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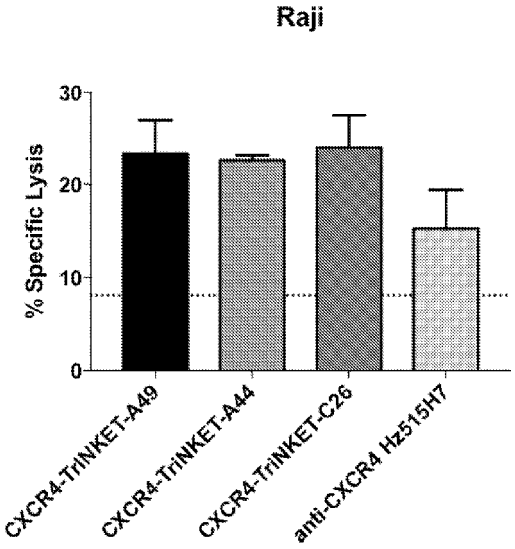
FIG. 37



(57) Abstract: Multi-specific binding proteins that bind the NKG2D receptor, CD 16, and a tumor-associated antigen are described, as well as pharmaceutical compositions and therapeutic methods useful for the treatment of cancer.

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PROTEINS BINDING NKG2D, CD16 AND A TUMOR-ASSOCIATED ANTIGEN

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of and priority to U.S. Provisional Patent Application No. 62/549,201, filed August 23, 2017, the disclosure of which is hereby incorporated by reference in its entirety for all purposes; U.S. Provisional Patent Application No. 62/558,509, filed September 14, 2017, the disclosure of which is hereby incorporated by reference in its entirety for all purposes; U.S. Provisional Patent Application No. 62/558,510, filed September 14, 2017; U.S. Provisional Patent Application No. 62/558,511, filed September 14, 2017, the disclosure of which is hereby incorporated by reference in its entirety for all purposes; U.S. Provisional Patent Application No. 62/558,514, filed September 14, 2017, the disclosure of which is hereby incorporated by reference in its entirety for all purposes; U.S. Provisional Patent Application No. 62/566,828, filed October 2, 2017, the disclosure of which is hereby incorporated by reference in its entirety for all purposes; U.S. Provisional Patent Application No. 62/581,357, filed November 3, 2017, the disclosure of which is hereby incorporated by reference in its entirety for all purposes; and U.S. Provisional Patent Application No. 62/608,384, filed December 20, 2017, the disclosure of which is hereby incorporated by reference in its entirety for all purposes.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on August 22, 2018, is named DFY-034WO_SL.txt and is 448,772 bytes in size.

FIELD OF THE INVENTION

[0003] The invention relates to multi-specific binding proteins that bind to NKG2D, CD16, and a tumor-associated antigen.

BACKGROUND

[0004] Cancer continues to be a significant health problem despite the substantial research efforts and scientific advances reported in the literature for treating this disease. Some of the most frequently diagnosed cancers include prostate cancer, breast cancer, lung cancer, and colorectal cancer. Prostate cancer is the most common form of cancer in men.

Breast cancer remains a leading cause of death in women. Blood and bone marrow cancers are also frequently diagnosed cancer types, including multiple myelomas, leukemia, and lymphomas. Current treatment options for these cancers are not effective for all patients and/or can have substantial adverse side effects. Other types of cancer also remain challenging to treat using existing therapeutic options.

[0005] Cancer immunotherapies are desirable because they are highly specific and can facilitate destruction of cancer cells using the patient's own immune system. Fusion proteins such as bi-specific T-cell engagers are cancer immunotherapies described in the literature that bind to tumor cells and T-cells to facilitate destruction of tumor cells. Antibodies that bind to certain tumor-associated antigens and to certain immune cells have been described in the literature. See, for example WO 2016/134371 and WO 2015/095412.

[0006] Natural killer (NK) cells are a component of the innate immune system and make up approximately 15% of circulating lymphocytes. NK cells infiltrate virtually all tissues and were originally characterized by their ability to kill tumor cells effectively without the need for prior sensitization. Activated NK cells kill target cells by means similar to cytotoxic T cells – *i.e.*, via cytolytic granules that contain perforin and granzymes as well as via death receptor pathways. Activated NK cells also secrete inflammatory cytokines such as IFN-gamma and chemokines that promote the recruitment of other leukocytes to the target tissue.

[0007] NK cells respond to signals through a variety of activating and inhibitory receptors on their surface. For example, when NK cells encounter healthy self-cells, their activity is inhibited through activation of the killer-cell immunoglobulin-like receptors (KIRs). Alternatively, when NK cells encounter foreign cells or cancer cells, they are activated via their activating receptors (*e.g.*, NKG2D, NCRs, DNAM1). NK cells are also activated by the constant region of some immunoglobulins through CD16 receptors on their surface. The overall sensitivity of NK cells to activation depends on the sum of stimulatory and inhibitory signals.

[0008] Chemokines mediate numerous physiological and pathological processes related primarily to cell homing and migration. The human chemokine system currently includes more than 40 chemokines and 18 chemokine receptors. CXCR4 is one of the most studied chemokine receptors. It is a 352 amino acid rhodopsin-like G-protein coupled receptor that selectively binds chemokine CXCL12, and mediates chemotaxis, enhanced intracellular calcium, cell adhesion, survival, proliferation, and gene transcription through multiple

divergent pathways. CXCR4 is overexpressed in more than 23 different types of human cancers including kidney, lung, brain, prostate, breast, pancreas, ovarian, and melanomas and this aberrant expression strongly promotes tumor proliferation, migration and invasion through multiple signal pathways. CXCR4 is also important in the homing of malignant cells, such as in acute myeloid leukemia and multiple myeloma, to niches in the bone marrow, which have been described to promote resistance to chemotherapy.

[0009] Regulatory T cells (T_{regs}) protect against autoimmunity, but in cancer, T_{regs} infiltrate even the earliest neoplastic lesions and undermine anti-tumor effector T cells. T_{reg} development and homeostasis are critically dependent on interleukin-2 (IL-2), and most T_{regs} express high levels of CD25, the cell surface α chain of the IL-2 receptor. CD25 monoclonal antibody have been shown to deplete $CD25^{+}T_{regs}$ in vivo and enhance tumor immunity and immunotherapy. Therefore, CD25 blockage represents an approach to circumvent a major element of immune suppression in patients with cancer, including acute myeloid leukemia, chronic lymphocytic leukemia, glioblastoma, bladder cancer, colon cancer, germ cell tumors, lung cancer, osteosarcoma, melanoma, ovarian cancer, multiple myeloma, head and neck cancer, renal cell cancer, and breast cancer.

