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg
                325                 330                 335

Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp
            340                 345                 350

Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        355                 360                 365
```

```
Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    370                 375                 380

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
385                 390                 395                 400

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
                405                 410                 415

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            420                 425                 430

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        435                 440                 445

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    450                 455                 460

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
465                 470                 475                 480

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                485                 490                 495

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 287
<211> 515
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 287

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Tyr Val
        35                  40                  45

Ser Ala Ile Ser Ser Asn Gly Gly Ser Thr Tyr Tyr Ala Asn Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Gly Ser Leu Arg Ala Glu Asp Met Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Leu Glu Tyr His Gly Phe Arg Gln Tyr Gly Leu Arg Tyr Trp
            100                 105                 110

His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
                245                 250                 255
```

```
Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
            260                 265                 270

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
        275                 280                 285

Asp Phe Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu
    290                 295                 300

Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
305                 310                 315                 320

Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
                325                 330                 335

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
            340                 345                 350

Pro Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu
        355                 360                 365

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
    370                 375                 380

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
385                 390                 395                 400

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
                405                 410                 415

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
            420                 425                 430

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
        435                 440                 445

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
    450                 455                 460
```

```
Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
465                 470                 475                 480


Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
                485                 490                 495


Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
            500                 505                 510


Pro Pro Arg
        515
```

<210> 288
<211> 514
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 288

```
Gln Leu Gln Leu Gln Glu Ser Gly Ser Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Ser Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Arg Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Ser Ile Lys Phe Trp Phe Ala Gly Ile Asn Tyr Phe Phe Pro
            100                 105                 110
```

```
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
                245                 250                 255

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
            260                 265                 270

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
        275                 280                 285

Phe Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala
    290                 295                 300

Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg
305                 310                 315                 320

Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro
                325                 330                 335
```

```
Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro
            340                 345                 350

Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu
        355                 360                 365

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
    370                 375                 380

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
385                 390                 395                 400

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
                405                 410                 415

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
            420                 425                 430

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
        435                 440                 445

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
    450                 455                 460

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
465                 470                 475                 480

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
                485                 490                 495

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
            500                 505                 510

Pro Arg
```

<210> 289
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 289

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45


Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Gly Phe Leu Gly Met Gly Ser Asn Phe Ile Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140


Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190
```

```
Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415
```

```
Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 290
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 290

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Leu Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
```

```
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Ser Gly Asp Arg Ala Arg Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285
```

```
Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 291
<211> 514
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 291

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45


Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Tyr Pro Arg Gly Tyr His Gln Met Val Asp Ala Phe Asp Ile
            100                 105                 110


Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
    130                 135                 140


Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160


Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175
```

```
Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
                245                 250                 255

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
            260                 265                 270

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
        275                 280                 285

Phe Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala
    290                 295                 300

Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg
305                 310                 315                 320

Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro
                325                 330                 335

Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro
            340                 345                 350

Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu
        355                 360                 365

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
    370                 375                 380
```

```
Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
385                 390                 395                 400


Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
                405                 410                 415


Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
            420                 425                 430


Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
        435                 440                 445


Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
    450                 455                 460


Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
465                 470                 475                 480


Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
                485                 490                 495


Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
            500                 505                 510


Pro Arg
```

<210> 292
<211> 517
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 292

```
Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30
```

```
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Val Arg Phe Leu Ala Ala Arg Thr Thr Ile Pro Glu Ala
            100                 105                 110

Asn Phe Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp
    130                 135                 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro
                245                 250                 255
```

```
Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
            260                 265                 270

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
        275                 280                 285

Gly Leu Asp Phe Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly
    290                 295                 300

Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe
305                 310                 315                 320

Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn
                325                 330                 335

Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr
            340                 345                 350

Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys
        355                 360                 365

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
    370                 375                 380

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
385                 390                 395                 400

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
                405                 410                 415

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
            420                 425                 430

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
        435                 440                 445

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
    450                 455                 460
```

```
Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
465                 470                 475                 480


Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
                485                 490                 495


Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
            500                 505                 510


Ala Leu Pro Pro Arg
        515
```

<210> 293
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 293

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Val Leu Ser Arg Ala Arg Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110
```

```
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335
```

```
Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505
```

<210> 294
<211> 508
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 294

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Leu Arg Gly Arg Val Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205
```

```
Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
                245                 250                 255

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
            260                 265                 270

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp
        275                 280                 285

Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val
    290                 295                 300

Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu
305                 310                 315                 320

Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr
                325                 330                 335

Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr
            340                 345                 350

Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
        355                 360                 365

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
    370                 375                 380

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
385                 390                 395                 400

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
                405                 410                 415

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
            420                 425                 430
```

```
Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
        435                 440                 445

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
    450                 455                 460

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
465                 470                 475                 480

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
                485                 490                 495

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505
```

<210> 295
<211> 514
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 295

```
Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95
```

```
Cys Ala Arg Ile Lys Phe Thr Ser Phe Leu Tyr Val His Gly Phe Leu
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
                245                 250                 255

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
            260                 265                 270

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
        275                 280                 285

Phe Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala
    290                 295                 300
```

```
Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg
305                 310                 315                 320

Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro
                325                 330                 335

Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro
            340                 345                 350

Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu
        355                 360                 365

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
    370                 375                 380

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
385                 390                 395                 400

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
                405                 410                 415

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
            420                 425                 430

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
        435                 440                 445

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
    450                 455                 460

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
465                 470                 475                 480

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
                485                 490                 495

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
            500                 505                 510

Pro Arg
```

<210> 296
<211> 513
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 296

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Gln Arg Trp Leu Tyr Leu Gly Gly Ile Arg Arg His Trp
            100                 105                 110


Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140


Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160


Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175
```

```
Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380
```

```
Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400


Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415


Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            420                 425                 430


Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        435                 440                 445


Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
    450                 455                 460


Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465                 470                 475                 480


Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
                485                 490                 495


Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
            500                 505                 510


Arg
```

<210> 297
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 297

```
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 Gly Gly Ser Ile Ser Ser Tyr
            20                  25                  30
```

```
Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Glu Trp Ile Pro Ser Arg Pro Tyr Tyr Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255
```

```
Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460
```

```
Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480


Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495


Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  298
<211>  511
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  298

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Ser Thr Gly Thr Gly Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110


Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350
```

```
Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 299
<211> 513
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 299

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Arg Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Asn Trp Asn Gly Gly Ser Thr Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr His Cys
                85                  90                  95

Ala Arg Glu Arg Tyr Arg Arg Val Leu His Trp Tyr Phe Asp Leu Trp
            100                 105                 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220
```

```
Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            420                 425                 430

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        435                 440                 445
```

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
450 455 460

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465 470 475 480

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
485 490 495

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
500 505 510

Arg

<210> 300
<211> 507
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 300

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Glu Pro Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val
            100                 105                 110

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
    130                 135                 140

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
145                 150                 155                 160

Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
                165                 170                 175

Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro
            180                 185                 190

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser
    210                 215                 220

Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225                 230                 235                 240

Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
                245                 250                 255

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
            260                 265                 270

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp Val
        275                 280                 285

Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr
    290                 295                 300
```

```
Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu
305                 310                 315                 320

His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg
                325                 330                 335

Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg
            340                 345                 350

Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
        355                 360                 365

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
    370                 375                 380

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
385                 390                 395                 400

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
                405                 410                 415

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
            420                 425                 430

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
        435                 440                 445

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
    450                 455                 460

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
465                 470                 475                 480

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
                485                 490                 495

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505
```

<210> 301
<211> 513

<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 301

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu His Met Gly Thr Ile Pro Tyr Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
165 170 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
180 185 190

```
Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400
```

```
Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415


Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            420                 425                 430


Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        435                 440                 445


Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
    450                 455                 460


Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465                 470                 475                 480


Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
                485                 490                 495


Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
            500                 505                 510


Arg
```

<210> 302
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 302

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45
```

```
Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Glu Phe Gly Tyr Gly Asp Val Leu Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270
```

```
Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480
```

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
485 490 495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505 510

<210> 303
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 303

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Asp Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Asp Val Val Lys Gly Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
130 135 140

```
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365
```

```
Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 304
<211> 512
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 304

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Asp Phe Ser His Lys Leu Gly Tyr Phe Gln His Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240
```

```
Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
                245                 250                 255

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
            260                 265                 270

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
        275                 280                 285

Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
    290                 295                 300

Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys
305                 310                 315                 320

Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg
                325                 330                 335

Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp
            340                 345                 350

Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        355                 360                 365

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    370                 375                 380

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
385                 390                 395                 400

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
                405                 410                 415

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            420                 425                 430

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        435                 440                 445

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    450                 455                 460
```

```
Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
465                 470                 475                 480


Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                485                 490                 495


Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  305
<211>  505
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  305

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


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

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
145                 150                 155                 160

Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                165                 170                 175

Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg
            180                 185                 190

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
        195                 200                 205

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser
    210                 215                 220

Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
225                 230                 235                 240

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
                245                 250                 255

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
            260                 265                 270

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp Val Leu Val
        275                 280                 285

Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala
    290                 295                 300

Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser
305                 310                 315                 320

Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His
                325                 330                 335
```

```
Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser Lys
            340                 345                 350

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
        355                 360                 365

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
    370                 375                 380

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
385                 390                 395                 400

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
                405                 410                 415

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
            420                 425                 430

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
        435                 440                 445

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
    450                 455                 460

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
465                 470                 475                 480

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
                485                 490                 495

Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505
```

<210> 306
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 306

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Asp Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Arg Arg Asp Trp Asp Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220
```

```
Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430
```

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435   440   445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450   455   460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465   470   475   480

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485   490   495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500   505   510

<210> 307
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 307

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gly
1   5   10   15

Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Ser
            20   25   30

Asn Trp Trp Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35   40   45

Ile Gly Glu Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu
    50   55   60

Lys Ser Arg Val Thr Ile Ser Val Asp Lys Ser Lys Asn Gln Phe Ser
65   70   75   80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

```
Ala Arg Asp Gln Gln Ala Leu Lys Tyr Arg Val Asp Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320
```

```
Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 308
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 308

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asp Leu Thr Leu Gly Cys Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140


Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175


Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190
```

```
Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415
```

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
420 425 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
435 440 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
450 455 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465 470 475 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
485 490 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505

<210> 309
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 309

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Asp Gly Ser Asn Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285
```

```
Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505
```

<210> 310
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 310

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ala Phe Leu Phe Leu Ser Phe Ser Val Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140


Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175
```

```
Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380
```

```
Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400


Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415


Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430


Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445


Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460


Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480


Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495


Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505


<210>  311
<211>  512
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  311

Glu Val Gln Leu Val Glu Ser Gly Gly Val Val Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30


Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Leu Ile Ser Trp Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Ile Phe Tyr Ser Ser Lys Glu Asp Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
                245                 250                 255

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
            260                 265                 270
```

```
Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
        275                 280                 285

Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
    290                 295                 300

Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys
305                 310                 315                 320

Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg
                325                 330                 335

Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp
            340                 345                 350

Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        355                 360                 365

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    370                 375                 380

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
385                 390                 395                 400

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
                405                 410                 415

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            420                 425                 430

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        435                 440                 445

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    450                 455                 460

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
465                 470                 475                 480
```

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
485 490 495

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505 510

<210> 312
<211> 515
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 312

Glu Val Gln Leu Val Glu Ser Gly Gly Val Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Leu Ile Ser Trp Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Lys Asp Ile Trp Ile Phe Tyr Ser Ser Asn Pro Lys Pro Thr Val
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
130 135 140

```
Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
                245                 250                 255

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
            260                 265                 270

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
        275                 280                 285

Asp Phe Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu
    290                 295                 300

Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
305                 310                 315                 320

Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
                325                 330                 335

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
            340                 345                 350

Pro Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu
        355                 360                 365
```

```
Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
    370                 375                 380

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
385                 390                 395                 400

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
                405                 410                 415

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
            420                 425                 430

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
        435                 440                 445

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
    450                 455                 460

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
465                 470                 475                 480

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
                485                 490                 495

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
            500                 505                 510

Pro Pro Arg
        515
```

<210> 313
<211> 513
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 313

```
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15
```

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe
    50                  55                  60

Thr Gly Arg Phe Val Phe Ser Phe Asp Thr Ser Val Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Cys Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Lys Asp Gln Thr Leu Thr Tyr Gly Asn Trp Phe Asp Pro Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220
```

```
Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            420                 425                 430

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        435                 440                 445
```

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
    450   455   460

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465   470   475   480

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
                485   490   495

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
            500   505   510

Arg

<210> 314
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 314

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 Gly Gly Ser Val Ser Ser Gly
            20   25   30

Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35   40   45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser
    50   55   60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65   70   75   80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85   90   95

```
Cys Ala Arg Asp His Tyr Glu Arg Gly Leu Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300
```

```
Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505

<210>  315
<211>  509
```

<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 315

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Met Tyr Asn Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
130 135 140

Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Gln Gly Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
180 185 190

```
Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ala Asn Ser Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400
```

```
Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415


Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430


Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445


Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460


Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480


Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495


Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505


<210>  316
<211>  508
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  316

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Arg Arg Pro Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Gly Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Ala Asn Ser Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
                245                 250                 255

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
            260                 265                 270

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp
        275                 280                 285
```

```
Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val
    290                 295                 300

Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu
305                 310                 315                 320

Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr
                325                 330                 335

Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr
            340                 345                 350

Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
        355                 360                 365

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
    370                 375                 380

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
385                 390                 395                 400

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
                405                 410                 415

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
            420                 425                 430

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
        435                 440                 445

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
    450                 455                 460

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
465                 470                 475                 480

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
                485                 490                 495
```

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505

<210> 317
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 317

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Val His Leu Lys Arg Arg Pro Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

```
Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380
```

```
Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400


Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415


Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430


Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445


Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460


Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480


Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495


Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  318
<211>  509
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  318

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Val His Lys Lys Pro Ile Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255
```

```
Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480
```

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
485 490 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505

<210> 319
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 319

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Thr Ser Arg Arg Cys Thr Phe Gln His Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
130 135 140

```
Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350
```

```
Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505
```

<210> 320
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 320

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Thr Ser Pro Arg Pro Leu Phe Gln His Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240
```

```
Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445
```

```
Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460


Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480


Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495


Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505


<210>  321
<211>  511
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  321

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Pro Tyr Gln Val Arg Gly Val Tyr Phe Asp Tyr Trp Gly Gln
            100                 105                 110
```

```
Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335
```

```
Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 322
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 322

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Pro Tyr Lys Lys Arg Arg Thr Val Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205
```

```
Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430
```

```
Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445


Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460


Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480


Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495


Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  323
<211>  510
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  323

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Ser Leu Gln Arg Gly Leu Ala Leu Phe Gln His Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300
```

```
Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 324
<211> 509

<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 324

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Ile Leu Ser Val Pro Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140


Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175


Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190
```

```
Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400
```

```
Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415


Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430


Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445


Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460


Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480


Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495


Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505


<210>  325
<211>  514
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  325

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Gly Trp Ile Arg Val Pro Leu Arg Leu Pro Leu Phe Gln His
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser
            180                 185                 190

Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
                245                 250                 255

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
            260                 265                 270

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
        275                 280                 285
```

```
Phe Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala
    290                 295                 300

Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg
305                 310                 315                 320

Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro
                325                 330                 335

Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro
            340                 345                 350

Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu
        355                 360                 365

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
    370                 375                 380

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
385                 390                 395                 400

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
                405                 410                 415

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
            420                 425                 430

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
        435                 440                 445

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
    450                 455                 460

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
465                 470                 475                 480

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
                485                 490                 495
```

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
500 505 510

Pro Arg

<210> 326
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 326

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Thr Ile Phe Ala Ile 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 Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
130 135 140

```
Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175


Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190


Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205


Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220


Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240


Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255


Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270


Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285


Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300


Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320


Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335


Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350


Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365
```

```
Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
        435                 440                 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
    450                 455                 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465                 470                 475                 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
                485                 490                 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505


<210>  327
<211>  510
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  327

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30
```

```
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Gly Arg Gly Phe Val His Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240
```

```
Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460
```

```
Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480


Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495


Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  328
<211>  511
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  328

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Thr Ser Arg Gly Leu Cys Val Leu Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335
```

```
Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 329
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 329

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Gly Pro Ser Ser Tyr Trp Tyr Phe Asp Leu Trp Gly Arg
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220
```

```
Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430
```

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435   440   445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450   455   460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465   470   475   480

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485   490   495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500   505   510

<210> 330
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 330

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

```
Ala Arg Asn Ile Tyr Met Gly Gly Ile Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320
```

```
Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 331
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 331

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Leu Thr Val Arg Thr Gly Ala Phe Asp Ile Trp Gly Gln Gly
            100                 105                 110


Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140


Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190
```

```
Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415
```

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
420 425 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
435 440 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
450 455 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465 470 475 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
485 490 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505 510

<210> 332
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 332

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Leu Arg Thr Ala His Leu Asp Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285
```

```
Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 333
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 333

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Asp Leu Ile Phe Pro Val Val Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140


Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175
```

```
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380
```

```
Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400


Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415


Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430


Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445


Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460


Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480


Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495


Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  334
<211>  513
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  334

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Gly Tyr Arg Lys Tyr Gly Tyr Val Phe Phe Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
            180                 185                 190

Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270
```

```
Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            420                 425                 430

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        435                 440                 445

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
    450                 455                 460