[0010] Antigens highly expressed on T_{regs} can be exploited in an anti-cancer therapy that targets a specific antigen for depletion of tumor resident T_{regs} and thereby relieves immune suppression in patients with cancer. These antigens include CCR8, which specifically binds and responds to cytokines of the CC chemokine family; CD7, also known as leu-9 or GP40, which is a cell surface glycoprotein; CTLA4, also known as CD152, which is a protein receptor and functions as an immune checkpoint; CX3CR1, also known as the fractalkine receptor or G-protein coupled receptor 13 (GPR13), which is a receptor for chemokine CX3CL1; ENTPD1, also known as CD39 or NTPDase1, which is an ectonucleotidase that catalyzes the hydrolysis of γ- and β-phosphate residues of triphospho- and diphosphonucleosides to the monophosphonucleoside derivative; HAVCR2, also known as TIM-3; IL1R2, also known as CD121b, which is a receptor for interleukin-1α (IL1A), interleukin-1β (IL1B), and interleukin 1 receptor antagonist (IL1Ra), preventing them from binding to their regular receptors and thereby inhibiting the transduction of their signaling; PDCD1LG2, also known as B7DC, CD273 or PD-L2, which is a ligand of PD-1 and negatively regulates T cell activation; TIGIT, which is an immune receptor on T_{regs} and functions as an immune checkpoint; TNFRSF4, also known as CD134 or OX40; TNFRSF8, also known as CD30; TNFRSF9, also known as CD137; GEM, a member of the RAD/GEM

family of GTP-binding proteins; NT5E, also known as CD73, which converts AMP to adenosine; and TNFRSF18, also known as GITR or CD357.

[0011] VLA4, CD44, CD13, CD15, CD47, and CD81 are associated with a variety of tumors. Very late antigen-4 (VLA-4) is a key adhesion molecule that acts as a receptor for the extracellular matrix protein fibronectin, and the cellular counter-receptor VCAM-1. It is expressed by numerous cells of hematopoietic origin and possesses a key function in the cellular immune response, *e.g.*, by mediating leukocyte tethering, rolling, binding, and finally transmigration of the vascular wall at inflammatory sites. In addition, VLA-4 is expressed in leukemic cells and different solid tumors such as acute myeloid leukemia, multiple myeloma, chronic lymphocytic leukemia, breast cancer, glioblastoma.

[0012] CD44 is a transmembrane glycoprotein that has various functions in cell-cell interactions, cell adhesion and migration. It is also abundantly expressed in several cancers, including acute myeloid leukemia, breast cancer, head and neck cancer, ovarian cancer, prostate cancer, and melanoma.

[0013] CD13, also known as aminopeptidase N, is a Zn^{2+}dependent membrane-bound ectopeptidase that degrades preferentially proteins and peptides with a *N*-terminal neutral amino acid. CD13 has been associated with malignant development, such as tumor cell invasion, differentiation, proliferation and apoptosis, motility and angiogenesis in acute myeloid leukemia, lung cancer, pancreatic cancer, liver cancer, and gastric cancer.

[0014] CD15 (3-fucosyl-N-acetyl-lactosamine) is a carbohydrate adhesion molecule that can be expressed on glycoproteins, glycolipids and proteoglycans. It is expressed in patients with acute myeloid leukemia, Hodgkin lymphoma, chronic lymphocytic leukemia, acute lymphoblastic leukemia, lung cancer and thyroid cancer.

[0015] CD47 (also known as integrin-associated protein) is a ubiquitously expressed glycoprotein of the immunoglobulin superfamily that plays a critical role in self-recognition. Various solid and hematologic cancers exploit CD47 expression in order to evade immunological eradication, and its overexpression is clinically correlated with poor prognoses. It has been demonstrated that overexpression of CD47 occurs in nearly all types of tumors, some of which include acute myeloid leukemia, multiple myeloma, B cell lymphoma, T cell lymphoma, ovarian cancer, lung cancer, bladder cancer, and breast cancer.

[0016] CD81, is a cell surface glycoprotein that is known to complex with integrins. It is a member of the tetraspanin family, most of which are cell-surface proteins that are

characterized by the presence of four hydrophobic domains, and mediate signal transduction events that play a role in the regulation of cell development, activation, growth and motility. CD81 participates in a variety of important cellular processes such as membrane organization, protein trafficking, cellular fusion and cell-cell interactions. CD81 has also been shown to contribute to tumor growth and metastasis, and to be expressed in most types of cancer, including acute myeloid leukemia, multiple myeloma, lymphoma, breast, lung, prostate, melanoma, and brain cancer.

[0017] CD23 is a type II integral membrane protein belonging to the calcium-dependent lectin superfamily. It is found on mature B cells, activated macrophages, eosinophils, follicular dendritic cells, and platelets. CD23 is also overexpressed in most B cell malignancies including chronic lymphocytic leukemia and Non-Hodgkin lymphoma.

[0018] CD40 is a molecule of the family of tumor necrosis factor receptors (TNFR), which is expressed throughout B-cell development and is implicated in cell survival and differentiation. The broad range of expression of CD40 on normal healthy cells translates to its extensive expression on a variety of tumors. It has been shown that CD40 is widely expressed on melanoma, prostate, lung cancers, and carcinomas of the nasopharynx, bladder, cervix, ovary and kidney. CD40 expression has also been reported on most B cell malignancies and other hematologic malignancies, such as non-Hodgkin lymphomas, Hodgkin lymphomas, chronic lymphocytic leukemia, multiple myeloma, diffuse large B cell lymphoma, and follicular lymphoma.

[0019] CD70 is a member of the tumor necrosis factor superfamily expressed primarily on activated lymphocytes. CD70 interacts with CD27 to regulate B and T cell functions. Among normal, non-lymphoid tissues, CD70 is only expressed on stromal cells of the thymic medulla and mature dendritic cells. CD70 is also expressed constitutively on a subset of B cell malignancies including Non-Hodgkin lymphoma and chronic lymphocytic leukemia, T cell lymphoma, renal cancer, glioblastoma, and head and neck cancer.