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465                 470                 475                 480
```

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
485 490 495

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
500 505 510

Arg

<210> 335
<211> 513
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 335

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Gly Arg Tyr Arg Arg Phe Trp His Ala Phe Asp Ile Trp
100 105 110

Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
            180                 185                 190

Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350
```

```
Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            420                 425                 430

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        435                 440                 445

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
    450                 455                 460

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465                 470                 475                 480

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
                485                 490                 495

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
            500                 505                 510

Arg
```

<210> 336
<211> 509
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 336

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala His Ile Arg Gly Tyr Phe Asp Leu Trp Gly Arg Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205
```

```
Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Phe Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe
        275                 280                 285

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300

Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320

Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335

Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350

Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
        355                 360                 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
    370                 375                 380

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385                 390                 395                 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
                405                 410                 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
            420                 425                 430
```

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
435 440 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
450 455 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465 470 475 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
485 490 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505

<210> 337
<211> 512
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 337

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Thr Trp Met Gly Gly Gly Gly Arg Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
                245                 250                 255

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
            260                 265                 270

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
        275                 280                 285

Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
    290                 295                 300
```

```
Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys
305                 310                 315                 320

Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg
                325                 330                 335

Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp
            340                 345                 350

Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        355                 360                 365

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    370                 375                 380

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
385                 390                 395                 400

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
                405                 410                 415

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            420                 425                 430

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        435                 440                 445

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    450                 455                 460

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
465                 470                 475                 480

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                485                 490                 495

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 338
<211> 510

<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 338

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Thr Ser Arg Thr Thr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
180 185 190

```
Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400
```

```
Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415


Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430


Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445


Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460


Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480


Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495


Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  339
<211>  512
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  339

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Trp Met Gly Gly Gly Gly Arg Leu Tyr Phe Asp Leu Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
                245                 250                 255

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
            260                 265                 270

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
        275                 280                 285
```

```
Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
    290                 295                 300

Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys
305                 310                 315                 320

Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg
                325                 330                 335

Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp
            340                 345                 350

Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        355                 360                 365

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    370                 375                 380

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
385                 390                 395                 400

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
                405                 410                 415

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            420                 425                 430

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        435                 440                 445

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    450                 455                 460

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
465                 470                 475                 480

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                485                 490                 495
```

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505 510

<210> 340
<211> 511
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 340

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Trp Gly Gly Arg Leu Tyr Trp Tyr Phe Asp Leu Trp Gly Arg
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

```
Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
    290                 295                 300

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
305                 310                 315                 320

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
                325                 330                 335

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
            340                 345                 350

Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
        355                 360                 365

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
    370                 375                 380
```

```
Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
385                 390                 395                 400


Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
                405                 410                 415


Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
            420                 425                 430


Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
        435                 440                 445


Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
    450                 455                 460


Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
465                 470                 475                 480


Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
                485                 490                 495


Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510


<210>  341
<211>  510
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  single chain variable fragment

<400>  341

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Ile Arg Gln Leu Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255
```

```
Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480
```

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
485 490 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505 510

<210> 342
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 342

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Phe Ala Asn Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
130 135 140

```
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350
```

```
Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 343
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 343

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Asp Arg Thr Thr Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240
```

```
Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445
```

```
Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 344
<211> 513
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 344

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Arg Trp Gly Lys Asp Gly Pro Tyr Trp Tyr Phe Asp Leu Trp
            100                 105                 110
```

```
Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
            180                 185                 190

Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335
```

```
Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            420                 425                 430

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        435                 440                 445

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
    450                 455                 460

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465                 470                 475                 480

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
                485                 490                 495

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
            500                 505                 510

Arg
```

<210> 345
<211> 513
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 345

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Arg Arg Asp Ser Tyr Gly Pro Tyr Trp Tyr Phe Asp Leu Trp
            100                 105                 110


Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr
    130                 135                 140


Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160


Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln
                165                 170                 175


Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
            180                 185                 190
```

```
Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
                245                 250                 255

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
            260                 265                 270

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
        275                 280                 285

Ala Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
    290                 295                 300

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
305                 310                 315                 320

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
                325                 330                 335

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
            340                 345                 350

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        355                 360                 365

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    370                 375                 380

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
385                 390                 395                 400

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                405                 410                 415
```

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
420 425 430

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
435 440 445

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
450 455 460

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
465 470 475 480

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
485 490 495

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
500 505 510

Arg

<210> 346
<211> 512
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 346

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Asn Arg Pro Pro Pro Gly Tyr Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
                245                 250                 255

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
            260                 265                 270
```

```
Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
        275                 280                 285

Cys Asp Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
    290                 295                 300

Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys
305                 310                 315                 320

Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg
                325                 330                 335

Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp
            340                 345                 350

Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        355                 360                 365

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    370                 375                 380

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
385                 390                 395                 400

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
                405                 410                 415

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            420                 425                 430

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        435                 440                 445

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    450                 455                 460

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
465                 470                 475                 480

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                485                 490                 495
```

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505 510

<210> 347
<211> 510
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain variable fragment

<400> 347

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Arg Arg Phe Ser Trp Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Ala Ile Gln Leu Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

```
Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
    290                 295                 300

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
305                 310                 315                 320

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
                325                 330                 335

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
            340                 345                 350

Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
        355                 360                 365
```

```
Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
    370                 375                 380

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
385                 390                 395                 400

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
                405                 410                 415

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
            420                 425                 430

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
        435                 440                 445

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
    450                 455                 460

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
465                 470                 475                 480

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
                485                 490                 495

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            500                 505                 510
```

<210> 348
<211> 500
<212> PRT
<213> Unknown

<220>
<223> inhibitory receptor

<400> 348

```
Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1               5                   10                  15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
            20                  25                  30
```

```
Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
                85                  90                  95

Ser His Val Pro Arg Thr Ser Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly
    130                 135                 140

Ala Ser Val Arg Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser
145                 150                 155                 160

Tyr His Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp
                165                 170                 175

Ile Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys
            180                 185                 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
        195                 200                 205

Tyr Met His Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
    210                 215                 220

Cys Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240

Thr Ser Val Thr Val Ser Ser Tyr Gly Ser Gln Ser Ser Lys Pro Tyr
                245                 250                 255
```

```
Leu Leu Thr His Pro Ser Asp Pro Leu Glu Leu Val Val Ser Gly Pro
            260                 265                 270

Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro Thr Ser Thr Ser Gly
        275                 280                 285

Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly
    290                 295                 300

Leu Gly Arg His Leu Gly Val Val Ile Gly Ile Leu Val Ala Val Ile
305                 310                 315                 320

Leu Leu Leu Leu Leu Leu Leu Leu Leu Phe Leu Ile Leu Arg His Arg
                325                 330                 335

Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg Lys Ala Asp Phe Gln
            340                 345                 350

His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr Asp Arg Gly Leu Gln
        355                 360                 365

Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu Glu Asn Leu Tyr Ala
    370                 375                 380

Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu Met Asp Thr Arg
385                 390                 395                 400

Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr Ala Glu Val Lys
                405                 410                 415

His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro Ser Pro Leu Ser
            420                 425                 430

Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu Glu Asp Arg Gln
        435                 440                 445

Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr
    450                 455                 460
```

```
Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala Thr Glu Pro Pro
465                 470                 475                 480


Pro Ser Gln Glu Gly Pro Ser Pro Ala Val Pro Ser Ile Tyr Ala Thr
                485                 490                 495


Leu Ala Ile His
            500


<210>  349
<211>  46
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  B2M shRNA

<400>  349
gcactcaaag cttgttaaga tcgaaatctt aacaagcttt gagtgc                    46


<210>  350
<211>  46
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  B2M shRNA

<400>  350
gttaacttcc aatttacata ccgaagtatg taaattggaa gttaac                    46


<210>  351
<211>  21
<212>  PRT
<213>  Unknown

<220>
<223>  T2A self-cleaving polypeptide

<400>  351

Gly Ser Gly Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp Val Glu
1               5                   10                  15


Glu Asn Pro Gly Pro
            20
```

<210> 352
<211> 64
<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 352

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp
1 5 10 15

Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro
20 25 30

Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
35 40 45

Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
50 55 60

<210> 353
<211> 64
<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 353

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp
1 5 10 15

Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro
20 25 30

Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
35 40 45

Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
50 55 60

<210> 354
<211> 44

<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 354

Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro
1   5   10   15

Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser
            20   25   30

Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
        35   40

<210> 355
<211> 64
<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 355

Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro Ser Asp
1   5   10   15

Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro
            20   25   30

Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr
        35   40   45

Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
    50   55   60

<210> 356
<211> 44
<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 356

Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro
1 5 10 15

Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser
20 25 30

Asp Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val
35 40

<210> 357
<211> 71
<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 357

Ser Ser Tyr Gly Ser Gln Ser Ser Lys Pro Tyr Leu Leu Thr His Pro
1 5 10 15

Ser Asp Pro Leu Glu Leu Val Val Ser Gly Pro Ser Gly Gly Pro Ser
20 25 30

Ser Pro Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro
35 40 45

Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu
50 55 60

Gly Val Val Ile Gly Ile Leu
65 70

<210> 358
<211> 39
<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 358

```
Ser Ser Thr Thr Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro
1               5                   10                  15


Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Leu
            20                  25                  30


Gly Val Val Ile Gly Ile Leu
        35


<210>  359
<211>  74
<212>  PRT
<213>  Unknown

<220>
<223>  HLA-A*02 scFv LIR-1 inhibitory receptor

<400>  359

Ser Ser Ala Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Pro Val
1               5                   10                  15


Pro Ser Thr Pro Pro Thr Pro Ser Pro Ser Thr Pro Pro Thr Pro Ser
            20                  25                  30


Pro Ser Gly Gly Ser Gly Asn Ser Ser Gly Ser Gly Gly Ser Pro Val
        35                  40                  45


Pro Ser Thr Pro Pro Thr Pro Ser Pro Ser Thr Pro Pro Thr Pro Ser
    50                  55                  60


Pro Ser Ala Ser Val Val Ile Gly Ile Leu
65                  70


<210>  360
<211>  82
<212>  PRT
<213>  Unknown

<220>
<223>  HLA-A*02 scFv LIR-1 inhibitory receptor

<400>  360

Ser Ser Ala Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Pro Val
1               5                   10                  15
```

```
Pro Ser Thr Pro Pro Thr Asn Ser Ser Ser Thr Pro Pro Thr Pro Ser
            20                  25                  30

Pro Ser Pro Val Pro Ser Thr Pro Pro Thr Asn Ser Ser Ser Thr Pro
        35                  40                  45

Pro Thr Pro Ser Pro Ser Pro Val Pro Ser Thr Pro Pro Thr Asn Ser
    50                  55                  60

Ser Ser Thr Pro Pro Thr Pro Ser Pro Ser Ala Ser Val Val Ile Gly
65                  70                  75                  80

Ile Leu
```

<210> 361
<211> 92
<212> PRT
<213> Unknown

<220>
<223> HLA-A*02 scFv LIR-1 inhibitory receptor

<400> 361

```
Ser Ser Val Val Ser Gly Pro Ser Gly Gly Pro Ser Ser Pro Thr Thr
1               5                   10                  15

Gly Pro Thr Ser Thr Ser Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr
            20                  25                  30

Gly Ser Asp Pro Gln Ser Gly Leu Gly Arg His Val Val Ser Gly Pro
        35                  40                  45

Ser Gly Gly Pro Ser Ser Pro Thr Thr Gly Pro Thr Ser Thr Ser Gly
    50                  55                  60

Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Ser Asp Pro Gln Ser Gly
65                  70                  75                  80