[0020] The CD79a protein together with the related CD79b protein, forms a dimer associated with membrane-bound immunoglobulin in B-cells, forming the B-cell antigen receptor (BCR). The CD79a/b heterodimer plays multiple and diverse roles in B cell development and function. It associates non-covalently with the immunoglobulin heavy chain through its transmembrane region, thus forming the BCR along with the immunoglobulin light chain. Association of the CD79a/b heterodimer with the immunoglobulin heavy chain is

required for surface expression of the BCR and BCR induced calcium flux and protein tyrosine phosphorylation. The CD79a/b protein is present on the surface of B-cells throughout their life cycle, and is absent on all other healthy cells. The protein remains present when B-cells transform into active plasma cells, and is also present in virtually all B-cell malignancies, including B-cell lymphomas, Non-Hodgkin lymphoma, chronic lymphocytic leukemia, multiple myeloma, diffuse large B cell lymphoma, and follicular lymphoma.

[0021] CD80 is a member of the B7 family of immune coregulatory proteins that mediate both immune activation and suppression. CD80 in particular has recently been shown to play an important role in supporting immune suppression through interactions with B7-H1. It has been shown that CD80 is expressed on malignant B cells in essentially all cases of follicular lymphoma, the majority of cases of diffuse large B-cell lymphoma, marginal zone lymphoma, mantle cell lymphoma, Non-Hodgkin lymphoma, and chronic lymphocytic leukemia.

[0022] CRLF2 is a type I cytokine receptor also known as thymic stromal lymphopoietin (TSLP) receptor (TSLPR). It forms a functional complex with TSLP and IL7R, capable of stimulating cell proliferation through activation of STAT3, STAT5 and JAK2 pathways and is implicated in the development of the hematopoietic system. It has been shown that CRLF2 is overexpressed in B cell malignancies including acute lymphoblastic leukemia, Non-Hodgkin lymphoma, chronic lymphocytic leukemia.

[0023] Multiple myeloma is a cancer of plasma cells, a type of white blood cells responsible for producing antibodies. Surface antigens SLAMF7, CD138 and CD38 are universally overexpressed in multiple myeloma. SLAMF7 (also named CD319) is a member of the signaling lymphocytic activation molecule (SLAM) family receptors, and plays an important role in immune cell regulation. CD138 is a heparin sulphate proteoglycan, specific for terminally differentiated normal plasma cells. It is highly expressed in multiple myeloma, controlling tumor cell survival, growth, adhesion and bone cell differentiation. CD38 is a multifunctional ectoenzyme that catalyzes the synthesis and hydrolysis of cyclic ADP-ribose (cADPR) from NAD^+ to ADP-ribose. Monoclonal antibodies targeting SLAMF7, CD138 or CD38 have been used as therapies for multiple myeloma.

[0024] T-cell lymphomas and leukemias are aggressive, treatment-resistant cancers with poor prognosis. The T-cell receptor, or TCR, is a molecule found on the surface of T cells, or

T lymphocytes that is responsible for recognizing fragments of antigen as peptides bound to major histocompatibility complex (MHC) molecules. The TCR is composed of two different protein chains. In humans, in 95% of T cells the TCR consists of an alpha (α) chain and a beta (β) chain, whereas in 5% of T cells the TCR consists of gamma and delta (γ/δ) chains. The β-constant region of TCR comprises 2 functionally identical genes: TRBC1 (*T cell receptor* beta *constant* 1) and TRBC2 (*T cell receptor* beta *constant* 2). Each T-cell expresses only one of these. Hence, normal T-cells will be a mixture of individual cells expressing either TRBC1 or 2. A clonal T-cell cancer expresses TRBC1 or TRBC2 in its entirety, which can be exploited to treat T cell cancer.

[0025] Leukocyte immunoglobulin-like receptors (LILR) are a family of at least 13 receptors mainly expressed on lymphoid and myelomonocytic cells. They are divided into two subfamilies LILRBs and LILRAs, which are involved in the inhibition and stimulation of the immune system respectively. LILRBs have 5 members LILRB1-LILRB5, and they are predominantly expressed in hematopoietic lineage cells and to suppress activation of various types of immune cells. In addition to leukocytes, LILRBs and related receptors are expressed by tumor cells and were suggested to have direct tumor-sustaining activity. For example, LILRB1 is expressed on human acute myeloid leukemia (AML) cells (especially in monocytic AML cells), neoplastic B cells (including B cell leukemia, B cell lymphoma, and multiple myeloma cells), T cell leukemia and lymphoma cells, and gastric cancer cells. LILRB2, also known as LIR-2, ILT-4, MIR-10, and CD85d, is expressed on AML cells, *e.g.*, the monocytic subtype, chronic lymphoblastic leukemia (CLL) cells, primary ductal and lobular breast cancer cells, and human non-small cell lung cancer cells. LILRB3 is expressed on myeloid leukemia, B lymphoid leukemia, and myeloma cells. LILRB4 is expressed on AML cells, *e.g.,* the M4 and the M5 subtype, and about 50% of B cell chronic lymphocytic leukemia (B-CLL) cells. LILRBs are also specifically expressed or up-regulated on lung cancer, gastric cancer, breast cancer, and pancreas cancer cells.

SUMMARY

[0026] The invention provides multi-specific binding proteins that bind to a tumor-associated antigen (selected from any one of the antigens provided in Table 15) and to the NKG2D receptor and CD16 receptor on natural killer cells. Such proteins can engage more than one kind of NK activating receptor, and may block the binding of natural ligands to NKG2D. In certain embodiments, the proteins can agonize NK cells in humans, and in other

species such as rodents and cynomolgus monkeys. Various aspects and embodiments of the invention are described in further detail below.

[0027] Accordingly, one aspect of the invention provides a protein that incorporates a first antigen-binding site that binds NKG2D; a second antigen-binding site that binds CXCR4; and an antibody Fc domain, a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16. The antigen-binding sites may each incorporate an antibody heavy chain variable domain and an antibody light chain variable domain (*e.g.* arranged as in an antibody, or fused together to from an scFv), or one or more of the antigen-binding sites may be a single domain antibody, such as a V_HH antibody like a camelid antibody or a V_{NAR} antibody like those found in cartilaginous fish.