Leu Gly Arg His Leu Gly Val Val Ile Gly Ile Leu
                85                  90
```

<210> 362
<211> 22
<212> PRT
<213> Unknown

<220>
<223> signal sequence

<400> 362

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1   5   10   15

Leu Arg Gly Ala Arg Cys
            20

<210> 363
<211> 711
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 363
caggtgcagc tggtgcagtc tggggctgag gtggagaagc ctggggcctc agtgaaggtc   60

tcctgcaagg cttctggata caccttcacc gactactata tgcactgggt gcgacaggcc   120

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat   180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac   240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gtctggctgg   300

gactttgact actggggcca gggaaccctg gtcaccgtgt cctcaggcgg aggtggaagc   360

ggaggggggag gatctggcgg cggaggaagc ggaggcgaca tcgtgatgac ccagtcttcc   420

tccctgtctg catctgtcgg agacagagtc accatcactt gccgggccag tcagagcatt   480

aggtactatt taagttggta tcagcagaaa ccaggaaaag cccctaagct cctgatctat   540

actgcatcca ttttacaaaa tggggtccca tcaaggttca gtggcagtgg atctgggaca   600

gatttcactc tcaccatcag cagcctgcaa cctgaggatt ttgcaactta ttactgcctc   660

cagacttaca ctactccgga ctttggccca gggaccaagg tggaaatcaa a   711

<210> 364
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 364
caggtgcagc tggtgcagtc tggggctgag gtgagggcac ctggggcctc agtgaagatt 60

tcctgcaagg cttctggatt caccttcaga ggctactata tccactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaatc atcaacccta gtggtggtag cagagcctac 180

gcacagaagt tccagggcag ggtcaccatg accagggaca cttccacgag cacagtctac 240

atggagctga gcagcctgag atctgacgac acggccatgt attactgtgc gagaaccgca 300

agttgtggtg gtgactgcta ctaccttgac tactggggcc agggaaccct ggtcaccgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgac 420

atccagatga cccagtctcc tcccaccctg tctgcatctg taggagacag agtcaccatc 480

acttgccggg ccagtgagaa tgttaatatc tggttggcct ggtatcagca gaaaccaggg 540

aaagccccta agctcctgat ctataagtca tccagtttag caagtggggt cccatcaagg 600

ttcagtggca gtggatctgg ggcagaattc actctcacca tcagcagcct gcagcctgat 660

gattttgcaa cttattactg ccaacagtat caaagttacc ccctcacttt cggcggaggg 720

accaaggtgg aaatcaaa 738

<210> 365
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 365
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtt 60

tcctgcaagg cttctggata ctcattcacc ggctacacca tgaactgggt gaggcaggcc 120

cctggacaaa gacttgagtg gatgggactt atcacccctt acaatggtgc ttctagctac 180

aaccagaagt tcaggggcag ggtcacaatc actagagaca cgtcagccag cacagcctac 240

atggagctct ccagcctgag atctgaagac actgcagtct attactgtgc aaggggggggt 300

tacgacggga ggggttttga ctactggggc cagggaacca cggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc cttcaagctt gtctgcatct gtaggagaca gggtcaccat cacttgcagt 480

gccagctcaa gtgtaagtta catgcactgg tatcagcaga aaccaggcaa ggcccctaag 540

agattgatct atgacacatc caaattagca agtggggtcc caagtcgctt cagtggcagt 600

ggatctggga ccgaattcac tctcaccatc agcagcttgc agcctgagga ttttgcaact 660

tattactgcc agcagtggag tggttaccct ctcacgttcg gtcaggggac aaagttggaa 720

atcaaa 726

<210> 366
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 366
caggtgcagc tgcagcagtc tgggcctgag ctggagaagc ctggggcctc agtgaagatt 60

tcctgcaagg cttctggata ctcattcacc ggctacacca tgaactgggt gaagcagagc 120

catggaaaaa gccttgagtg gattggactt atcacccctt acaatggtgc ttctagctac 180

aaccagaagt tcaggggcaa ggccacatta actgtagaca agtcatccag cacagcctac 240

atggacctcc tcagcctgac atctgaagac tctgcagtct atttctgtgc aaggggggggt 300

tacgacggga ggggttttga ctactggggc cagggaacca cggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catcgagctc 420

acccagtctc ctgcaatcat gtctgcatct ccaggagaga aggtcaccat gacttgcagt 480

gccagctcaa gtgtaagtta catgcactgg tatcagcaga aatcaggcac ctcccctaag 540

agatggatct atgacacatc caaattggca agtggggtcc caggtcgctt cagtggcagt 600

ggatctggga actcttactc tctcaccatc agcagcgtgg aggctgagga tgatgcaact 660

tattactgcc agcagtggag tggttaccct ctcacgttcg gtgctgggac aaagttggaa 720

atcaaa 726

<210> 367
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 367
gaagtgcagc tggtggaaag cggcggaggc ctggtgaaac ctggcggcag cctgagactg 60

agctgcgccg ccagcggctt caccttctcg aacgcctgga tgagctgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtcggacgg atcaagagca agaccgacgg cggcaccacc 180

gactacgctg cccccgtgaa gggccggttc accatcagcc gggacgacag caagaacacc 240

ctgtacctgc agatgaacag cctgaaaacc gaggacaccg ccgtgtatta ctgtaccaca 300

gatcttccta agcttaggaa ttttcatatt tggggccagg gaaccctggt caccgtgtcc 360

tcaggcggag gtggaagcgg agggggagga tctggcggcg gaggaagcgg aggcgacatc 420

cagatgaccc agtctccatc ctccctgtct gcatctgtag gagacagagt caccatcact 480

tgccgggcaa gtcagagcat tagcagctat ttaaattggt atcagcagaa accagggaaa 540

gcccctaagc tcctgatcta tgctgcatcc agtttgcaaa gtggggtccc atcaaggttc 600

agtggcagtg gatctgggac agatttcact ctcaccatca gcagtctgca acctgaagat 660

tttgcaactt actactgtca acagagttac agtacccctc tcactttcgg cggcggaaca 720

aaggtggaga tcaag 735

<210> 368
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 368
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctacgcca tgcactgggt ccgccaggcc 120

cctggcaagg gactggaata cgtgtccgcc atcagctcga acggcggcag cacctactac 180

gccaacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

ctgcagatgg gcagcctgcg ggccgaggat atggccgtgt attactgtgc gagcctagaa 300

taccatggct ttcgacaata tgggcttcgt tattggcatt ggggccaggg aaccctggtc 360

accgtgtcct caggcggagg tggaagcgga gggggaggat ctggcggcgg aggaagcgga 420

ggcgacatcc agatgaccca gtctccatcc tccctgtctg catctgtagg agacagagtc 480

accatcactt gccgggcaag tcagagcatt agcagctatt taaattggta tcagcagaaa 540

ccagggaaag cccctaagct cctgatctat gctgcatcca gtttgcaaag tggggtccca 600

tcaaggttca gtggcagtgg atctgggaca gatttcactc tcaccatcag cagtctgcaa 660

cctgaagatt ttgcaactta ctactgtcaa cagagttaca gtacccctct cactttcggc 720

ggcggaacaa aggtggagat caag 744

<210> 369
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 369
cagctgcagc tccaggaaag cggcagcggc ctggtgaaac ccagccagac cctgagcctg 60

acctgtgccg tgtccggcgg cagcatcagc agcggcggct acagctggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct accacagcgg ctcgacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acagaagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgccagcata 300

aaattctggt ttgcggggat taattatttt tttccgtggg gccagggaac cctggtcacc 360

gtgtcctcag gcggaggtgg aagcggaggg ggaggatctg gcggcggagg aagcggaggc 420

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 480

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 540

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 600

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 660

gaagattttg caacttacta ctgtcaacag agttacagta cccctctcac tttcggcggc 720

ggaacaaagg tggagatcaa g 741

<210> 370
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 370
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctactgga tgcactgggt ccgccaggcc 120

cctggcaagg gactggtctg ggtgtctcga atcaacagcg acggcagcag caccagctac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc aagcggattt 300

ttgggaatgg gctcgaattt tatttggggc cagggaaccc tggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagcccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 371
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 371
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg cagcatcagc agcggcggct actactggtc ctggatcaga 120

cagcaccccg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cctggtgaca atctccgtcg ataccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcaagcggg 300

gacagggcac ggtacttcga tctctggggc cgtggcaccc tggtcactgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagcccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 372
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 372
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctactgga tgcactgggt ccgccaggcc 120

cctggcaagg gactggtctg ggtgtctcga atcaacagcg acggcagcag caccagctac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc aagatatcca 300

cgtggatatc atcagatggt tgatgctttt gatatctggg gccaagggac aatggtcacc 360

gtgtcctcag gcggaggtgg aagcggaggg ggaggatctg gcggcggagg aagcggaggc 420

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 480

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 540

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 600

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 660

gaagattttg caacttacta ctgtcaacag agttacagta cccctctcac tttcggcggc 720

ggaacaaagg tggagatcaa g 741

<210> 373
<211> 750
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 373
cagctgcagc tccaggaaag cggccctggc ctggtgaaac ccagcgagac actgagcctg 60

acctgcaccg tgtccggcgg cagcatcagc agcagcagct actactgggg ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctcgatct actacagcgg ctccacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagagta 300

cgatttttgg ctgctcgcac tactattccg gaggcgaatt ttctttgggg ccagggaacc 360

ctggtcaccg tgtcctcagg cggaggtgga agcggagggg gaggatctgg cggcggagga 420

agcggaggcg acatccagat gacccagtct ccatcctccc tgtctgcatc tgtaggagac 480

agagtcacca tcacttgccg ggcaagtcag agcattagca gctatttaaa ttggtatcag 540

cagaaaccag ggaaagcccc taagctcctg atctatgctg catccagttt gcaaagtggg 600

gtcccatcaa ggttcagtgg cagtggatct gggacagatt tcactctcac catcagcagt 660

ctgcaacctg aagattttgc aacttactac tgtcaacaga gttacagtac ccctctcact 720

ttcggcggcg gaacaaaggt ggagatcaag 750

<210> 374
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 374
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctacagca tgaactgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcagctccac catctactac 180

gccgacagcg tgaagggtcg attcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagtactc 300

tccagggcta ggtttgacta ctggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacat ccagatgacc 420

cagtctccat cctccctgtc tgcatctgta ggagacagag tcaccatcac ttgccgggca 480

agtcagagca ttagcagcta tttaaattgg tatcagcaga aaccagggaa agcccctaag 540

ctcctgatct atgctgcatc cagtttgcaa agtggggtcc catcaaggtt cagtggcagt 600

ggatctggga cagatttcac tctcaccatc agcagtctgc aacctgaaga ttttgcaact 660

tactactgtc aacagagtta cagtacccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 375
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 375
gaagtgcagc tggtggaaag cggcggaggc ctggtgaaac ctggcggcag cctgagactg 60

agctgcgccg ccagcggctt caccttcagc agctacagca tgaactgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtcctcg atcagcagca gcagctccta catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagattacga 300

gggagggtgt tcgacccctg gggccaggga accctggtca ccgtgtcctc aggcggaggt 360

ggaagcggag ggggaggatc tggcggcgga ggaagcggag gcgacatcca gatgacccag 420

tctccatcct ccctgtctgc atctgtagga gacagagtca ccatcacttg ccgggcaagt 480

cagagcatta gcagctattt aaattggtat cagcagaaac cagggaaagc ccctaagctc 540

ctgatctatg ctgcatccag tttgcaaagt ggggtcccat caaggttcag tggcagtgga 600

tctgggacag atttcactct caccatcagc agtctgcaac ctgaagattt tgcaacttac 660

tactgtcaac agagttacag taccctctc actttcggcg gcggaacaaa ggtggagatc 720

aag 723

<210> 376
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 376
cagctgcagc tccaggaaag cggccctggc ctggtgaaac ccagcgagac actgagcctg 60

acctgcaccg tgtccggcgg cagcatcagc agcagcagct actactgggg ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctcgatct actacagcgg ctccacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagaata 300

aaatttacca gctttttata tgttcatggt tttctgtggg gccagggaac cctggtcacc 360

gtgtcctcag gcggaggtgg aagcggaggg ggaggatctg gcggcggagg aagcggaggc 420

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 480

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 540

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 600

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 660

gaagattttg caacttacta ctgtcaacag agttacagta cccctctcac tttcggcggc 720

ggaacaaagg tggagatcaa g 741

<210> 377
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 377
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg ccagcggcta caccttcacc agctacgcca tgcactgggt tcgacaggcc 120

cctggccaga gactggaatg gatgggctgg atcaacgccg gcaacggcaa caccaagtac 180

agccagaaat tccagggcag agtgaccatc acccgggaca ccagcgccag caccgcctac 240

atggaactga gcagcctgcg gagcgaggac accgctgtgt attactgtgc gagaggccag 300

agatggctgt acctcggggg gattcgtcgg cattggggcc agggaaccct ggtcaccgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgac 420

atccagatga cccagtctcc atcctccctg tctgcatctg taggagacag agtcaccatc 480

acttgccggg caagtcagag cattagcagc tatttaaatt ggtatcagca gaaaccaggg 540

aaagccccta agctcctgat ctatgctgca tccagtttgc aaagtggggt cccatcaagg 600

ttcagtggca gtggatctgg gacagatttc actctcacca tcagcagtct gcaacctgaa 660

gattttgcaa cttactactg tcaacagagt tacagtaccc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

<210> 378
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 378
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagcgagac actgagcctg 60

acctgcaccg tgtccggcgg cagcatcagc agctactact ggtcctggat cagacagccc 120

cctggcaagg gcctggaatg gatcggctac atctactaca gcggcagcac caactacaac 180

cccagcctga agtccagagt gaccatctcc gtcgatacca gcaagaacca gttcagcctg 240

aagctgagca gcgtgacagc cgccgacacc gctgtgtatt actgtgcgag agaatggatt 300

cccagccgtc cgtactactt tgactactgg ggccagggaa ccctggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgacatccag 420

atgacccagt ctccatcctc cctgtctgca tctgtaggag acagagtcac catcacttgc 480

cgggcaagtc agagcattag cagctattta aattggtatc agcagaaacc agggaaagcc 540

cctaagctcc tgatctatgc tgcatccagt ttgcaaagtg gggtcccatc aaggttcagt 600

ggcagtggat ctgggacaga tttcactctc accatcagca gtctgcaacc tgaagatttt 660

gcaacttact actgtcaaca gagttacagt acccctctca ctttcggcgg cggaacaaag 720

gtggagatca ag 732

<210> 379
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 379
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagagaa 300

agtaccggta caggagcttt tgatatctgg ggccaaggga caatggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgacatccag 420

atgacccagt ctccatcctc cctgtctgca tctgtaggag acagagtcac catcacttgc 480

cgggcaagtc agagcattag cagctattta aattggtatc agcagaaacc agggaaagcc 540

cctaagctcc tgatctatgc tgcatccagt ttgcaaagtg gggtcccatc aaggttcagt 600

ggcagtggat ctgggacaga tttcactctc accatcagca gtctgcaacc tgaagatttt 660

gcaacttact actgtcaaca gagttacagt acccctctca ctttcggcgg cggaacaaag 720

gtggagatca ag 732

<210> 380
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 380
gaagtgcagc tggtggaaag cggaggcgga gtggttcgac ctggcggaag cctgagactg 60

tcttgcgccg ccagcggctt cacctttgac gactacggca tgagctgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtccggc atcaactgga acggcggcag caccggctac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccttgt atcactgtgc gagagagagg 300

tacaggcggg tactccactg gtacttcgat ctctggggcc gtggcaccct ggtcactgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgac 420

atccagatga cccagtctcc atcctccctg tctgcatctg taggagacag agtcaccatc 480

acttgccggg caagtcagag cattagcagc tatttaaatt ggtatcagca gaaaccaggg 540

aaagccccta agctcctgat ctatgctgca tccagtttgc aaagtggggt cccatcaagg 600

ttcagtggca gtggatctgg gacagatttc actctcacca tcagcagtct gcaacctgaa 660

gattttgcaa cttactactg tcaacagagt tacagtaccc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

<210> 381
<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 381
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg ccagcggcta caccttcacc agctacgaca tcaactgggt ccgccaggcc 120

accggacagg gcctggaatg gatgggctgg atgaacccca acagcggcaa caccggctac 180

gcccagaaat tccagggcag agtgaccatg acccggaaca cctcgatcag caccgcctac 240

atggaactga gcagcctgcg gagcgaggac accgctgtgt attactgtgc gagagaaccg 300

gatgcttttg atatctgggg ccaagggaca atggtcaccg tgtcctcagg cggaggtgga 360

agcggagggg gaggatctgg cggcggagga agcggaggcg acatccagat gacccagtct 420

ccatcctccc tgtctgcatc tgtaggagac agagtcacca tcacttgccg ggcaagtcag 480

agcattagca gctatttaaa ttggtatcag cagaaaccag ggaaagcccc taagctcctg 540

atctatgctg catccagttt gcaaagtggg gtcccatcaa ggttcagtgg cagtggatct 600

gggacagatt tcactctcac catcagcagt ctgcaacctg aagattttgc aacttactac 660

tgtcaacaga gttacagtac ccctctcact ttcggcggcg gaacaaaggt ggagatcaag 720

<210> 382
<211> 738

<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 382
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagagaa 300

catatgggga cgattccgta ctactttgac tactggggcc agggaaccct ggtcaccgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgac 420

atccagatga cccagtctcc atcctccctg tctgcatctg taggagacag agtcaccatc 480

acttgccggg caagtcagag cattagcagc tatttaaatt ggtatcagca gaaaccaggg 540

aaagccccta agctcctgat ctatgctgca tccagtttgc aaagtggggt cccatcaagg 600

ttcagtggca gtggatctgg gacagatttc actctcacca tcagcagtct gcaacctgaa 660

gattttgcaa cttactactg tcaacagagt tacagtaccc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

<210> 383
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 383
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg ctcgatcagc agcggcggct actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagagaa 300

gagtttggtt atggggacgt cctctactgg ggccagggaa ccctggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgacatccag 420

atgacccagt ctccatcctc cctgtctgca tctgtaggag acagagtcac catcacttgc 480

cgggcaagtc agagcattag cagctattta aattggtatc agcagaaacc agggaaagcc 540

cctaagctcc tgatctatgc tgcatccagt ttgcaaagtg gggtcccatc aaggttcagt 600

ggcagtggat ctgggacaga tttcactctc accatcagca gtctgcaacc tgaagatttt 660

gcaacttact actgtcaaca gagttacagt acccctctca ctttcggcgg cggaacaaag 720

gtggagatca ag 732

<210> 384
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 384
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg cagcatcagc agcggcgact actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc tcgagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgccagagag 300

gacgtagtca aaggcgcttt tgatatctgg ggccaaggga caatggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgacatccag 420

atgacccagt ctccatcctc cctgtctgca tctgtaggag acagagtcac catcacttgc 480

cgggcaagtc agagcattag cagctattta aattggtatc agcagaaacc agggaaagcc 540

cctaagctcc tgatctatgc tgcatccagt ttgcaaagtg gggtcccatc aaggttcagt 600

ggcagtggat ctgggacaga tttcactctc accatcagca gtctgcaacc tgaagatttt 660

gcaacttact actgtcaaca gagttacagt acccctctca ctttcggcgg cggaacaaag 720

gtggagatca ag 732

<210> 385
<211> 735

<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 385
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctacagca tgaactgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcagctccac catctactac 180

gccgacagcg tgaagggtcg attcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagaagac 300

ttctcgcata agctagggta cttccagcac tggggccagg gcaccctggt caccgtgtcc 360

tcaggcggag gtggaagcgg agggggagga tctggcggcg gaggaagcgg aggcgacatc 420

cagatgaccc agtctccatc ctccctgtct gcatctgtag gagacagagt caccatcact 480

tgccgggcaa gtcagagcat tagcagctat ttaaattggt atcagcagaa accagggaaa 540

gcccctaagc tcctgatcta tgctgcatcc agtttgcaaa gtggggtccc atcaaggttc 600

agtggcagtg gatctgggac agatttcact ctcaccatca gcagtctgca acctgaagat 660

tttgcaactt actactgtca acagagttac agtacccctc tcactttcgg cggcggaaca 720

aaggtggaga tcaag 735

<210> 386
<211> 714
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 386
caggtgcagc tggtggaaag cggcggaggc ctggtgaaac ctggcggcag cctgagactg 60

agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagattac 300

gattacgtgt ggggccaggg aaccctggtc accgtgtcct caggcggagg tggaagcgga 360

ggggggaggat ctggcggcgg aggaagcgga ggcgacatcc agatgaccca gtctccatcc 420

tccctgtctg catctgtagg agacagagtc accatcactt gccgggcaag tcagagcatt 480

agcagctatt taaattggta tcagcagaaa ccagggaaag cccctaagct cctgatctat 540

gctgcatcca gtttgcaaag tggggtccca tcaaggttca gtggcagtgg atctgggaca 600

gatttcactc tcaccatcag cagtctgcaa cctgaagatt ttgcaactta ctactgtcaa 660

cagagttaca gtacccctct cactttcggc ggcggaacaa aggtggagat caag 714

<210> 387
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 387
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagccagac cctgagcctg 60

acctgcacag tgtccggcgg cagcatcagc agcggcgact actactggtc ctggatcaga 120

cagccccctg gcaagggcct ggaatggatc ggctacatct actacagcgg cagcacctac 180

tacaacccca gcctgaagtc tcgagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgccagagat 300

cgccgtgatt gggactggtt cgacccctgg ggccagggaa ccctggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgacatccag 420

atgacccagt ctccatcctc cctgtctgca tctgtaggag acagagtcac catcacttgc 480

cgggcaagtc agagcattag cagctattta attggtatc agcagaaacc agggaaagcc 540

cctaagctcc tgatctatgc tgcatccagt ttgcaaagtg gggtcccatc aaggttcagt 600

ggcagtggat ctgggacaga tttcactctc accatcagca gtctgcaacc tgaagatttt 660

gcaacttact actgtcaaca gagttacagt acccctctca ctttcggcgg cggaacaaag 720

gtggagatca ag 732

<210> 388
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 388
caggtgcagc tgcaggaaag cggccctggc ctggtgaaac ccagcggcac cctgagcctg 60

acctgtgccg tgtctggcgg cagcatcagc agcagcaact ggtggtcctg ggtccgccag 120

cctcccggca agggcctcga atggatcggc gagatctacc acagcggcag caccaactac 180

aaccccagcc tgaagtccag agtgaccatc agcgtggaca agagcaagaa ccagttcagc 240

ctgaagctga gcagcgtgac agccgccgac accgctgtgt attactgtgc gagagatcag 300

caggcgttga aataccgtgt ggattggggc cagggaaccc tggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcaagtcaga gcattagcag ctatttaaat tggtatcagc agaaaccagg gaaagccct 540

aagctcctga tctatgctgc atccagtttg caaagtgggg tcccatcaag gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagtc tgcaacctga agattttgca 660

acttactact gtcaacagag ttacagtacc cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 389
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 389
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg ccagcggcta caccttcacc agctacggca tcagctgggt ccgccaggct 120

cctggacagg gactggaatg gatgggctgg atcagcgcct acaacggcaa caccaactac 180

gcccagaaac tgcagggcag agtgaccatg accaccgaca ccagcaccag caccgcctac 240

atggaacttc gaagcctgag aagcgacgac accgccgtgt attactgtgc gagagatctt 300

acgctaggat gctttgacta ctggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgacat ccagatgacc 420

cagtctccat cctccctgtc tgcatctgta ggagacagag tcaccatcac ttgccgggca 480

agtcagagca ttagcagcta tttaaattgg tatcagcaga aaccagggaa agcccctaag 540

ctcctgatct atgctgcatc cagtttgcaa agtggggtcc catcaaggtt cagtggcagt 600

ggatctggga cagatttcac tctcaccatc agcagtctgc aacctgaaga ttttgcaact 660

tactactgtc aacagagtta cagtacccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 390
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 390
gaagtgcagc tggtggaaag cggcggaggc ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccgtgtcc agcaactaca tgagctgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtccgtg atctacagcg gcggcagcac ctactacgcc 180

gacagcgtga agggtcgatt caccatcagc cgggacaaca gcaagaacac cctgtacctg 240

cagatgaaca gcctgcgggc cgaggacacc gccgtgtatt actgtgcgag agatgggtca 300

aactcttggt acttcgatct ctggggccgt ggcaccctgg tcactgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgacat ccagatgacc 420

cagtctccat cctccctgtc tgcatctgta ggagacagag tcaccatcac ttgccgggca 480

agtcagagca ttagcagcta tttaaattgg tatcagcaga aaccagggaa agcccctaag 540

ctcctgatct atgctgcatc cagtttgcaa agtggggtcc catcaaggtt cagtggcagt 600

ggatctggga cagatttcac tctcaccatc agcagtctgc aacctgaaga ttttgcaact 660

tactactgtc aacagagtta cagtacccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 391
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 391
caggtgcagc tggtggaaag cggcggaggc gtggtgcagc ccggcagaag ccttcgactg 60

agctgcgccg ccagcggctt caccttcagc agctacggca tgcactgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtggccgtg atttggtacg acggcagcaa caagtactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagggcattt 300

ttattcctgt ctttttcggt ttggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacat ccagatgacc 420

cagtctccat cctccctgtc tgcatctgta ggagacagag tcaccatcac ttgccgggca 480

agtcagagca ttagcagcta tttaaattgg tatcagcaga aaccagggaa agcccctaag 540

ctcctgatct atgctgcatc cagtttgcaa agtggggtcc catcaaggtt cagtggcagt 600

ggatctggga cagatttcac tctcaccatc agcagtctgc aacctgaaga ttttgcaact 660

tactactgtc aacagagtta cagtacccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 392
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 392
gaagtgcagc tggtggaatc tggcggcgtg gtggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcgac gactacacca tgcactgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtccctg atcagctggg acggcggctc tacctactac 180

gccgactccg tgaagggccg gttcaccatc agccgggaca acagcaagaa cagcctgtac 240

ctgcagatga acagcctgcg gaccgaggac accgccttgt attactgtgc aaaagggata 300

ttctactcga gtaaagagga ttttgactac tggggccagg gaaccctggt caccgtgtcc 360

tcaggcggag gtggaagcgg agggggagga tctggcggcg gaggaagcgg aggcgacatc 420

cagatgaccc agtctccatc ctccctgtct gcatctgtag gagacagagt caccatcact 480

tgccgggcaa gtcagagcat tagcagctat ttaaattggt atcagcagaa accagggaaa 540

gcccctaagc tcctgatcta tgctgcatcc agtttgcaaa gtggggtccc atcaaggttc 600

agtggcagtg gatctgggac agatttcact ctcaccatca gcagtctgca acctgaagat 660

tttgcaactt actactgtca acagagttac agtacccctc tcactttcgg cggcggaaca 720

aaggtggaga tcaag 735

<210> 393
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 393
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tcttgcgccg ccagcggctt caccttcgac gactacacca tgcactgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtccctg atcagctggg acggcggctc tacctactac 180

gccgactccg tgaagggccg gttcaccatc agccgggaca acagcaagaa cagcctgtac 240

ctgcagatga acagcctgcg gaccgaggac accgccttgt attactgtgc aaaagatata 300

tggatattct actcgagtaa tccaaagccg acggtctact ggggccaggg aaccctggtc 360

accgtgtcct caggcggagg tggaagcgga gggggaggat ctggcggcgg aggaagcgga 420

ggcgacatcc agatgaccca gtctccatcc tccctgtctg catctgtagg agacagagtc 480

accatcactt gccgggcaag tcagagcatt agcagctatt taaattggta tcagcagaaa 540

ccagggaaag cccctaagct cctgatctat gctgcatcca gtttgcaaag tggggtccca 600

tcaaggttca gtggcagtgg atctgggaca gatttcactc tcaccatcag cagtctgcaa 660

cctgaagatt ttgcaactta ctactgtcaa cagagttaca gtacccctct cactttcggc 720

ggcggaacaa aggtggagat caag 744

<210> 394
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 394
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tcctgcaagg ccagcggcta caccttcacc agctacgcca tgaactgggt ccgccaggcc 120

ccaggccagg gactggaatg gatgggctgg atcaacacca acaccggcaa ccccacctac 180

gcccagggct tcaccggcag attcgtgttc agcttcgaca ccagcgtgtc caccgcctac 240

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cagacgctga cctacggaaa ctggttcgac ccctggggcc agggaaccct ggtcaccgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgac 420

atccagatga cccagtctcc atcctccctg tctgcatctg taggagacag agtcaccatc 480

acttgccggg caagtcagag cattagcagc tatttaaatt ggtatcagca gaaaccaggg 540

aaagccccta agctcctgat ctatgctgca tccagtttgc aaagtggggt cccatcaagg 600

ttcagtggca gtggatctgg gacagatttc actctcacca tcagcagtct gcaacctgaa 660

gattttgcaa cttactactg tcaacagagt tacagtaccc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

<210> 395
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 395
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acctgcaccg tgtccggcgg ctctgtgtcc agcggctcct actactggtc ctggatcaga 120

cagccccctg gcaagggcct cgaatggatc ggctacatct actacagcgg cagcaccaac 180

tacaacccca gcctgaagtc cagagtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gacagccgcc gacaccgctg tgtattactg tgcgagagat 300

cattacgagc gggggctcta ctggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgacat ccagatgacc 420

cagtctccat cctccctgtc tgcatctgta ggagacagag tcaccatcac ttgccgggca 480

agtcagagca ttagcagcta tttaaattgg tatcagcaga aaccagggaa agcccctaag 540

ctcctgatct atgctgcatc cagtttgcaa agtggggtcc catcaaggtt cagtggcagt 600

ggatctggga cagatttcac tctcaccatc agcagtctgc aacctgaaga ttttgcaact 660

tactactgtc aacagagtta cagtacccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 396
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 396
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagatatatg 300

tataactggt acttcgatct ctggggccgt ggcaccctgg tcactgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgacat ccagatgacc 420

cagagcccca gcagcgtgtc cgccagcgtg ggcgatcgag tgaccatcac ctgtcgggcc 480

tcccagggca tcagcagctg gctggcctgg tatcagcaga agcccggcaa ggcccccaag 540

ctgctgatct acgccgccag cagcctgcag agcggcgtgc caagcagatt cagcggcagc 600

ggctccggca ccgacttcac cctgaccatc agctccctgc agcccgagga cttcgccacc 660

tactactgcc agcaggctaa cagtttccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 397
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 397
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagatcga 300

aggcctgctt ttgatatctg gggccaaggg acaatggtca ccgtgtcctc aggcggaggt 360

ggaagcggag ggggaggatc tggcggcgga ggaagcggag gcgacatcca gatgacccag 420

agccccagca gcgtgtccgc cagcgtgggc gatcgagtga ccatcacctg tcgggcctcc 480

cagggcatca gcagctggct ggcctggtat cagcagaagc ccggcaaggc ccccaagctg 540

ctgatctacg ccgccagcag cctgcagagc ggcgtgccaa gcagattcag cggcagcggc 600

tccggcaccg acttcaccct gaccatcagc tccctgcagc ccgaggactt cgccacctac 660

tactgccagc aggctaacag tttccctctc actttcggcg gcggaacaaa ggtggagatc 720

aag 723

<210> 398
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 398
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc ggtacatttg 300

aaacgacgtc cctactttga ctactggggc cagggaaccc tggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcgc catccagctg 420

acccagagcc ccagcagcct gagcgccagc gtgggcgata gagtgaccat cacctgtcgc 480

gccagccagg gcatcagcag cgctctggcc tggtatcagc agaagcccgg caaggccccc 540

aagctgctga tctacgacgc cagctccctg gaaagcggcg tgcccagcag attcagcggc 600

agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taatagttac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 399
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 399
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagcgtacat 300

aagaaaccca tctttgacta ctggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgccat ccagctgacc 420

cagagcccca gcagcctgag cgccagcgtg ggcgatagag tgaccatcac ctgtcgcgcc 480

agccagggca tcagcagcgc tctggcctgg tatcagcaga agcccggcaa ggcccccaag 540

ctgctgatct acgacgccag ctccctggaa agcggcgtgc ccagcagatt cagcggcagc 600

ggctccggca ccgacttcac cctgaccatc agcagcctgc agcccgagga cttcgccacc 660

tactactgcc agcagtttaa tagttaccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 400
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 400
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagtaccagt 300

cggcgctgta ccttccagca ctggggccag ggcaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgccat ccagctgacc 420

cagagcccca gcagcctgag cgccagcgtg ggcgatagag tgaccatcac ctgtcgcgcc 480

agccagggca tcagcagcgc tctggcctgg tatcagcaga agcccggcaa ggcccccaag 540

ctgctgatct acgacgccag ctccctggaa agcggcgtgc ccagcagatt cagcggcagc 600

ggctccggca ccgacttcac cctgaccatc agcagcctgc agcccgagga cttcgccacc 660

tactactgcc agcagtttaa tagttaccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 401
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 401
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagtaccagc 300

ccgcgtcctc tcttccagca ctggggccag ggcaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgccat ccagctgacc 420

cagagcccca gcagcctgag cgccagcgtg ggcgatagag tgaccatcac ctgtcgcgcc 480

agccagggca tcagcagcgc tctggcctgg tatcagcaga agcccggcaa ggcccccaag 540

ctgctgatct acgacgccag ctccctggaa agcggcgtgc ccagcagatt cagcggcagc 600

ggctccggca ccgacttcac cctgaccatc agcagcctgc agcccgagga cttcgccacc 660

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atcaag 726

<210> 402
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 402
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagcccttac 300

caagtccgag gagtctactt tgactactgg ggccagggaa ccctggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgccatccag 420

ctgacccaga gccccagcag cctgagcgcc agcgtgggcg atagagtgac catcacctgt 480

cgcgccagcc agggcatcag cagcgctctg gcctggtatc agcagaagcc cggcaaggcc 540

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ggcagcggct ccggcaccga cttcaccctg accatcagca gcctgcagcc cgaggacttc 660

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gtggagatca ag 732

<210> 403
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 403
caggtgcagc tggtggaaag cggcggaggc ctggtgaaac ctggcggcag cctgagactg 60

agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagcccctat 300

aagaaacgac gaacggtctt tgactactgg ggccagggaa ccctggtcac cgtgtcctca 360

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ctgacccaga gccccagcag cctgagcgcc agcgtgggcg atagagtgac catcacctgt 480

cgcgccagcc agggcatcag cagcgctctg gcctggtatc agcagaagcc cggcaaggcc 540

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ggcagcggct ccggcaccga cttcaccctg accatcagca gcctgcagcc cgaggacttc 660

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gtggagatca ag 732

<210> 404
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 404
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

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agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taatagttac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 405
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 405
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

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ggctccggca ccgacttcac cctgaccatc agcagcctgc agcccgagga cttcgccacc 660

tactactgcc agcagtttaa tagttaccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 406
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 406
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

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attcgtgtac ctttacgatt gcccctcttc cagcactggg gccagggcac cctggtcacc 360

gtgtcctcag gcggaggtgg aagcggaggg ggaggatctg gcggcggagg aagcggaggc 420

gccatccagc tgacccagag ccccagcagc ctgagcgcca gcgtgggcga tagagtgacc 480

atcacctgtc gcgccagcca gggcatcagc agcgctctgg cctggtatca gcagaagccc 540

ggcaaggccc ccaagctgct gatctacgac gccagctccc tggaaagcgg cgtgcccagc 600

agattcagcg gcagcggctc cggcaccgac ttcaccctga ccatcagcag cctgcagccc 660

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ggaacaaagg tggagatcaa g 741

<210> 407
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 407
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

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atatttgcga tatttgatat ctggggccaa gggacaatgg tcaccgtgtc ctcaggcgga 360

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cagagcccca gcagcctgag cgccagcgtg ggcgatagag tgaccatcac ctgtcgcgcc 480

agccagggca tcagcagcgc tctggcctgg tatcagcaga agcccggcaa ggcccccaag 540

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ggctccggca ccgacttcac cctgaccatc agcagcctgc agcccgagga cttcgccacc 660

tactactgcc agcagtttaa tagttaccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 408
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 408
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

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cgtggattcg ttcattttga tctctggggc cgtggcaccc tggtcactgt gtcctcaggc 360

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acccagagcc ccagcagcct gagcgccagc gtgggcgata gagtgaccat cacctgtcgc 480

gccagccagg gcatcagcag cgctctggcc tggtatcagc agaagcccgg caaggccccc 540

aagctgctga tctacgacgc cagctccctg gaaagcggcg tgcccagcag attcagcggc 600

agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taatagttac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 409
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 409
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

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ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gaggacgtca 300

agaggtttgt gtgttttatt tgactactgg ggccagggaa ccctggtcac cgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgccatccag 420

ctgacccaga gccccagcag cctgagcgcc agcgtgggcg atagagtgac catcacctgt 480

cgcgccagcc agggcatcag cagcgctctg gcctggtatc agcagaagcc cggcaaggcc 540

cccaagctgc tgatctacga cgccagctcc ctggaaagcg gcgtgcccag cagattcagc 600

ggcagcggct ccggcaccga cttcaccctg accatcagca gcctgcagcc cgaggacttc 660

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gtggagatca ag 732

<210> 410
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 410
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cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagaagtggg 300

cccagtagct actggtactt cgatctctgg ggccgtggca ccctggtcac tgtgtcctca 360

ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgccatccag 420

ctgacccaga gccccagcag cctgagcgcc agcgtgggcg atagagtgac catcacctgt 480

cgcgccagcc agggcatcag cagcgctctg gcctggtatc agcagaagcc cggcaaggcc 540

cccaagctgc tgatctacga cgccagctcc ctggaaagcg gcgtgcccag cagattcagc 600

ggcagcggct ccggcaccga cttcaccctg accatcagca gcctgcagcc cgaggacttc 660

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gtggagatca ag 732

<210> 411
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

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cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagaaacatt 300

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ggcggaggtg gaagcggagg gggaggatct ggcggcggag gaagcggagg cgccatccag 420

ctgacccaga gccccagcag cctgagcgcc agcgtgggcg atagagtgac catcacctgt 480

cgcgccagcc agggcatcag cagcgctctg gcctggtatc agcagaagcc cggcaaggcc 540

cccaagctgc tgatctacga cgccagctcc ctggaaagcg gcgtgcccag cagattcagc 600

ggcagcggct ccggcaccga cttcaccctg accatcagca gcctgcagcc cgaggacttc 660

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gtggagatca ag 732

<210> 412
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 412
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagacttaca 300

gtccgcactg gagcttttga tatctggggc caagggacaa tggtcaccgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcgc catccagctg 420

acccagagcc ccagcagcct gagcgccagc gtgggcgata gagtgaccat cacctgtcgc 480

gccagccagg gcatcagcag cgctctggcc tggtatcagc agaagcccgg caaggccccc 540

aagctgctga tctacgacgc cagctccctg gaaagcggcg tgcccagcag attcagcggc 600

agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taatagttac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 413
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 413
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagactaaga 300

actgcccacc tggacttcga tctctggggc cgtggcaccc tggtcactgt gtcctcaggc 360

ggaggtggaa gcggaggggg aggatctggc ggcggaggaa gcggaggcgc catccagctg 420

acccagagcc ccagcagcct gagcgccagc gtgggcgata gagtgaccat cacctgtcgc 480

gccagccagg gcatcagcag cgctctggcc tggtatcagc agaagcccgg caaggccccc 540

aagctgctga tctacgacgc cagctccctg gaaagcggcg tgcccagcag attcagcggc 600

agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taatagttac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

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<220>
<223> MSLN scFv domain

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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagatctc 300

atatttccag tagtctttga ctactggggc cagggaaccc tggtcaccgt gtcctcaggc 360

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acccagagcc ccagcagcct gagcgccagc gtgggcgata gagtgaccat cacctgtcgc 480

gccagccagg gcatcagcag cgctctggcc tggtatcagc agaagcccgg caaggccccc 540

aagctgctga tctacgacgc cagctccctg gaaagcggcg tgcccagcag attcagcggc 600

agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taatagttac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 415
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 415
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagatgga 300

tatcgcaaat atggttacgt atttttttgat atctggggcc aagggacaat ggtcaccgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgcc 420

atccagctga cccagagccc cagcagcctg agcgccagcg tgggcgatag agtgaccatc 480

acctgtcgcg ccagccaggg catcagcagc gctctggcct ggtatcagca gaagcccggc 540

aaggccccca agctgctgat ctacgacgcc agctccctgg aaagcggcgt gcccagcaga 600

ttcagcggca gcggctccgg caccgacttc accctgacca tcagcagcct gcagcccgag 660

gacttcgcca cctactactg ccagcagttt aatagttacc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

<210> 416
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 416
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagatggg 300

aggtacaggc ggttctggca tgcttttgat atctggggcc aagggacaat ggtcaccgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgcc 420

atccagctga cccagagccc cagcagcctg agcgccagcg tgggcgatag agtgaccatc 480

acctgtcgcg ccagccaggg catcagcagc gctctggcct ggtatcagca gaagcccggc 540

aaggccccca agctgctgat ctacgacgcc agctccctgg aaagcggcgt gcccagcaga 600

ttcagcggca gcggctccgg caccgacttc accctgacca tcagcagcct gcagcccgag 660

gacttcgcca cctactactg ccagcagttt aatagttacc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

<210> 417
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 417
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agctgcgccg ccagcggctt caccttcagc gactactaca tgagctggat cagacaggcc 120

cctggcaagg gactggaatg ggtgtcctac atcagcagca gcggctcgac catctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt attactgtgc gagagcccat 300

atacgggggt acttcgatct ctggggccgt ggcaccctgg tcactgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgccat ccagctgacc 420

cagagcccca gcagcctgag cgccagcgtg ggcgatagag tgaccatcac ctgtcgcgcc 480

agccagggca tcagcagcgc tctggcctgg tatcagcaga agcccggcaa ggcccccaag 540

ctgctgatct acgacgccag ctccctggaa agcggcgtgc ccagcagatt cagcggcagc 600

ggctccggca ccgacttcac cctgaccatc agcagcctgc agcccgagga cttcgccacc 660

tactactgcc agcagtttaa tagttaccct ctcactttcg gcggcggaac aaaggtggag 720

atcaag 726

<210> 418
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

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gggggcgggg gacgatggta cttcgatctc tggggccgtg gcaccctggt cactgtgtcc 360

tcaggcggag gtggaagcgg agggggagga tctggcggcg gaggaagcgg aggcgccatc 420

cagctgaccc agagccccag cagcctgagc gccagcgtgg gcgacagagt gaccatcacc 480

tgtcgggcca gccagggcat cagcagcgct ctggcctggt atcagcagaa gcccggcaag 540

gcccccaagc tgctgatcta cgacgcgtcc tccctggaaa gcggcgtgcc cagcagattc 600

agcggcagcg gctccggcac cgacttcacc ctgaccatca gcagcctgca gcccgaggac 660

ttcgccacct actactgcca gcagtttaat aattaccctc tcactttcgg cggcggaaca 720

aaggtggaga tcaag 735

<210> 419
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 419
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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

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gccagccagg gcatcagcag cgctctggcc tggtatcagc agaagcccgg caaggccccc 540

aagctgctga tctacgacgc gtcctccctg gaaagcggcg tgcccagcag attcagcggc 600

agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

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gagatcaag 729

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<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

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cagctgaccc agagccccag cagcctgagc gccagcgtgg gcgacagagt gaccatcacc 480

tgtcgggcca gccagggcat cagcagcgct ctggcctggt atcagcagaa gcccggcaag 540

gcccccaagc tgctgatcta cgacgcgtcc tccctggaaa gcggcgtgcc cagcagattc 600

agcggcagcg gctccggcac cgacttcacc ctgaccatca gcagcctgca gcccgaggac 660

ttcgccacct actactgcca gcagtttaat aattaccctc tcactttcgg cggcggaaca 720

aaggtggaga tcaag 735

<210> 421
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 421
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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

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ctgacccaga gccccagcag cctgagcgcc agcgtgggcg acagagtgac catcacctgt 480

cgggccagcc agggcatcag cagcgctctg gcctggtatc agcagaagcc cggcaaggcc 540

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gtggagatca ag 732

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<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

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acctactact gccagcagtt taataattac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

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<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

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agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taataattac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 424
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 424
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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

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aggactacct ggtacttcga tctctggggc cgtggcaccc tggtcactgt gtcctcaggc 360

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aagctgctga tctacgacgc gtcctccctg gaaagcggcg tgcccagcag attcagcggc 600

agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

acctactact gccagcagtt taataattac cctctcactt tcggcggcgg aacaaaggtg 720

gagatcaag 729

<210> 425
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 425
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tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

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ggtaaggatg gtccttactg gtacttcgat ctctggggcc gtggcaccct ggtcactgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgcc 420

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aaggccccca agctgctgat ctacgacgcg tcctccctgg aaagcggcgt gcccagcaga 600

ttcagcggca gcggctccgg caccgacttc accctgacca tcagcagcct gcagcccgag 660

gacttcgcca cctactactg ccagcagttt aataattacc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

<210> 426
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> MSLN scFv domain

<400> 426
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cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtat attactgtgc gaaaagaaga 300

gacagttatg gtccttactg gtacttcgat ctctggggcc gtggcaccct ggtcactgtg 360

tcctcaggcg gaggtggaag cggaggggga ggatctggcg gcggaggaag cggaggcgcc 420

atccagctga cccagagccc cagcagcctg agcgccagcg tgggcgacag agtgaccatc 480

acctgtcggg ccagccaggg catcagcagc gctctggcct ggtatcagca gaagcccggc 540

aaggccccca agctgctgat ctacgacgcg tcctccctgg aaagcggcgt gcccagcaga 600

ttcagcggca gcggctccgg caccgacttc accctgacca tcagcagcct gcagcccgag 660

gacttcgcca cctactactg ccagcagttt aataattacc ctctcacttt cggcggcgga 720

acaaaggtgg agatcaag 738

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<220>
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<400> 427
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cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtat attactgtgc gaagaatcgt 300

cccccgcccg ggtactggta cttcgatctc tggggccgtg gcaccctggt cactgtgtcc 360

tcaggcggag gtggaagcgg agggggagga tctggcggcg gaggaagcgg aggcgccatc 420

cagctgaccc agagccccag cagcctgagc gccagcgtgg gcgacagagt gaccatcacc 480

tgtcgggcca gccagggcat cagcagcgct ctggcctggt atcagcagaa gcccggcaag 540

gcccccaagc tgctgatcta cgacgcgtcc tccctggaaa gcggcgtgcc cagcagattc 600

agcggcagcg gctccggcac cgacttcacc ctgaccatca gcagcctgca gcccgaggac 660

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aaggtggaga tcaag 735

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<220>
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cctggcaagg gactcgaatg ggtgtccgcc atcagcggca gcggcggcag cacctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtat attactgtgc gaagggaaga 300

cgatttagct ggtacttcga tctctggggc cgtggcaccc tggtcactgt gtcctcaggc 360

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acccagagcc ccagcagcct gagcgccagc gtgggcgaca gagtgaccat cacctgtcgg 480

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agcggctccg gcaccgactt caccctgacc atcagcagcc tgcagcccga ggacttcgcc 660

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gagatcaag 729

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<400> 429

Asn Ala Trp Met Ser
1 5

<210> 430
<211> 5
<212> PRT
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<220>
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<400> 430

Ser Tyr Ala Met His
1 5

<210> 431
<211> 7
<212> PRT
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<400> 431

Ser Gly Gly Tyr Ser Trp Ser
1 5

<210> 432
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<400> 432

Ser Gly Gly Tyr Tyr Trp Ser
1 5

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<400> 433

Ser Ser Ser Tyr Tyr Trp Gly
1 5

<210> 434
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<400> 434

Ser Tyr Ser Met Asn
1 5

<210> 435
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<400> 435

Ser Tyr Tyr Trp Ser
1 5

<210> 436
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<400> 436

Asp Tyr Gly Met Ser
1 5

<210> 437
<211> 5
<212> PRT
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<400> 437

Ser Tyr Asp Ile Asn
1 5

<210> 438
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<220>
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<400> 438

Ser Gly Asp Tyr Tyr Trp Ser
1 5

<210> 439
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<220>
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<400> 439

Asp Tyr Tyr Met Ser
1 5

<210> 440
<211> 6
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<213> Artificial Sequence

<220>
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<400> 440

Ser Ser Asn Trp Trp Ser
1 5

<210> 441
<211> 5
<212> PRT
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<220>
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<400> 441

Ser Tyr Gly Ile Ser
1 5

<210> 442
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<212> PRT
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<400> 442

Ser Asn Tyr Met Ser
1 5

<210> 443
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<400> 443

Ser Tyr Gly Met His
1   5

<210> 444
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<400> 444

Asp Tyr Thr Met His
1   5

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<220>
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<400> 445

Ser Tyr Ala Met Asn
1   5

<210> 446
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<400> 446

Ser Gly Ser Tyr Tyr Trp Ser
1   5

<210> 447
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<212> PRT
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<220>
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<400> 447

Ser Tyr Ala Met Ser
1   5

<210> 448
<211> 5
<212> PRT
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<220>
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<400> 448

Gly Tyr Thr Met Asn
1   5

<210> 449
<211> 5
<212> PRT
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<220>
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<400> 449

Ser Tyr Trp Met His
1   5

<210> 450
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<212> PRT
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<220>
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<400> 450

Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala Pro
1   5   10   15

Val Lys Gly

<210> 451
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 451

Ala Ile Ser Ser Asn Gly Gly Ser Thr Tyr Tyr Ala Asn Ser Val Lys
1 5 10 15

Gly

<210> 452
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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<400> 452

Tyr Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 453
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 453

Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 454
<211> 16

<212> PRT
<213> Artificial Sequence

<220>
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<400> 454

Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 455
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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<400> 455

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 456
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 456

Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 457
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 457

Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 458
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 458

Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe Gln
1 5 10 15

Gly

<210> 459
<211> 16
<212> PRT
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<220>
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<400> 459

Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 460
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 460

Gly Ile Asn Trp Asn Gly Gly Ser Thr Gly Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 461
<211> 17
<212> PRT
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<220>
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<400> 461

Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 462
<211> 17
<212> PRT
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<220>
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<400> 462

Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 463
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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<400> 463

Glu Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 464
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 464

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> 465
<211> 16
<212> PRT
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<220>
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<400> 465

Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
1 5 10 15

<210> 466
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR2

<400> 466

Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 467
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR2

<400> 467

Leu Ile Ser Trp Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 468
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR2

<400> 468

Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe Thr
1   5   10   15

Gly

<210> 469
<211> 17
<212> PRT
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<220>
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<400> 469

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 470
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
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<400> 470

Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys Phe Arg
1   5   10   15

Gly

<210> 471
<211> 10
<212> PRT
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<220>
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<400> 471

Asp Leu Pro Lys Leu Arg Asn Phe His Ile
1   5   10

<210> 472
<211> 15
<212> PRT
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<220>
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<400> 472

Leu Glu Tyr His Gly Phe Arg Gln Tyr Gly Leu Arg Tyr Trp His
1   5   10   15

<210> 473
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
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<400> 473

Ile Lys Phe Trp Phe Ala Gly Ile Asn Tyr Phe Phe Pro
1   5   10

<210> 474
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<400> 474

Gly Phe Leu Gly Met Gly Ser Asn Phe Ile
1 5 10

<210> 475
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 475

Gly Asp Arg Ala Arg Tyr Phe Asp Leu
1 5

<210> 476
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
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<400> 476

Tyr Pro Arg Gly Tyr His Gln Met Val Asp Ala Phe Asp Ile
1 5 10

<210> 477
<211> 16
<212> PRT
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<220>
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<400> 477

Val Arg Phe Leu Ala Ala Arg Thr Thr Ile Pro Glu Ala Asn Phe Leu
1   5   10   15

<210> 478
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<212> PRT
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<220>
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<400> 478

Val Leu Ser Arg Ala Arg Phe Asp Tyr
1   5

<210> 479
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<212> PRT
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<220>
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<400> 479

Leu Arg Gly Arg Val Phe Asp Pro
1   5

<210> 480
<211> 13
<212> PRT
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<220>
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<400> 480

Ile Lys Phe Thr Ser Phe Leu Tyr Val His Gly Phe Leu
1   5   10

<210> 481
<211> 13
<212> PRT
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<220>
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<400> 481

Gly Gln Arg Trp Leu Tyr Leu Gly Gly Ile Arg Arg His
1 5 10

<210> 482
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<212> PRT
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<220>
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<400> 482

Glu Trp Ile Pro Ser Arg Pro Tyr Tyr Phe Asp Tyr
1 5 10

<210> 483
<211> 10
<212> PRT
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<220>
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<400> 483

Glu Ser Thr Gly Thr Gly Ala Phe Asp Ile
1 5 10

<210> 484
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
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<400> 484

Glu Arg Tyr Arg Arg Val Leu His Trp Tyr Phe Asp Leu
1 5 10

<210> 485
<211> 7
<212> PRT
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<220>

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<400> 485

Glu Pro Asp Ala Phe Asp Ile
1   5

<210> 486
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<212> PRT
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<220>
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<400> 486

Glu His Met Gly Thr Ile Pro Tyr Tyr Phe Asp Tyr
1   5   10

<210> 487
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<400> 487

Glu Glu Phe Gly Tyr Gly Asp Val Leu Tyr
1   5   10

<210> 488
<211> 10
<212> PRT