[0028] The invention provides multi-specific binding proteins that bind the NKG2D receptor, CD16, and an antigen selected from CXCR4, CD25, VLA4, CD44, CD13, CD15, CD47, CD81, CD23, CD40, CD70, CD79a, CD79b, CD80, CRLF2, SLAMF7, CD38, CD138, T-cell receptor beta-1 chain C region (TRBC1), T-cell receptor beta-2 chain C region (TRBC2), a leukocyte immunoglobulin-like receptor family member selected from LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, LILRA1, LILRA2, LILRA3, LILRA4, LILRA5, and LILRA6, a regulatory T cell expressing protein selected from CC chemokine receptor 8 (CCR8), Cluster of Differentiation 7 (CD7), cytotoxic T-lymphocyte-associated protein 4 (CTLA4), CX3C chemokine receptor 1 (CX3CR1), Ectonucleoside Triphosphate Diphosphohydrolase-1 (ENTPD1), hepatitis A virus cellular receptor 2 (HAVCR2), interleukin 1 receptor type II (IL-1R2), programmed cell death 1 ligand 2 (PDCD1LG2), T cell immunoreceptor with Ig and ITIM domains (TIGIT), tumor necrosis factor receptor superfamily member 4 (TNFRSF4), tumor necrosis factor receptor superfamily member 8 (TNFRSF8), tumor necrosis factor receptor superfamily member 9 (TNFRSF9), GTP-binding protein GEM, ecto-5'-nucleotidase (NT5E), and tumor necrosis factor superfamily member 18 (TNFRSF18).

[0029] The first antigen-binding site, which binds to NKG2D, in some embodiments, can incorporate a heavy chain variable domain related to SEQ ID NO:1, such as by having an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:1, and/or incorporating amino acid sequences identical to the CDR1 (SEQ ID NO:105), CDR2 (SEQ ID NO:106), and CDR3 (SEQ ID NO:107) sequences of SEQ ID NO:1. The heavy chain variable domain related to SEQ ID NO:1 can be coupled with a variety of light chain variable domains to form an NKG2D

binding site. For example, the first antigen-binding site that incorporates a heavy chain variable domain related to SEQ ID NO:1 can further incorporate a light chain variable domain selected from any one of the sequences related to SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, and 40. For example, the first antigen-binding site incorporates a heavy chain variable domain with amino acid sequences at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:1 and a light chain variable domain with amino acid sequences at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to any one of the sequences selected from SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, and 40.

[0030] Alternatively, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:41 and a light chain variable domain related to SEQ ID NO:42. For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:41, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:43), CDR2 (SEQ ID NO:44), and CDR3 (SEQ ID NO:45) sequences of SEQ ID NO:41. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:42, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:46), CDR2 (SEQ ID NO:47), and CDR3 (SEQ ID NO:48) sequences of SEQ ID NO:42.

[0031] In other embodiments, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:49 and a light chain variable domain related to SEQ ID NO:50. For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:49, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:51), CDR2 (SEQ ID NO:52), and CDR3 (SEQ ID NO:53) sequences of SEQ ID NO:49. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:50, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:54), CDR2 (SEQ ID NO:55), and CDR3 (SEQ ID NO:56) sequences of SEQ ID NO:50.

[0032] Alternatively, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:57 and a light chain variable domain related to SEQ ID NO:58, such as by having amino acid sequences at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:57 and at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:58, respectively.

[0033] In another embodiment, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:59 and a light chain variable domain related to SEQ ID NO:60, For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:59, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:517), CDR2 (SEQ ID NO:518), and CDR3 (SEQ ID NO:519) sequences of SEQ ID NO:59. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:60, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:520), CDR2 (SEQ ID NO:521), and CDR3 (SEQ ID NO:355) sequences of SEQ ID NO:60.

[0034] The first antigen-binding site, which binds to NKG2D, in some embodiments, can incorporate a heavy chain variable domain related to SEQ ID NO:61 and a light chain variable domain related to SEQ ID NO:62. For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:61, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:63), CDR2 (SEQ ID NO:64), and CDR3 (SEQ ID NO:65) sequences of SEQ ID NO:61. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:62, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:66), CDR2 (SEQ ID NO:67), and CDR3 (SEQ ID NO:68) sequences of SEQ ID NO:62.

[0035] In some embodiments, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:69 and a light chain variable domain related to SEQ ID NO:70. For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:69, and/or incorporate amino acid sequences identical to the CDR1

(SEQ ID NO:71), CDR2 (SEQ ID NO:72), and CDR3 (SEQ ID NO:73) sequences of SEQ ID NO:69. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:70, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:74), CDR2 (SEQ ID NO:75), and CDR3 (SEQ ID NO:76) sequences of SEQ ID NO:70.

[0036] In some embodiments, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:77 and a light chain variable domain related to SEQ ID NO:78. For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:77, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:79), CDR2 (SEQ ID NO:80), and CDR3 (SEQ ID NO:81) sequences of SEQ ID NO:77. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:78, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:82), CDR2 (SEQ ID NO:83), and CDR3 (SEQ ID NO:84) sequences of SEQ ID NO:78.

[0037] In some embodiments, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:85 and a light chain variable domain related to SEQ ID NO:86. For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:85, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:87), CDR2 (SEQ ID NO:88), and CDR3 (SEQ ID NO:89) sequences of SEQ ID NO:85. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:86, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:90), CDR2 (SEQ ID NO:91), and CDR3 (SEQ ID NO:92) sequences of SEQ ID NO:86.

[0038] In some embodiments, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:93 and a light chain variable domain related to SEQ ID NO:94. For example, the heavy chain variable domain of the first antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:93, and/or incorporate amino acid sequences identical to the CDR1

(SEQ ID NO:95), CDR2 (SEQ ID NO:96), and CDR3 (SEQ ID NO:97) sequences of SEQ ID NO:93. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:94, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:98), CDR2 (SEQ ID NO:99), and CDR3 (SEQ ID NO:100) sequences of SEQ ID NO:94.

[0039] In some embodiments, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:101 and a light chain variable domain related to SEQ ID NO:102, such as by having amino acid sequences at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:101 and at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:102, respectively.

[0040] In some embodiments, the first antigen-binding site can incorporate a heavy chain variable domain related to SEQ ID NO:103 and a light chain variable domain related to SEQ ID NO:104, such as by having amino acid sequences at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:103 and at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:104, respectively.

[0041] In some embodiments, the second antigen-binding site can bind to CXCR4 and can incorporate a heavy chain variable domain related to SEQ ID NO:109 and a light chain variable domain related to SEQ ID NO:110. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:109, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:111), CDR2 (SEQ ID NO:112), and CDR3 (SEQ ID NO:113) sequences of SEQ ID NO:109. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:110, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:114), CDR2 (SEQ ID NO:115), and CDR3 (SEQ ID NO:116) sequences of SEQ ID NO:110.

[0042] In some embodiments, the second antigen-binding site can bind to CXCR4 and can incorporate a heavy chain variable domain related to SEQ ID NO:117 and a light chain variable domain related to SEQ ID NO:118. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:117, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:119), CDR2 (SEQ ID NO:120), and CDR3 (SEQ ID NO:121) sequences of SEQ ID NO:117. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:118, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:122), CDR2 (SEQ ID NO:123), and CDR3 (SEQ ID NO:124) sequences of SEQ ID NO:118.

[0043] In some embodiments, the second antigen-binding site can bind to CXCR4 and can incorporate a heavy chain variable domain related to SEQ ID NO:125 and a light chain variable domain related to SEQ ID NO:126. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:125, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:127), CDR2 (SEQ ID NO:128), and CDR3 (SEQ ID NO:129) sequences of SEQ ID NO:125. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:126, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:130), CDR2 (SEQ ID NO:131), and CDR3 (SEQ ID NO:132) sequences of SEQ ID NO:126.

[0044] In some embodiments, the second antigen-binding site can bind to CXCR4 and can incorporate a heavy chain variable domain related to SEQ ID NO:522 and a light chain variable domain related to SEQ ID NO:526. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:522, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:523), CDR2 (SEQ ID NO:524), and CDR3 (SEQ ID NO:525) sequences of SEQ ID NO:522. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:526, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:527), CDR2 (SEQ ID NO:528), and CDR3 (SEQ ID NO:529) sequences of SEQ ID NO:526.

[0045] In some embodiments, the second antigen-binding site can bind to CD25 and can incorporate a heavy chain variable domain related to SEQ ID NO:134 and a light chain variable domain related to SEQ ID NO:135. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:134, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:136), CDR2 (SEQ ID NO:137), and CDR3 (SEQ ID NO:138) sequences of SEQ ID NO:134. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:135, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:139), CDR2 (SEQ ID NO:140), and CDR3 (SEQ ID NO:141) sequences of SEQ ID NO:135.

[0046] In some embodiments, the second antigen-binding site can bind to CD25 and can incorporate a heavy chain variable domain related to SEQ ID NO:142 and a light chain variable domain related to SEQ ID NO:143. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:142, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:144), CDR2 (SEQ ID NO:145), and CDR3 (SEQ ID NO:146) sequences of SEQ ID NO:142. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:143, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:147), CDR2 (SEQ ID NO:148), and CDR3 (SEQ ID NO:149) sequences of SEQ ID NO:143.

[0047] In some embodiments, the second antigen-binding site can bind to CD25 and can incorporate a heavy chain variable domain related to SEQ ID NO:150 and a light chain variable domain related to SEQ ID NO:151. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:150, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:152), CDR2 (SEQ ID NO:153), and CDR3 (SEQ ID NO:154) sequences of SEQ ID NO:150. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:151, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:155), CDR2 (SEQ ID NO:156), and CDR3 (SEQ ID NO:157) sequences of SEQ ID NO:151.

[0048] In some embodiments, the second antigen-binding site can bind to VLA4 and can incorporate a heavy chain variable domain related to SEQ ID NO:166 and a light chain variable domain related to SEQ ID NO:167. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:166, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:168), CDR2 (SEQ ID NO:169), and CDR3 (SEQ ID NO:170) sequences of SEQ ID NO:166. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:167, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:171), CDR2 (SEQ ID NO:172), and CDR3 (SEQ ID NO:173) sequences of SEQ ID NO:167.

[0049] In some embodiments, the second antigen-binding site can bind to CD44 and can incorporate a heavy chain variable domain related to SEQ ID NO:174 and a light chain variable domain related to SEQ ID NO:175. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:174, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:176), CDR2 (SEQ ID NO:177), and CDR3 (SEQ ID NO:178) sequences of SEQ ID NO:174. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:175, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:179), CDR2 (SEQ ID NO:180), and CDR3 (SEQ ID NO:181) sequences of SEQ ID NO:175.

[0050] In some embodiments, the second antigen-binding site can bind to CD47 and can incorporate a heavy chain variable domain related to SEQ ID NO:182 and a light chain variable domain related to SEQ ID NO:183. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:182, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:184), CDR2 (SEQ ID NO:185), and CDR3 (SEQ ID NO:186) sequences of SEQ ID NO:182. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:183, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:187), CDR2 (SEQ ID NO:188), and CDR3 (SEQ ID NO:189) sequences of SEQ ID NO:183.

[0051] In some embodiments, the second antigen-binding site can bind to CD23 and can incorporate a heavy chain variable domain related to SEQ ID NO:197 and a light chain variable domain related to SEQ ID NO:198. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:197, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:199), CDR2 (SEQ ID NO:200), and CDR3 (SEQ ID NO:201) sequences of SEQ ID NO:197. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:198, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:202), CDR2 (SEQ ID NO:203), and CDR3 (SEQ ID NO:204) sequences of SEQ ID NO:198.

[0052] In some embodiments, the second antigen-binding site can bind to CD40 and can incorporate a heavy chain variable domain related to SEQ ID NO:205 and a light chain variable domain related to SEQ ID NO:206. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:205, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:207), CDR2 (SEQ ID NO:208), and CDR3 (SEQ ID NO:209) sequences of SEQ ID NO:205. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:206, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:210), CDR2 (SEQ ID NO:211), and CDR3 (SEQ ID NO:212) sequences of SEQ ID NO:206.