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<220>
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<400> 488

Glu Asp Val Val Lys Gly Ala Phe Asp Ile
1   5   10

<210> 489
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<220>
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<400> 489

Glu Asp Phe Ser His Lys Leu Gly Tyr Phe Gln His
1   5   10

<210> 490
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<212> PRT
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<220>
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<400> 490

Asp Tyr Asp Tyr Val
1   5

<210> 491
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<400> 491

Asp Arg Arg Asp Trp Asp Trp Phe Asp Pro
1   5   10

<210> 492
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<400> 492

Asp Gln Gln Ala Leu Lys Tyr Arg Val Asp
1   5   10

<210> 493
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<212> PRT
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<220>
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<400> 493

Asp Leu Thr Leu Gly Cys Phe Asp Tyr
1   5

<210> 494
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<212> PRT
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<220>
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<400> 494

Asp Gly Ser Asn Ser Trp Tyr Phe Asp Leu
1   5   10

<210> 495
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<220>
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<400> 495

Ala Phe Leu Phe Leu Ser Phe Ser Val
1   5

<210> 496
<211> 12
<212> PRT
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<220>
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<400> 496

Gly Ile Phe Tyr Ser Ser Lys Glu Asp Phe Asp Tyr
1   5   10

<210> 497
<211> 15
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<220>
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<400> 497

Asp Ile Trp Ile Phe Tyr Ser Ser Asn Pro Lys Pro Thr Val Tyr
1 5 10 15

<210> 498
<211> 13
<212> PRT
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<220>
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<400> 498

Lys Asp Gln Thr Leu Thr Tyr Gly Asn Trp Phe Asp Pro
1 5 10

<210> 499
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<212> PRT
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<220>
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<400> 499

Asp His Tyr Glu Arg Gly Leu Tyr
1 5

<210> 500
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<212> PRT
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<220>
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<400> 500

Tyr Met Tyr Asn Trp Tyr Phe Asp Leu
1 5

<210> 501
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<212> PRT
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<220>
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<400> 501

Asp Arg Arg Pro Ala Phe Asp Ile
1   5

<210> 502
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<400> 502

His Leu Lys Arg Arg Pro Tyr Phe Asp Tyr
1   5   10

<210> 503
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<212> PRT
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<220>
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<400> 503

Val His Lys Lys Pro Ile Phe Asp Tyr
1   5

<210> 504
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<212> PRT
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<220>
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<400> 504

Thr Ser Arg Arg Cys Thr Phe Gln His
1 5

<210> 505
<211> 9
<212> PRT
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<220>
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<400> 505

Thr Ser Pro Arg Pro Leu Phe Gln His
1 5

<210> 506
<211> 11
<212> PRT
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<220>
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<400> 506

Pro Tyr Gln Val Arg Gly Val Tyr Phe Asp Tyr
1 5 10

<210> 507
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<212> PRT
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<220>
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<400> 507

Pro Tyr Lys Lys Arg Arg Thr Val Phe Asp Tyr
1 5 10

<210> 508
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 508

Leu Gln Arg Gly Leu Ala Leu Phe Gln His
1 5 10

<210> 509
<211> 9
<212> PRT
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<220>
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<400> 509

Ile Leu Ser Val Pro Tyr Phe Asp Leu
1 5

<210> 510
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<212> PRT
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<220>
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<400> 510

Gly Trp Ile Arg Val Pro Leu Arg Leu Pro Leu Phe Gln His
1 5 10

<210> 511
<211> 9
<212> PRT
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<220>
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<400> 511

Val Thr Ile Phe Ala Ile Phe Asp Ile
1 5

<210> 512
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

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<400> 512

Val Gly Arg Gly Phe Val His Phe Asp Leu
1   5   10

<210> 513
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
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<400> 513

Thr Ser Arg Gly Leu Cys Val Leu Phe Asp Tyr
1   5   10

<210> 514
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<400> 514

Ser Gly Pro Ser Ser Tyr Trp Tyr Phe Asp Leu
1   5   10

<210> 515
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
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<400> 515

Asn Ile Tyr Met Gly Gly Ile Trp Phe Asp Pro
1   5   10

<210> 516
<211> 10
<212> PRT
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<220>
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<400> 516

Leu Thr Val Arg Thr Gly Ala Phe Asp Ile
1   5   10

<210> 517
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<223> MSLN scFv domain HC CDR3

<400> 517

Leu Arg Thr Ala His Leu Asp Phe Asp Leu
1   5   10

<210> 518
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 518

Asp Leu Ile Phe Pro Val Val Phe Asp Tyr
1   5   10

<210> 519
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 519

Asp Gly Tyr Arg Lys Tyr Gly Tyr Val Phe Phe Asp Ile
1   5   10

<210> 520
<211> 13

<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 520

Asp Gly Arg Tyr Arg Arg Phe Trp His Ala Phe Asp Ile
1   5   10

<210> 521
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 521

Ala His Ile Arg Gly Tyr Phe Asp Leu
1   5

<210> 522
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 522

Trp Met Gly Gly Gly Gly Arg Trp Tyr Phe Asp Leu
1   5   10

<210> 523
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 523

Thr Ser Arg Thr Thr Trp Tyr Phe Asp Leu
1   5   10

<210> 524
<211> 12
<212> PRT
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<220>
<223> MSLN scFv domain HC CDR3

<400> 524

Trp Met Gly Gly Gly Gly Arg Leu Tyr Phe Asp Leu
1 5 10

<210> 525
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 525

Trp Gly Gly Arg Leu Tyr Trp Tyr Phe Asp Leu
1 5 10

<210> 526
<211> 10
<212> PRT
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<220>
<223> MSLN scFv domain HC CDR3

<400> 526

Val Ile Arg Gln Leu Trp Tyr Phe Asp Leu
1 5 10

<210> 527
<211> 10
<212> PRT
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<220>
<223> MSLN scFv domain HC CDR3

<400> 527

Val Phe Ala Asn Ser Trp Tyr Phe Asp Leu
1 5 10

<210> 528
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 528

Val Asp Arg Thr Thr Trp Tyr Phe Asp Leu
1 5 10

<210> 529
<211> 13
<212> PRT
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<220>
<223> MSLN scFv domain HC CDR3

<400> 529

Arg Trp Gly Lys Asp Gly Pro Tyr Trp Tyr Phe Asp Leu
1 5 10

<210> 530
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 530

Arg Arg Asp Ser Tyr Gly Pro Tyr Trp Tyr Phe Asp Leu
1 5 10

<210> 531
<211> 12
<212> PRT
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<220>
<223> MSLN scFv domain HC CDR3

<400> 531

Asn Arg Pro Pro Pro Gly Tyr Trp Tyr Phe Asp Leu
1 5 10

<210> 532
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 532

Gly Arg Arg Phe Ser Trp Tyr Phe Asp Leu
1 5 10

<210> 533
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 533

Cys Ala Arg Glu Asp Val Val Lys Gly Ala Phe Asp Ile Trp
1 5 10

<210> 534
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain HC CDR3

<400> 534

Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr
1 5 10

<210> 535
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR1

<400> 535

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 536
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR1

<400> 536

Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
1 5 10

<210> 537
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR1

<400> 537

Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala
1 5 10

<210> 538
<211> 10
<212> PRT
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<220>
<223> MSLN scFv domain LC CDR1

<400> 538

Ser Ala Ser Ser Ser Val Ser Tyr Met His
1 5 10

<210> 539
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<223> MSLN scFv domain LC CDR2

<400> 539

Ala Ala Ser Ser Leu Gln Ser
1   5

<210> 540
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR2

<400> 540

Asp Ala Ser Ser Leu Glu Ser
1   5

<210> 541
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR2

<400> 541

Asp Thr Ser Lys Leu Ala Ser
1   5

<210> 542
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR3

<400> 542

Gln Gln Ser Tyr Ser Thr Pro Leu Thr
1   5

<210> 543
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR3

<400> 543

Gln Gln Ala Asn Ser Phe Pro Leu Thr
1   5

<210> 544
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR3

<400> 544

Gln Gln Phe Asn Ser Tyr Pro Leu Thr
1   5

<210> 545
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> MSLN scFv domain LC CDR3

<400> 545

Gln Gln Trp Ser Gly Tyr Pro Leu Thr
1   5

<210> 546
<211> 4
<212> PRT
<213> Unknown

<220>
<223> immunoreceptor tyrosine-based activation motif

<220>
<221> SITE
<222> (2)..(3)
<223> Xaa is any amino acid

<220>
<221> SITE

<222> (4)..(4)
<223> Xaa is Leu or Ile

<400> 546

Tyr Xaa Xaa Xaa
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<210> 547
<211> 6
<212> PRT
<213> Unknown

<220>
<223> immunoreceptor tyrosine-based activation motif

<220>
<221> SITE
<222> (1)..(1)
<223> Xaa is Ser, Ile, Val or Leu

<220>
<221> SITE
<222> (2)..(2)
<223> Xaa is any amino acid

<220>
<221> SITE
<222> (4)..(5)
<223> Xaa is any amino acid

<220>
<221> SITE
<222> (6)..(6)
<223> Xaa is Ile, Val or Leu

<400> 547

Xaa Xaa Tyr Xaa Xaa Xaa
1   5

<210> 548
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

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tacctgcaga aaccaggcca gtctccaaag ctcctgatct acaaagtttc caaccgattt 180

tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240

agtagagtgg aggctgagga tctgggagtt tattactgct ttcaaggttc acatgttcct 300

cggacgtccg gtggaggcac caagctggaa atcaaaggcg gaggtggaag cggagggggа 360

ggatctggcg gcggaggaag cggaggccag gtccagctgc agcagtctgg acctgagctg 420

gtgaagcctg gggcttcagt gaggatatcc tgcaaggctt ctggctacac cttcacaagt 480

taccatatac attgggtgaa gcagaggcct ggacagggac ttgagtggat tggatggatt 540

tatcctggaa atgttaatac tgagtacaat gagaagttca agggcaaggc cacactgact 600

gcagacaaat cgtccagcac agcctacatg cacctcagca gcctgacctc tgaggactct 660

gcggtctatt tctgtgccag agaggagatt acctatgcta tggactactg gggtcaagga 720

acctcagtca ccgtgtcctc a 741

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<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

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cccggacaag ggcttgagtg gatgggatgg atctaccctg gcaatgttaa cacagaatat 180

aatgagaagt tcaagggcaa agccaccatt accgcggaca aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagggaggaa 300

attacctacg ctatggacta ctggggccag ggaaccacag tcaccgtgtc ctcaggcgga 360

ggtggaagcg gagggggagg atctggcggc ggaggaagcg gaggcgagat tgtattgacc 420

cagagcccag gcaccctgag cctctctcca ggagagcggg ccaccctcag ttgtagatcc 480

agtcagagta ttgtacacag taatgggaac acctatttgg aatggtatca gcagaaacca 540

ggtcaagccc caagattgct catctacaaa gtctctaaca gatttagtgg tattccagac 600

aggttcagcg gttccggaag tggtactgat ttcaccctca cgatctccag gctcgagcca 660

gaagatttcg ccgtttatta ctgttttcaa ggttcacatg tgccgcgcac attcggtggg 720

ggtactaaag tagaaatcaa a 741

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<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

<400> 550
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cccggacaag ggcttgagtg gatgggatgg atctaccctg gcaatgttaa cacagaatat 180

aatgagaagt tcaagggcaa agccaccatt accgcggaca aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagggaggaa 300

attacctacg ctatggacta ctggggccag ggaaccacag tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacat tgtaatgacc 420

cagaccccac tcagcctgcc cgtcactcca ggagagccgg ccagcatcag ttgtagatcc 480

agtcagagta ttgtacacag taatgggaac acctatttgg aatggtatct gcagaaacca 540

ggtcaatccc cacaattgct catctacaaa gtctctaaca gatttagtgg tgtaccagac 600

aggttcagcg gttccggaag tggtactgat ttcaccctca agatctccag ggtcgaggca 660

gaagatgtcg gcgtttatta ctgttttcaa ggttcacatg tgccgcgcac attcggtggg 720

ggtactaaag tagaaatcaa a 741

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<400> 551
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cccggaaaag ggcttgagtg ggtgggatgg atctaccctg gcaatgttaa cacagaatat 180

aatgagaagt tcaagggcag attcaccatt agcagggacg attccaagaa cacactctac 240

ctgcagatga acagcctgaa aactgaagac acggctgtgt attactgtgc gagggaggaa 300

attacctacg ctatggacta ctggggccag ggaaccacag tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacat tcaaatgacc 420

cagagcccat ccagcctgag cgcatctgta ggtgaccggg tcaccatcac ttgtagatcc 480

agtcagagta ttgtacacag taatgggaac acctatttgg aatggtatca gcagaaacca 540

ggtaaagccc caaaattgct catctacaaa gtctctaaca gatttagtgg tgtaccaagc 600

aggttcagcg gttccggaag tggtactgat ttcaccctca cgatctcctc tctccagcca 660

gaagatttcg ccacttatta ctgttttcaa ggttcacatg tgccgcgcac attcggtggg 720

ggtactaaag tagaaatcaa a 741

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tcctgcaagg cttctggata caccttcact agctatcata tacattgggt gcgccaggcc 120

cccggacaag ggcttgagtg gatcggatgg atctaccctg gcaatgttaa cacagaatat 180

aatgagaagt tcaagggcaa agccaccatt accgcggacg aatccacgaa cacagcctac 240

atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagggaggaa 300

attacctacg ctatggacta ctggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacat tcaaatgacc 420

cagagcccat ccaccctgag cgcatctgta ggtgaccggg tcaccatcac ttgtagatcc 480

agtcagagta ttgtacacag taatgggaac acctatttgg aatggtatca gcagaaacca 540

ggtaaagccc caaaattgct catctacaaa gtctctaaca gatttagtgg tgtaccagcc 600

aggttcagcg gttccggaag tggtactgaa ttcaccctca cgatctcctc tctccagcca 660

gatgatttcg ccacttatta ctgttttcaa ggttcacatg tgccgcgcac attcggtcag 720

ggtactaaag tagaagtcaa a 741

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cccggacaag ggcttgagtg gatcggatac atctaccctg gcaatgttaa cacagaatat 180

aatgagaagt tcaagggcaa agccaccctt accgcggaca aatccacgaa cacagcctac 240

atggagctga gcagcctgag atctgaagac acggctgtgt atttctgtgc gagggaggaa 300

attacctacg ctatggacta ctggggccag ggaaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacgt tcaaatgacc 420

cagagcccat ccaccctgag cgcatctgta ggtgaccggg tcaccatcac ttgtagctcc 480

agtcagagta ttgtacacag taatgggaac acctatatgg aatggtatca gcagaaacca 540

ggtaaagccc caaaattgct catctacaaa gtctctaaca gatttagtgg tgtaccagac 600

aggttcagcg gttccggaag tggtactgaa ttcaccctca cgatctcctc tctccagcca 660

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cctggacaag ggcttgagtg gatcggatgg atctaccctg gcgatggtag tacacagtat 180

aatgagaagt tcaagggcaa aaccaccctt accgcggaca aatcctccag cacagcctac 240

atgttgctga gcagcctgac ctctgaagac tctgctatct atttctgtgc gagggagggg 300

acctactacg ctatggacta ctggggccag ggaacctcag tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgatgt tttgatgacc 420

cagactccac tctccctgcc tgtctctctt ggagaccaag tctccatctc ttgtagatcc 480

agtcagagta ttgtacacag taatgggaac acctatttag aatggtatct gcagaaacca 540

ggtcagtctc caaagttgct catctacaaa gtctctaaca gatttagtgg tgtaccagac 600

aggttcagcg gttccggaag tggtactgat ttcaccctca agatctcgag agtggaggct 660

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ggtactaaac tggaaatcaa a 741

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cctggaaaag ggcttgagtg gatcggatgg atctaccctg gcgatggttc aacacagtac 180

aatgagaagt tcaagggcag agccacgatt agcgtggaca catccaagaa ccaattctcc 240

ctgaacctgg acagcgtgag tgctgcggac acggccattt attactgtgc gagagaggga 300

acttactacg ctatggacta ctggggcaaa gggagcacgg tcaccgtgtc ctcaggcgga 360

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cctggacaag ggcttgagtg gatcggatgg atctaccctg gcgatggttc aacacagtac 180

aatgagaagt tcaagggcaa agccacgctt accgtggaca aatccacgaa cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtat attactgtgc gagagaggga 300

acttactacg ctatggacta ctggggccaa gggaccctgg tcaccgtgtc ctcaggcgga 360

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cagagcccat ccaccctgag tgcgtccgtg ggcgaccgcg tgaccatcac ttgcagatcc 480

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cctggacaag ggcttgagtg gatgggatgg atctaccctg gcgatggttc aacacagtac 180

aatgagaagt tcaagggcag agtcacgatt accgcggaca aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtat attactgtgc gagagaggga 300

acttactacg ctatggacta ctggggccaa gggaccacgg tcaccgtgtc ctcaggcgga 360

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cgcttctcag ggtccggctc ggggacggat ttcaccctca cgattagccg cttggagccc 660

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<210> 558
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<212> DNA
<213> Artificial Sequence

<220>
<223> HLA scFv binding domain

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cctggacaag ggcttgagtg gttgggaagg atctaccctg gcgatggttc aacacagtac 180

aatgagaagt tcaagggcaa agtcacgatt accgcggaca aatccatgga cacatccttc 240

atggagctga ccagcctgac atctgaggac acggccgtat attactgtgc gagagaggga 300

acttactacg ctatggacct ctggggccaa gggaccctgg tcaccgtgtc ctcaggcgga 360

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cctggacaaa ggcttgagtg gatgggatgg atctaccctg gcgatggttc aacacagtac 180

aatgagaagt tcaagggcaa agtcacgatt acccgggaca catccgcgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtat attactgtgc gagagaggga 300

acttactacg ctatggacta ctggggccaa gggaccctgg tcaccgtgtc ctcaggcgga 360

ggtggaagcg gaggggggagg atctggcggc ggaggaagcg gaggcgacat cgtcatgacc 420

cagaccccac tgtccctgcc tgtgaccccg ggcgagcccg cgagcatcag ttgcagatcc 480

tctcagtcca tcgtgcactc caacggcaac acgtacctcg actggtacct gcagaagccc 540

gggcagtccc cgcaactgct catctacaag gtgagcaacc ggttctccgg cgtccccgac 600

cgcttctcag ggtccggctc ggggacggat ttcaccctca agattagccg cgtggaggcc 660

gaagacgtcg gcgtgtacta ctgcatgcag ggaagtcacg tgccgcgtac cttcgggggg 720

ggcacgaaag tggaaattaa g 741

<210> 560
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 560

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30

Tyr Ser Trp His Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190

Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220
```

Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 561
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 561

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ser Gly
20 25 30

Tyr Ser Trp His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
35 40 45

Val Ser Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
50 55 60

Lys Ser Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
130 135 140

```
Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160


Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175


Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190


Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205


Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220


Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240


Val Glu Ile Lys
```

<210> 562
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 562

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Ser Trp His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45


Val Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
    50                  55                  60
```

```
Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Glu Ile Val Leu Thr Gln Ser
    130                 135                 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145                 150                 155                 160

Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190

Asp Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
    210                 215                 220

Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 563
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 563

```
Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Ser Trp His Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu Trp
        35                  40                  45


Leu Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
    50                  55                  60


Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80


Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Gly Gly Ser Gly Gly Glu Ile Val Leu Thr Gln Ser
    130                 135                 140


Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145                 150                 155                 160


Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175


Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190
```

Asp Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
210 215 220

Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 564
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 564

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ser Gly
20 25 30

Tyr Ser Trp His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
35 40 45

Val Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
50 55 60

Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
100 105 110

```
Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140


Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160


Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175


Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190


Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205


Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220


Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240


Val Glu Ile Lys
```

<210> 565
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 565

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30
```

```
Tyr Ser Trp His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Val Ser Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
    50                  55                  60

Lys Ser Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190

Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 566
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 566

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Ser Trp His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45


Val Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
    50                  55                  60


Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140


Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160


Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175
```

```
Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190

Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 567
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 567

```
Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30

Tyr Ser Trp His Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190

Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 568
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 568

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30

Tyr Ser Trp His Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190

Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220
```

Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 569
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-B*07 antigen binding domain

<400> 569

Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Tyr Ser Ile Thr Ser Gly
20 25 30

Tyr Ser Trp His Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu Trp
35 40 45

Leu Gly Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu
50 55 60

Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Val Val Ser His Tyr Ala Met Asp Cys Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
130 135 140

```
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160


Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175


Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Thr Tyr Leu Pro
            180                 185                 190


Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205


Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220


Cys Gln His Phe Trp Val Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240


Val Glu Ile Lys
```

<210> 570
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 570

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Val Ser Phe Asp Trp Phe Asp Pro Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
    130                 135                 140


Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
145                 150                 155                 160


Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
                165                 170                 175


Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro
            180                 185                 190


Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205


Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser
    210                 215                 220


Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225                 230                 235                 240


<210>  571
<211>  248
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  571
```

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Arg Ser Ile Ser Pro Tyr Tyr Tyr Tyr Tyr Met Asp
            100                 105                 110

Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220
```

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225 230 235 240

Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 572
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 572

Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Ser Val Ile Trp Tyr Trp Phe Asp Pro Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gln Ser Val Leu Thr Gln Pro
130 135 140

```
Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser
145                 150                 155                 160


Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn Trp Tyr Gln Gln
                165                 170                 175


Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Ser Asn Asn Gln Arg
            180                 185                 190


Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser
        195                 200                 205


Ala Ser Leu Ala Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr
    210                 215                 220


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


Gly Thr Lys Leu Thr Val Leu
                245


<210>  573
<211>  249
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  573

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60
```

```
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Glu Ile Leu Pro Arg Leu Ser Tyr Tyr Tyr Tyr Met
            100                 105                 110

Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
            180                 185                 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 574
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 574

```
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Ala Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe
    50                  55                  60


Thr Gly Arg Phe Val Phe Ser Phe Asp Thr Ser Val Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Ile Cys Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Gly Arg Ala His Ser Ser Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110


Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140


Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190
```

```
Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205


Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240


Lys Val Glu Ile Lys
                245


<210>  575
<211>  251
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  575

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Asp Arg Ile Lys Ile Leu Pro Arg Leu Gly Tyr Tyr Tyr
            100                 105                 110
```

```
Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140


Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
145                 150                 155                 160


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
                165                 170                 175


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
            180                 185                 190


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
        195                 200                 205


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
    210                 215                 220


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
225                 230                 235                 240


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  576
<211>  246
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  576

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30
```

```
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Thr Val Ile His Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 577
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 577

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Asp Val Ile Val Glu Val Phe Leu Ser Tyr Tyr Tyr Tyr
            100                 105                 110


Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp
    130                 135                 140


Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160


Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175
```

```
Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190


Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240


Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  578
<211>  246
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  578

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95
```

```
Cys Ala Arg Asp Ile Phe Ile His Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 579
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 579

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Gly Thr Phe Tyr Ser Tyr Ser Pro Tyr Tyr Phe Asp Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220
```

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 580
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 580

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Trp Ile Lys Ile Leu Pro Arg Leu Gly Tyr Tyr Tyr
100 105 110

Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
145                 150                 155                 160


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
                165                 170                 175


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
            180                 185                 190


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
        195                 200                 205


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
    210                 215                 220


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
225                 230                 235                 240


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  581
<211>  246
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  581

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60
```

```
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Arg Ser Leu Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 582
<211> 248
<212> PRT
<213> Artificial Sequence

<220>

<223> HLA-C*07 antigen binding domain

<400> 582

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                  10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Asp Lys Ile Leu Ala Pro Asn Tyr Tyr Tyr Tyr Met Asp
            100                 105                 110


Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190


Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205
```

```
Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245


<210>  583
<211>  250
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  583

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Lys Ser Trp Lys Tyr Phe Tyr Tyr Tyr Tyr Tyr Tyr
            100                 105                 110


Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly
        115                 120                 125
```

```
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp
    130                 135                 140


Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160


Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175


Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190


Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240


Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  584
<211>  249
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  584

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45
```

```
Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Asn Thr Ser Thr Ile Pro Tyr Tyr Tyr Tyr Tyr Met
            100                 105                 110

Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
            180                 185                 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 585
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 585

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Asp Val Asp Lys Asn Thr Ser Thr Ile Tyr Tyr Tyr
            100                 105                 110


Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130                 135                 140


Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
145                 150                 155                 160


Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
                165                 170                 175
```

```
Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
            180                 185                 190

Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe
        195                 200                 205

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
    210                 215                 220

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr
225                 230                 235                 240

Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250
```

<210> 586
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 586

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Asp Gly Gly Asp Ile Val Ser Ser Ser Ala Ile Tyr Trp Tyr
            100                 105                 110

Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Ala
    130                 135                 140

Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu
                165                 170                 175

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu Thr
225                 230                 235                 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  587
<211>  248
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  587

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Leu Ile Leu Pro Pro Tyr Tyr Tyr Tyr Tyr Met Asp
            100                 105                 110

Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240
```

Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 588
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 588

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Thr Trp Ile Lys Ile Leu Pro Arg Tyr Tyr Tyr Tyr
100 105 110

Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
145 150 155 160

```
Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
                165                 170                 175


Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
            180                 185                 190


Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe
        195                 200                 205


Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
    210                 215                 220


Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr
225                 230                 235                 240


Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  589
<211>  246
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  589

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
```

```
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Leu Ser Arg Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 590
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 590

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu His Ile Val Leu Cys Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Gly Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Glu
                165                 170                 175

Lys Ala Pro Lys Ser Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205
```

```
Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 591
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 591

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Lys Ile Leu Pro Arg Pro Tyr Tyr Tyr Tyr Tyr Met
            100                 105                 110

Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
            180                 185                 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 592
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 592

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Ser Asn Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala
    130                 135                 140

Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser
145                 150                 155                 160

Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Val Ser Lys Arg Pro Ser
            180                 185                 190

Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser
        195                 200                 205

Leu Thr Val Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys
    210                 215                 220

Ser Ser Tyr Ala Gly Ser Asn Asn Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu
```

<210> 593
<211> 242

<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 593

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe
50 55 60

Thr Gly Arg Phe Val Phe Ser Phe Asp Thr Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Cys Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Ser Tyr Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly
180 185 190

```
Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205


Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220


Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240


Ile Lys
```

<210> 594
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 594

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Glu Ile Val Glu Val Phe Tyr Tyr Tyr Tyr Met Asp
            100                 105                 110
```

```
Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190


Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 595
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 595

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Asp Asp Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225                 230                 235                 240
```

Lys

<210> 596
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 596

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Trp Ser Thr Asn Ile Leu Leu Ser Tyr Thr Lys Ala Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

```
Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 597
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 597

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
```

```
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Lys Thr Tyr Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 598
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 598

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Lys Tyr Phe His Asp Lys Tyr Phe His Asp Tyr Tyr
            100                 105                 110

Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
145                 150                 155                 160

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
                165                 170                 175

Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
            180                 185                 190

Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe
        195                 200                 205

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
    210                 215                 220
```

```
Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr
225                 230                 235                 240


Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  599
<211>  246
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  599

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Asp Thr Ser Val Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110


Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140
```

```
Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160


Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175


Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190


Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205


Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220


Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240


Thr Lys Val Glu Ile Lys
                245


<210>  600
<211>  248
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  600

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60
```

```
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Lys Ile Leu Pro Tyr Tyr Tyr Tyr Tyr Tyr Met Asp
            100                 105                 110

Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 601
<211> 257
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 601

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Ile Gln Trp Ile Tyr Ile Tyr Ile Asn Pro Arg Gly Phe Ile Phe
            100   105   110

Leu His Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val
        115   120   125

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130   135   140

Ser Gly Gly Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr
145   150   155   160

Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile
                165   170   175

Gly Ser Asn Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro
            180   185   190

Lys Leu Leu Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp
195 200 205

Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser
210 215 220

Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp
225 230 235 240

Asp Ser Leu Asn Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val
245 250 255

Leu

<210> 602
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 602

Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
20 25 30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
50 55 60

Val Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

```
Tyr Tyr Cys Ala Lys Glu Asp Val Asp Phe His His Asp Ala Phe Asp
            100                 105                 110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 603
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 603

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Gly Val Asp Lys Asn Thr Ser Thr Ile Tyr Tyr Tyr
            100                 105                 110

Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
145                 150                 155                 160

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
                165                 170                 175

Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
            180                 185                 190

Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe
        195                 200                 205

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
    210                 215                 220

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr
225                 230                 235                 240
```

Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
245 250

<210> 604
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 604

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Arg Gly Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
130 135 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145 150 155 160

```
Gln Gly Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys
                165                 170                 175

Ala Pro Lys Ser Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Tyr Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys
```

<210> 605
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 605

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Thr Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Tyr Met His Trp Val Gln Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Asp Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Gly Ile His Val Asp Ile Arg Ser Met Glu Asp Trp Phe Asp
            100                 105                 110

Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 606
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 606

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Asp Ile Gly Thr Ser Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110


Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140


Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160


Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175


Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190


Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205
```

```
Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220


Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240


Thr Lys Val Glu Ile Lys
                245


<210>  607
<211>  249
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  607

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Val Val Glu Val Phe Leu Tyr Tyr Tyr Tyr Tyr Met
            100                 105                 110


Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
            180                 185                 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 608
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 608

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45
```

```
Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Leu Tyr Tyr Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 609
<211> 256

<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 609

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Ser Trp Lys Tyr Phe Tyr Pro Arg Gly Ser Ile Phe
            100                 105                 110


Ile His Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val
        115                 120                 125


Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140


Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
145                 150                 155                 160


Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
                165                 170                 175


Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
            180                 185                 190
```

```
Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro
        195                 200                 205


Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
    210                 215                 220


Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser
225                 230                 235                 240


Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250                 255


<210>  610
<211>  248
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-C*07 antigen binding domain

<400>  610

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Asp Arg Ile Val Glu Val Phe Tyr Tyr Tyr Tyr Met Asp
            100                 105                 110
```

```
Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190


Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 611
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 611

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30
```

```
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Lys Tyr Phe His Asp Trp Leu Tyr Tyr Tyr Tyr Tyr
            100                 105                 110

Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp
    130                 135                 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240
```

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
245 250

<210> 612
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 612

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Leu Val Asp Lys Asn Thr Ser Tyr Tyr Tyr Tyr Tyr
100 105 110

Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp
130 135 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145 150 155 160

```
Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250
```

<210> 613
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 613

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Gln Asn Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala
    130                 135                 140

Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser
145                 150                 155                 160

Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Val Ser Lys Arg Pro Ser
            180                 185                 190

Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser
        195                 200                 205

Leu Thr Val Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys
    210                 215                 220

Ser Ser Tyr Ala Gly Ser Asn Asn Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu
```

<210> 614
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-C*07 antigen binding domain

<400> 614

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Ala Asn Trp Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly
145                 150                 155                 160

Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195                 200                 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn
    210                 215                 220
```

Ser Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 615
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 615

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Arg Val Ser Gln Arg Gly Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

```
Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 616
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 616

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Pro Asp Lys Asp Pro Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 617
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 617

```
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 Gly Gly Ser Val Ser Ser Gly
            20                  25                  30

Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Phe Tyr Cys Thr Asn Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205
```

```
Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240


Lys Val Glu Ile Lys
                245


<210>  618
<211>  244
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*03 scFv

<400>  618

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 Gly Gly Ser Ile Ser Ser Tyr
            20                  25                  30


Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60


Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80


Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Arg Glu Ser Ser Ser Gly Ser Tyr Trp Tyr Phe Asp Leu Trp Gly Arg
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 619
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 619

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60

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

Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp
    130                 135                 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
                245                 250
```

<210> 620
<211> 249

<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 620

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asp Leu Ser His Tyr Tyr Tyr Tyr Met Asp Val Trp
100 105 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gln Thr Val Val Thr
130 135 140

Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr
145 150 155 160

Cys Ala Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn Trp
165 170 175

Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Ala Leu Ile Tyr Ser Thr
180 185 190

Ser Asn Lys His Ser Trp Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu
        195   200   205

Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu
    210   215   220

Ala Glu Tyr Tyr Cys Leu Leu Tyr Tyr Gly Gly Ala Gln Trp Val Phe
225   230   235   240

Gly Gly Gly Thr Lys Leu Thr Val Leu
                245

<210> 621
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 621

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50   55   60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Glu Asn Arg Arg Tyr Asn Ser Cys Tyr Tyr Phe Asp Tyr Trp
            100   105   110

```
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 622
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 622

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
```

```
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Asp Leu Ser His Tyr Tyr Tyr Tyr Leu Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gln Thr Val Val Thr
    130                 135                 140

Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr
145                 150                 155                 160

Cys Ala Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn Trp
                165                 170                 175

Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Ala Leu Ile Tyr Ser Thr
            180                 185                 190

Ser Asn Lys His Ser Trp Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu
        195                 200                 205

Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu
    210                 215                 220

Ala Glu Tyr Tyr Cys Leu Leu Tyr Tyr Gly Gly Ala Gln Trp Val Phe
225                 230                 235                 240
```

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 623
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 623

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ala Thr Leu Leu Ser Leu Ser Tyr Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145 150 155 160

```
Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys
                245
```

<210> 624
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 624

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Asp Leu Ser His Tyr Tyr Tyr Met Asp Val Trp Gly
            100                 105                 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gln Thr Val Val Thr Gln
    130                 135                 140

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
145                 150                 155                 160

Ala Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn Trp Phe
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Ala Leu Ile Tyr Ser Thr Ser
            180                 185                 190

Asn Lys His Ser Trp Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
        195                 200                 205

Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala
    210                 215                 220

Glu Tyr Tyr Cys Leu Leu Tyr Tyr Gly Gly Ala Gln Trp Val Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Leu Thr Val Leu
                245
```

<210> 625
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 625

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala 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 Arg Glu Arg Asp Arg Trp Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220
```

Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

<210> 626
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 626

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Thr Pro Pro Ser Leu Gly Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gln Ser Ala Leu Thr Gln Pro
130 135 140

```
Pro Ser Ala Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr
145                 150                 155                 160


Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln
                165                 170                 175


Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Val Ser Lys
            180                 185                 190


Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn
        195                 200                 205


Thr Ala Ser Leu Thr Val Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp
    210                 215                 220


Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser Asn Asn Trp Val Phe Gly Gly
225                 230                 235                 240


Gly Thr Lys Leu Thr Val Leu
                245


<210>  627
<211>  251
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*03 scFv

<400>  627

Gln Leu 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 Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30


Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60
```

```
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Ala Tyr Cys Leu Ser Asp Ser Tyr Trp Tyr Phe Asp
            100                 105                 110

Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gln Ser Val
    130                 135                 140

Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val Thr
145                 150                 155                 160

Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
                165                 170                 175

Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys
        195                 200                 205

Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln Ser Glu Asp
    210                 215                 220

Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu Asn Gly Trp
225                 230                 235                 240

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
                245                 250
```

<210> 628
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*03 scFv

<400> 628

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Ser Trp Lys Tyr Phe Tyr Pro Arg Gly Tyr Met Asp
            100                 105                 110


Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190
```

```
Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245


<210>  629
<211>  248
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*01 scFv

<400>  629

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Gly Trp Thr Ala Trp Tyr Tyr Tyr Met Asp Val Trp Gly
            100                 105                 110
```

```
Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gln Thr Val Val Thr Gln
    130                 135                 140


Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
145                 150                 155                 160


Ala Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn Trp Phe
                165                 170                 175


Gln Gln Lys Pro Gly Gln Ala Pro Arg Ala Leu Ile Tyr Ser Thr Ser
            180                 185                 190


Asn Lys His Ser Trp Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
        195                 200                 205


Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala
    210                 215                 220


Glu Tyr Tyr Cys Leu Leu Tyr Tyr Gly Gly Ala Gln Trp Val Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Leu Thr Val Leu
                245


<210>  630
<211>  244
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*01 scFv

<400>  630

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala Lys Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gln Ser Val Leu Thr Gln Pro Pro Ser Ala
    130                 135                 140

Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser
145                 150                 155                 160

Ser Asn Ile Gly Ser Asn Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly
                165                 170                 175

Thr Ala Pro Lys Leu Leu Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
        195                 200                 205

Ala Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
    210                 215                 220

Ala Trp Asp Asp Ser Leu Asn Gly Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu
```