[0053] In some embodiments, the second antigen-binding site can bind to CD40 and can incorporate a heavy chain variable domain related to SEQ ID NO:213 and a light chain variable domain related to SEQ ID NO:214. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:213, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:215), CDR2 (SEQ ID NO:216), and CDR3 (SEQ ID NO:217) sequences of SEQ ID NO:213. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:214, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:218), CDR2 (SEQ ID NO:219), and CDR3 (SEQ ID NO:220) sequences of SEQ ID NO:214.

[0054] In some embodiments, the second antigen-binding site can bind to CD40 and can incorporate a heavy chain variable domain related to SEQ ID NO:221 and a light chain variable domain related to SEQ ID NO:222. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:221, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:223), CDR2 (SEQ ID NO:224), and CDR3 (SEQ ID NO:225) sequences of SEQ ID NO:221. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:222, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:226), CDR2 (SEQ ID NO:227), and CDR3 (SEQ ID NO:228) sequences of SEQ ID NO:222.

[0055] In some embodiments, the second antigen-binding site can bind to CD40 and can incorporate a heavy chain variable domain related to SEQ ID NO:229 and a light chain variable domain related to SEQ ID NO:230. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:229, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:231), CDR2 (SEQ ID NO:232), and CDR3 (SEQ ID NO:233) sequences of SEQ ID NO:229. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:230, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:234), CDR2 (SEQ ID NO:235), and CDR3 (SEQ ID NO:236) sequences of SEQ ID NO:230.

[0056] In some embodiments, the second antigen-binding site can bind to CD70 and can incorporate a heavy chain variable domain related to SEQ ID NO:237 and a light chain variable domain related to SEQ ID NO:238. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:237, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:239), CDR2 (SEQ ID NO:240), and CDR3 (SEQ ID NO:241) sequences of SEQ ID NO:237. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:238, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:242), CDR2 (SEQ ID NO:243), and CDR3 (SEQ ID NO:244) sequences of SEQ ID NO:238.

[0057] In some embodiments, the second antigen-binding site can bind to CD79b and can incorporate a heavy chain variable domain related to SEQ ID NO:245 and a light chain variable domain related to SEQ ID NO:246. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:245, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:247), CDR2 (SEQ ID NO:248), and CDR3 (SEQ ID NO:249) sequences of SEQ ID NO:245. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:246, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:250), CDR2 (SEQ ID NO:251), and CDR3 (SEQ ID NO:252) sequences of SEQ ID NO:246.

[0058] In some embodiments, the second antigen-binding site can bind to CD80 and can incorporate a heavy chain variable domain related to SEQ ID NO:253 and a light chain variable domain related to SEQ ID NO:254. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:253, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:255), CDR2 (SEQ ID NO:256), and CDR3 (SEQ ID NO:257) sequences of SEQ ID NO:253. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:254, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:258), CDR2 (SEQ ID NO:259), and CDR3 (SEQ ID NO:260) sequences of SEQ ID NO:254.

[0059] In some embodiments, the second antigen-binding site can bind to CRLF2 and can incorporate a heavy chain variable domain related to SEQ ID NO:261 and a light chain variable domain related to SEQ ID NO:262. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:261, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:263), CDR2 (SEQ ID NO:264), and CDR3 (SEQ ID NO:265) sequences of SEQ ID NO:261. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:262, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:266), CDR2 (SEQ ID NO:267), and CDR3 (SEQ ID NO:268) sequences of SEQ ID NO:262.

[0060] In some embodiments, the second antigen-binding site can bind to SLAMF7 and can incorporate a heavy chain variable domain related to SEQ ID NO:272 and a light chain variable domain related to SEQ ID NO:273. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:272, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:274), CDR2 (SEQ ID NO:275), and CDR3 (SEQ ID NO:276) sequences of SEQ ID NO:272. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:273, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:277), CDR2 (SEQ ID NO:278), and CDR3 (SEQ ID NO:279) sequences of SEQ ID NO:273.

[0061] In some embodiments, the second antigen-binding site can bind to SLAMF7 and can incorporate a heavy chain variable domain related to SEQ ID NO:280 and a light chain variable domain related to SEQ ID NO:281. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:280, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:282), CDR2 (SEQ ID NO:283), and CDR3 (SEQ ID NO:284) sequences of SEQ ID NO:280. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:281, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:285), CDR2 (SEQ ID NO:286), and CDR3 (SEQ ID NO:287) sequences of SEQ ID NO:281.

[0062] In some embodiments, the second antigen-binding site can bind to CD138 and can incorporate a heavy chain variable domain related to SEQ ID NO:288 and a light chain variable domain related to SEQ ID NO:289. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:288, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:290), CDR2 (SEQ ID NO:291), and CDR3 (SEQ ID NO:292) sequences of SEQ ID NO:288. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:289, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:293), CDR2 (SEQ ID NO:294), and CDR3 (SEQ ID NO:295) sequences of SEQ ID NO:289.

[0063] In some embodiments, the second antigen-binding site can bind to CD38 and can incorporate a heavy chain variable domain related to SEQ ID NO:296 and a light chain variable domain related to SEQ ID NO:297. For example, the heavy chain variable domain of

the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:296, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:298), CDR2 (SEQ ID NO:299), and CDR3 (SEQ ID NO:300) sequences of SEQ ID NO:296. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:297, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:301), CDR2 (SEQ ID NO:302), and CDR3 (SEQ ID NO:303) sequences of SEQ ID NO:297.

[0064] In some embodiments, the second antigen-binding site can bind to CD38 and can incorporate a heavy chain variable domain related to SEQ ID NO:304 and a light chain variable domain related to SEQ ID NO:305. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:304, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:306), CDR2 (SEQ ID NO:307), and CDR3 (SEQ ID NO:308) sequences of SEQ ID NO:304. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:305, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:309), CDR2 (SEQ ID NO:310), and CDR3 (SEQ ID NO:311) sequences of SEQ ID NO:305.

[0065] In some embodiments, the second antigen-binding site can bind to CD7 and can incorporate a heavy chain variable domain related to SEQ ID NO:325. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:325, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:326), CDR2 (SEQ ID NO:327), and CDR3 (SEQ ID NO:328) sequences of SEQ ID NO:325.

[0066] In some embodiments, the second antigen-binding site can bind to CD7 and can incorporate a heavy chain variable domain related to SEQ ID NO:329. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:329, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:330), CDR2 (SEQ ID NO:331), and CDR3 (SEQ ID NO:332) sequences of SEQ ID NO:329.

[0067] In some embodiments, the second antigen-binding site can bind to CTLA4 and can incorporate a heavy chain variable domain related to SEQ ID NO:333 and a light chain variable domain related to SEQ ID NO:334. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:333, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:335), CDR2 (SEQ ID NO:336), and CDR3 (SEQ ID NO:337) sequences of SEQ ID NO:333. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:334, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:338), CDR2 (SEQ ID NO:339), and CDR3 (SEQ ID NO:340) sequences of SEQ ID NO:334.

[0068] In some embodiments, the second antigen-binding site can bind to CTLA4 and can incorporate a heavy chain variable domain related to SEQ ID NO:341 and a light chain variable domain related to SEQ ID NO:342. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:341, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:343), CDR2 (SEQ ID NO:344), and CDR3 (SEQ ID NO:345) sequences of SEQ ID NO:341. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:342, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:346), CDR2 (SEQ ID NO:347), and CDR3 (SEQ ID NO:348) sequences of SEQ ID NO:342.

[0069] In some embodiments, the second antigen-binding site can bind to CX3CR1 and can incorporate a heavy chain variable domain related to SEQ ID NO:349. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:349, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:350), CDR2 (SEQ ID NO:351), and CDR3 (SEQ ID NO:352) sequences of SEQ ID NO:349.

[0070] In some embodiments, the second antigen-binding site can bind to CX3CR1 and can incorporate a heavy chain variable domain related to SEQ ID NO:353. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID

NO:353, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:354), CDR2 (SEQ ID NO:356), and CDR3 (SEQ ID NO:357) sequences of SEQ ID NO:353.

[0071] In some embodiments, the second antigen-binding site can bind to ENTPD1 and can incorporate a heavy chain variable domain related to SEQ ID NO:358 and a light chain variable domain related to SEQ ID NO:359. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:358, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:360), CDR2 (SEQ ID NO:361), and CDR3 (SEQ ID NO:362) sequences of SEQ ID NO:358. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:359, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:363), CDR2 (SEQ ID NO:364), and CDR3 (SEQ ID NO:365) sequences of SEQ ID NO:359.

[0072] In some embodiments, the second antigen-binding site can bind to ENTPD1 and can incorporate a heavy chain variable domain related to SEQ ID NO:366 and a light chain variable domain related to SEQ ID NO:367. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:366, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:368), CDR2 (SEQ ID NO:369), and CDR3 (SEQ ID NO:370) sequences of SEQ ID NO:366. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:367, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:371), CDR2 (SEQ ID NO:372), and CDR3 (SEQ ID NO:373) sequences of SEQ ID NO:367.

[0073] In some embodiments, the second antigen-binding site can bind to HAVCR2 and can incorporate a heavy chain variable domain related to SEQ ID NO:374 and a light chain variable domain related to SEQ ID NO:375. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:374, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:376), CDR2 (SEQ ID NO:377), and CDR3 (SEQ ID NO:378) sequences of SEQ ID NO:374. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:375, and/or incorporate

amino acid sequences identical to the CDR1 (SEQ ID NO:379), CDR2 (SEQ ID NO:380), and CDR3 (SEQ ID NO:381) sequences of SEQ ID NO:375.

[0074] In some embodiments, the second antigen-binding site can bind to HAVCR2 and can incorporate a heavy chain variable domain related to SEQ ID NO:382 and a light chain variable domain related to SEQ ID NO:383. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:382, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:384), CDR2 (SEQ ID NO:385), and CDR3 (SEQ ID NO:386) sequences of SEQ ID NO:382. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:383, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:387), CDR2 (SEQ ID NO:388), and CDR3 (SEQ ID NO:389) sequences of SEQ ID NO:383.

[0075] In some embodiments, the second antigen-binding site can bind to PDCDILG2 and can incorporate a heavy chain variable domain related to SEQ ID NO:390 and a light chain variable domain related to SEQ ID NO:391. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:390, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:392), CDR2 (SEQ ID NO:393), and CDR3 (SEQ ID NO:394) sequences of SEQ ID NO:390. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:391, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:395), CDR2 (SEQ ID NO:396), and CDR3 (SEQ ID NO:397) sequences of SEQ ID NO:391.

[0076] In some embodiments, the second antigen-binding site can bind to PDCDILG2 and can incorporate a heavy chain variable domain related to SEQ ID NO:398 and a light chain variable domain related to SEQ ID NO:399. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:398, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:400), CDR2 (SEQ ID NO:401), and CDR3 (SEQ ID NO:402) sequences of SEQ ID NO:398. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:399, and/or

incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:403), CDR2 (SEQ ID NO:404), and CDR3 (SEQ ID NO:405) sequences of SEQ ID NO:399.

[0077] In some embodiments, the second antigen-binding site can bind to TIGIT and can incorporate a heavy chain variable domain related to SEQ ID NO:406 and a light chain variable domain related to SEQ ID NO:407. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:406, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:408), CDR2 (SEQ ID NO:409), and CDR3 (SEQ ID NO:410) sequences of SEQ ID NO:406. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:407, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:411), CDR2 (SEQ ID NO:412), and CDR3 (SEQ ID NO:413) sequences of SEQ ID NO:407.

[0078] In some embodiments, the second antigen-binding site can bind to TIGIT and can incorporate a heavy chain variable domain related to SEQ ID NO:414 and a light chain variable domain related to SEQ ID NO:415. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:414, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:416), CDR2 (SEQ ID NO:417), and CDR3 (SEQ ID NO:418) sequences of SEQ ID NO:414. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:415, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:419), CDR2 (SEQ ID NO:420), and CDR3 (SEQ ID NO:421) sequences of SEQ ID NO:415.

[0079] In some embodiments, the second antigen-binding site can bind to TNFRSF4 and can incorporate a heavy chain variable domain related to SEQ ID NO:422 and a light chain variable domain related to SEQ ID NO:423. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:422, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:424), CDR2 (SEQ ID NO:425), and CDR3 (SEQ ID NO:426) sequences of SEQ ID NO:422. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:423, and/or incorporate

amino acid sequences identical to the CDR1 (SEQ ID NO:427), CDR2 (SEQ ID NO:428), and CDR3 (SEQ ID NO:429) sequences of SEQ ID NO:423.