<210> 631
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*01 scFv

<400> 631

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Asp Gln Val Asp Lys Asn Thr Tyr Tyr Tyr Tyr Met Asp
            100                 105                 110


Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175
```

```
Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190


Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245


<210>  632
<211>  243
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*01 scFv

<400>  632

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Ala Cys Gln Leu Ala Glu Tyr Phe Gln His Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Ala Asn Ser Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys
```

<210> 633
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*01 scFv

<400> 633

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Asp Arg Val Asp Lys Asn Thr Ser Tyr Tyr Tyr Met Asp
            100                 105                 110

Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220
```

```
Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 634
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A*01 scFv

<400> 634

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Asp
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Tyr Ser Ile Ser Ser Ser
            20                  25                  30


Asn Trp Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45


Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu
    50                  55                  60


Lys Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80


Leu Lys Leu Ser Ser Val Thr Ala Val Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Arg Val Gln Leu Lys Leu Val His Trp Phe Asp Pro Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140
```

```
Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190


Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205


Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240


Lys Val Glu Ile Lys
                245


<210>  635
<211>  245
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*01 scFv

<400>  635

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
```

```
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Tyr Tyr Asp Tyr Val Thr Val Phe Tyr Phe Gln His Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys
                245
```

<210> 636
<211> 245
<212> PRT
<213> Artificial Sequence

<220>

<223> HLA-A*01 scFv

<400> 636

```
Gln Leu Gln Leu Gln Glu Ser Gly Ser Gly Leu Val Lys Pro Ser Gln
1               5                  10                  15


Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30


Gly Tyr Ser Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Arg Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Glu Ser Tyr Pro Ser Phe Tyr Ala Phe Asp Ile Trp Gly
            100                 105                 110


Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile Gln Met Thr Gln
    130                 135                 140


Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190


Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205
```

```
Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr
225                 230                 235                 240


Lys Val Glu Ile Lys
                245


<210>  637
<211>  249
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HLA-A*01 scFv

<400>  637

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1               5                   10                  15


Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
            20                  25                  30


Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
        35                  40                  45


Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser
    50                  55                  60


Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65                  70                  75                  80


Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
                85                  90                  95


Cys Ala His Ser Asn Met Trp Ser Tyr Ser Leu Asn Asp Tyr Tyr Phe
            100                 105                 110


Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
            180                 185                 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
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Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1               5                   10
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Ala Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1   5   10

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Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
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Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
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Arg Ala Ser Glu Asn Ile Tyr Ser Asn Leu Ala
1   5   10

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Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala
1   5   10

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Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
1   5   10

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Ala Ala Ser Ser Leu Gln Ser
1   5

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Ser Thr Ser Asn Lys His Ser
1   5

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Glu Val Ser Lys Arg Pro Ser
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Ser Asn Asn Gln Arg Pro Ser
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<400> 649

Ala Ala Thr Tyr Leu Pro Asp
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Gln Gln Ser Tyr Ser Thr Pro Leu Thr
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Leu Leu Tyr Tyr Gly Gly Ala Gln Trp Val
1   5   10

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Ser Ser Tyr Ala Gly Ser Asn Asn Trp Val
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Ala Ala Trp Asp Asp Ser Leu Asn Gly Trp Val
1   5   10

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Gln His Phe Trp Val Thr Pro Tyr Thr
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Gln Gln Tyr Asn Ser Tyr Pro Leu Thr
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Gln Gln Ala Asn Ser Phe Pro Leu Thr
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Ser Tyr Gly Ile Ser
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Ser Tyr Ser Met Asn
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Ser Gly Ser Tyr Tyr Trp Ser
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Ser Tyr Tyr Trp Ser
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Ser Tyr Trp Ile Gly
1 5

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Ser Asn Tyr Met Ser
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Ser Ser Ser Tyr Tyr Trp Gly
1 5

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Ser Gly Gly Tyr Tyr Trp Ser
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Ser Gly Tyr Ser Trp His
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Thr Ser Gly Val Gly Val Gly
1   5

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Ser Tyr Trp Met His
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Ser Tyr Ala Met Ser
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Ser Tyr Ala Met Asn
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Asp Tyr Tyr Met Ser
1   5

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Ser Asn Ser Ala Ala Trp Asn
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Asp Tyr Tyr Met His
1   5

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Ser Ser Asn Trp Trp Gly
1   5

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Ser Tyr Asp Ile Asn
1   5

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<400> 675

Ser Gly Gly Tyr Ser Trp Ser
1   5

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Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
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Gly

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Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

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<400> 678

Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

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Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> 680
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Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
1 5 10 15

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Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1   5   10   15

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Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1   5   10   15

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Tyr Ile His Phe Ser Gly Ser Thr His Tyr His Pro Ser Leu Lys Ser
1   5   10   15

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Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser Leu Lys Ser
1   5   10   15

<210> 685
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Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 686
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<400> 686

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 687
<211> 17
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<220>
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<400> 687

Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe Thr
1   5   10   15

Gly

<210> 688
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Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 689
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<400> 689

Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala Val Ser Val
1 5 10 15

Lys Ser

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Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe Gln
1 5 10 15

Gly

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Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

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<400> 692

Tyr Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

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<400> 693

Glu Arg Val Ser Gln Arg Gly Ala Phe Asp Ile
1 5 10

<210> 694
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Gly Asn Pro Asp Lys Asp Pro Phe Asp Tyr
1   5   10

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<400> 695

Asp Phe Tyr Cys Thr Asn Trp Tyr Phe Asp Leu
1   5   10

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<400> 696

Glu Ser Ser Ser Gly Ser Tyr Trp Tyr Phe Asp Leu
1   5   10

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Asp Ser Gly Tyr Lys Tyr Asn Leu Tyr Tyr Tyr Tyr Tyr Tyr Met Asp
1   5   10   15

Val

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<400> 698

Gly Gly Asp Leu Ser His Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

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Glu Asn Arg Arg Tyr Asn Ser Cys Tyr Tyr Phe Asp Tyr
1   5   10

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<400> 700

Gly Gly Asp Leu Ser His Tyr Tyr Tyr Tyr Leu Asp Val
1   5   10

<210> 701
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1   5   10

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Gly Gly Asp Leu Ser His Tyr Tyr Tyr Met Asp Val
1 5 10

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<400> 703

Glu Arg Asp Arg Trp Phe Asp Pro
1 5

<210> 704
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Glu Thr Pro Pro Ser Leu Gly Ala Phe Asp Ile
1 5 10

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Glu Ala Tyr Cys Leu Ser Asp Ser Tyr Trp Tyr Phe Asp Leu
1   5   10

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Glu Ser Trp Lys Tyr Phe Tyr Pro Arg Gly Tyr Met Asp Val
1   5   10

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Gly Gly Val Val Ser His Tyr Ala Met Asp Cys
1   5   10

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<400> 708

Ser Phe Asp Trp Phe Asp Pro
1   5

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<400> 709

Glu Arg Ser Ile Ser Pro Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10

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Asp Ser Val Ile Trp Tyr Trp Phe Asp Pro
1 5 10

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<400> 711

Glu Glu Ile Leu Pro Arg Leu Ser Tyr Tyr Tyr Tyr Met Asp Val
1 5 10 15

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Gly Gly Arg Ala His Ser Ser Trp Tyr Phe Asp Leu
1 5 10

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<400> 713

Asp Arg Ile Lys Ile Leu Pro Arg Leu Gly Tyr Tyr Tyr Tyr Met Asp
1   5   10   15

Val

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<400> 714

Asp Thr Val Ile His Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

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Asp Val Ile Val Glu Val Phe Leu Ser Tyr Tyr Tyr Tyr Met Asp Val
1   5   10   15

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Asp Ile Phe Ile His Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

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Asp Gly Thr Phe Tyr Ser Tyr Ser Pro Tyr Tyr Phe Asp Tyr
1 5 10

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<400> 718

Glu Trp Ile Lys Ile Leu Pro Arg Leu Gly Tyr Tyr Tyr Tyr Met Asp
1 5 10 15

Val

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<400> 719

Asp Arg Ser Leu Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10

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1 5 10

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Glu Lys Ser Trp Lys Tyr Phe Tyr Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10 15

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<400> 722

Glu Asn Thr Ser Thr Ile Pro Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10 15

<210> 723
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1 5 10 15

Met Asp Val

<210> 724
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<400> 724

Asp Gly Gly Asp Ile Val Ser Ser Ser Ala Ile Tyr Trp Tyr Phe Asp
1   5   10   15

Leu

<210> 725
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<400> 725

Asp Leu Ile Leu Pro Pro Tyr Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

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<400> 726

Glu Thr Trp Ile Lys Ile Leu Pro Arg Tyr Tyr Tyr Tyr Tyr Tyr Tyr
1   5   10   15

Met Asp Val

<210> 727
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<400> 727

Asp Leu Ser Arg Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10

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<400> 728

Glu His Ile Val Leu Cys Phe Asp Tyr
1 5

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<400> 729

Asp Lys Ile Leu Pro Arg Pro Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10 15

<210> 730
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<400> 730

Gly Ser Asn Glu Tyr Phe Gln His
1 5

<210> 731
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<400> 731

Gly Thr Ser Tyr Trp Tyr Phe Asp Leu
1   5

<210> 732
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<400> 732

Glu Glu Ile Val Glu Val Phe Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

<210> 733
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<220>
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<400> 733

Val Asp Asp Tyr Tyr Phe Asp Tyr
1   5

<210> 734
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<400> 734

Ser Thr Asn Ile Leu Leu Ser Tyr Thr Lys Ala Phe Asp Ile
1   5   10

<210> 735
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<400> 735

Asp Lys Thr Tyr Tyr Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

<210> 736
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<400> 736

Glu Lys Tyr Phe His Asp Lys Tyr Phe His Asp Tyr Tyr Tyr Tyr Tyr
1   5   10   15

Met Asp Val

<210> 737
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<400> 737

Asp Thr Ser Val Tyr Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

<210> 738
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<400> 738

Glu Lys Ile Leu Pro Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10

<210> 739
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<220>
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<400> 739

Gln Trp Ile Tyr Ile Tyr Ile Asn Pro Arg Gly Phe Ile Phe Leu His
1 5 10 15

Asp Ala Phe Asp Ile
20

<210> 740
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Glu Asp Val Asp Phe His His Asp Ala Phe Asp Ile
1 5 10

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Glu Gly Val Asp Lys Asn Thr Ser Thr Ile Tyr Tyr Tyr Tyr Tyr Tyr
1 5 10 15

Met Asp Val

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<400> 742

Asp Arg Arg Gly Tyr Phe Asp Leu
1 5

<210> 743
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Gly Ile His Val Asp Ile Arg Ser Met Glu Asp Trp Phe Asp Pro
1 5 10 15

<210> 744
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Asp Ile Gly Thr Ser Tyr Tyr Tyr Tyr Met Asp Val
1 5 10

<210> 745
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<400> 745

Glu Val Val Glu Val Phe Leu Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10 15

<210> 746
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<400> 746

Asp Leu Tyr Tyr Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10

<210> 747
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<223> CDR-H3

<400> 747

Glu Ser Trp Lys Tyr Phe Tyr Pro Arg Gly Ser Ile Phe Ile His Tyr
1 5 10 15

Tyr Tyr Tyr Met Asp Val
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<210> 748
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
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<400> 748

Asp Arg Ile Val Glu Val Phe Tyr Tyr Tyr Tyr Met Asp Val
1 5 10

<210> 749
<211> 16
<212> PRT
<213> Artificial Sequence

<220>

<223> CDR-H3

<400> 749

Glu Lys Tyr Phe His Asp Trp Leu Tyr Tyr Tyr Tyr Tyr Met Asp Val
1   5   10   15

<210> 750
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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<400> 750

Asp Leu Val Asp Lys Asn Thr Ser Tyr Tyr Tyr Tyr Tyr Met Asp Val
1   5   10   15

<210> 751
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<212> PRT
<213> Artificial Sequence

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<223> CDR-H3

<400> 751

Val Gln Asn Glu Tyr Phe Gln His
1   5

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<212> PRT
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<220>
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<400> 752

Ala Asn Trp Phe Asp Pro
1   5

<210> 753
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<212> PRT
<213> Artificial Sequence

<220>
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<400> 753

Gly Gly Trp Thr Ala Trp Tyr Tyr Tyr Met Asp Val
1   5   10

<210> 754
<211> 8
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<220>
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<400> 754

Ala Lys Tyr Tyr Tyr Met Asp Val
1   5

<210> 755
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<400> 755

Asp Gln Val Asp Lys Asn Thr Tyr Tyr Tyr Tyr Met Asp Val
1   5   10

<210> 756
<211> 10
<212> PRT
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<220>
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<400> 756

Ala Cys Gln Leu Ala Glu Tyr Phe Gln His
1   5   10

<210> 757
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<400> 757

Asp Arg Val Asp Lys Asn Thr Ser Tyr Tyr Tyr Met Asp Val
1   5   10

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<400> 758

Arg Val Gln Leu Lys Leu Val His Trp Phe Asp Pro
1   5   10

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<400> 759

Tyr Tyr Asp Tyr Val Thr Val Phe Tyr Phe Gln His
1   5   10

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<212> PRT
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<220>
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<400> 760

Glu Ser Tyr Pro Ser Phe Tyr Ala Phe Asp Ile
1   5   10

<210> 761
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H3

<400> 761

Ser Asn Met Trp Ser Tyr Ser Leu Asn Asp Tyr Tyr Phe Asp Tyr
1 5 10 15

<210> 762
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> extracellular ligand binding domain VL

<400> 762

Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Arg Thr Ser Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 763
<211> 118

<212> PRT
<213> Artificial Sequence

<220>
<223> extracellular ligand binding domain VH

<400> 763

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1 5 10 15

Ser Val Arg Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

His Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Glu Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met His Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Glu Glu Ile Thr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Val Thr Val Ser Ser
115

<210> 764
<211> 18
<212> PRT
<213> Unknown

<220>
<223> T2A self-cleaving peptide

<400> 764

Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp Val Glu Glu Asn Pro
1 5 10 15

Gly Pro

<210> 765
<211> 19
<212> PRT
<213> Unknown

<220>
<223> P2A self-cleaving peptide

<400> 765

Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn
1 5 10 15

Pro Gly Pro

<210> 766
<211> 20
<212> PRT
<213> Unknown

<220>
<223> E2A self-cleaving peptide

<400> 766

Gln Cys Thr Asn Tyr Ala Leu Leu Lys Leu Ala Gly Asp Val Glu Ser
1 5 10 15

Asn Pro Gly Pro
20

<210> 767
<211> 22
<212> PRT
<213> Unknown

<220>
<223> F2A self-cleaving peptide

<400> 767

Val Lys Gln Thr Leu Asn Phe Asp Leu Leu Lys Leu Ala Gly Asp Val
1 5 10 15

Glu Ser Asn Pro Gly Pro
20

<210> 768
<211> 63
<212> DNA
<213> Unknown

<220>
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ccc 63

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<212> RNA
<213> Homo sapiens

<400> 769
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ucacgucauc cagcagagaa uggaaaguca aauuuccuga auugcuaugu gucuggguuu 180

cauccauccg acauugaagu ugacuuacug aagaauggag agagaauuga aaaaguggag 240

cauucagacu ugucuuucag caaggacugg ucuuucuauc ucuuguacua cacugaauuc 300

acccccacug aaaaagauga guaugccugc cgugugaacc augugacuuu gucacagccc 360

aagauaguua agugggaucg agacauguaa gcagcaucau ggagguuuga agaugccgca 420

uuuggauugg augaauucca aauucugcuu gcuugcuuuu uaauauugau augcuuauac 480

acuuacacuu uaugcacaaa auguaggguu auaauaaugu uaacauggac augaucuucu 540

uuauaauucu acuuugagug cugucuccau guuugaugua ucugagcagg uugcuccaca 600

gguagcucua ggagggcugg caacuuagag guggggagca gagaauucuc uuauccaaca 660

ucaacaucuu ggucagauuu gaacucuuca aucucuugca cucaaagcuu guuaagauag 720

uuaagcgugc auaaguuaac uuccaauuua cauacucugc uuagaauuug ggggaaaauu 780

uagaaauaua auugacagga uuauuggaaa uuuguuauaa ugaaugaaac auuuugucau 840

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<213> Homo sapiens

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gatctgcaat ccaaataaaa taaattcatt gctaaccttt ttcttttctt ttcaggtttg 6120

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gggggaaaat ttagaaatat aattgacagg attattggaa atttgttata atgaatgaaa 6540

cattttgtca tataagattc atatttactt cttatacatt tgataaagta aggcatggtt 6600

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tttcttttct ccctctccca acctatgtag ggtccttctt cctggatact cacgacgcgg 180

acccagttct cactcccatt gggtgtcggg tttccagaga agccaatcag tgtcgtcgcg 240

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atggccgtca tggcgccccg aaccctcgtc ctgctactct cgggggctct ggccctgacc 360

cagacctggg cgggctctca ctccatgagg tatttcttca catccgtgtc ccggcccggc 420

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