[0080] In some embodiments, the second antigen-binding site can bind to TNFRSF4 and can incorporate a heavy chain variable domain related to SEQ ID NO:430 and a light chain variable domain related to SEQ ID NO:431. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:430, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:432), CDR2 (SEQ ID NO:433), and CDR3 (SEQ ID NO:434) sequences of SEQ ID NO:430. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:431, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:435), CDR2 (SEQ ID NO:436), and CDR3 (SEQ ID NO:437) sequences of SEQ ID NO:431.

[0081] In some embodiments, the second antigen-binding site can bind to TNFRSF8 and can incorporate a heavy chain variable domain related to SEQ ID NO:438 and a light chain variable domain related to SEQ ID NO:439. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:438, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:440), CDR2 (SEQ ID NO:441), and CDR3 (SEQ ID NO:442) sequences of SEQ ID NO:438. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:439, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:443), CDR2 (SEQ ID NO:444), and CDR3 (SEQ ID NO:445) sequences of SEQ ID NO:439.

[0082] In some embodiments, the second antigen-binding site can bind to TNFRSF8 and can incorporate a heavy chain variable domain related to SEQ ID NO:446 and a light chain variable domain related to SEQ ID NO:447. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:446, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:448), CDR2 (SEQ ID NO:449), and CDR3 (SEQ ID NO:450) sequences of SEQ ID NO:446. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:447, and/or incorporate

amino acid sequences identical to the CDR1 (SEQ ID NO:451), CDR2 (SEQ ID NO:452), and CDR3 (SEQ ID NO:453) sequences of SEQ ID NO:447.

[0083] In some embodiments, the second antigen-binding site can bind to TNFRSF9 and can incorporate a heavy chain variable domain related to SEQ ID NO:454 and a light chain variable domain related to SEQ ID NO:455. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:454, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:456), CDR2 (SEQ ID NO:457), and CDR3 (SEQ ID NO:458) sequences of SEQ ID NO:454. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:455, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:459), CDR2 (SEQ ID NO:460), and CDR3 (SEQ ID NO:461) sequences of SEQ ID NO:455.

[0084] In some embodiments, the second antigen-binding site can bind to TNFRSF9 and can incorporate a heavy chain variable domain related to SEQ ID NO:462 and a light chain variable domain related to SEQ ID NO:463. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:462, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:464), CDR2 (SEQ ID NO:465), and CDR3 (SEQ ID NO:466) sequences of SEQ ID NO:462. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:463, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:467), CDR2 (SEQ ID NO:468), and CDR3 (SEQ ID NO:469) sequences of SEQ ID NO:463.

[0085] In some embodiments, the second antigen-binding site can bind to NST5 and can incorporate a heavy chain variable domain related to SEQ ID NO:470 and a light chain variable domain related to SEQ ID NO:471. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:470, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:472), CDR2 (SEQ ID NO:473), and CDR3 (SEQ ID NO:474) sequences of SEQ ID NO:470. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:471, and/or incorporate

amino acid sequences identical to the CDR1 (SEQ ID NO:475), CDR2 (SEQ ID NO:476), and CDR3 (SEQ ID NO:477) sequences of SEQ ID NO:471.

[0086] In some embodiments, the second antigen-binding site can bind to NST5 and can incorporate a heavy chain variable domain related to SEQ ID NO:478 and a light chain variable domain related to SEQ ID NO:479. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:478, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:480), CDR2 (SEQ ID NO:481), and CDR3 (SEQ ID NO:482) sequences of SEQ ID NO:478. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:479, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:483), CDR2 (SEQ ID NO:484), and CDR3 (SEQ ID NO:485) sequences of SEQ ID NO:479.

[0087] In some embodiments, the second antigen-binding site can bind to TNFRSF18 and can incorporate a heavy chain variable domain related to SEQ ID NO:486 and a light chain variable domain related to SEQ ID NO:487. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:486, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:488), CDR2 (SEQ ID NO:489), and CDR3 (SEQ ID NO:490) sequences of SEQ ID NO:486. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:487, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:491), CDR2 (SEQ ID NO:492), and CDR3 (SEQ ID NO:493) sequences of SEQ ID NO:487.

[0088] In some embodiments, the second antigen-binding site can bind to TNFRSF18 and can incorporate a heavy chain variable domain related to SEQ ID NO:494 and a light chain variable domain related to SEQ ID NO:495. For example, the heavy chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:494, and/or incorporate amino acid sequences identical to the CDR1 (SEQ ID NO:496), CDR2 (SEQ ID NO:497), and CDR3 (SEQ ID NO:498) sequences of SEQ ID NO:494. Similarly, the light chain variable domain of the second antigen-binding site can be at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:495, and/or incorporate

amino acid sequences identical to the CDR1 (SEQ ID NO:499), CDR2 (SEQ ID NO:500), and CDR3 (SEQ ID NO:501) sequences of SEQ ID NO:495.

[0089] In some embodiments, the second antigen binding site incorporates a light chain variable domain having an amino acid sequence identical to the amino acid sequence of the light chain variable domain present in the first antigen binding site.

[0090] In some embodiments, the protein incorporates a portion of an antibody Fc domain sufficient to bind CD16, wherein the antibody Fc domain comprises hinge and CH2 domains, and/or amino acid sequences at least 90% identical to amino acid sequence 234-332 of a human IgG antibody.

[0091] Formulations containing one of these proteins; cells containing one or more nucleic acids expressing these proteins, and methods of enhancing tumor cell death using these proteins are also provided.

[0092] Another aspect of the invention provides a method of treating cancer in a patient. The method comprises administering to a patient in need thereof a therapeutically effective amount of the multi-specific binding protein described herein. Exemplary cancers for treatment using the multi-specific binding proteins include, for example, acute myeloid leukemia, diffuse large B cell lymphoma, thymoma, adenoid cystic carcinoma, gastrointestinal cancer, renal cancer, breast cancer, glioblastoma, lung cancer, ovarian cancer, brain cancer, prostate cancer, pancreatic cancer, and melanomas.

BRIEF DESCRIPTION OF THE DRAWINGS

[0093] **FIG. 1** is a representation of a heterodimeric, multi-specific antibody (a trispecific binding protein (TriNKET)). Each arm can represent either the NKG2D-binding domain, or the tumor associated antigen-binding domain. In some embodiments, the NKG2D- and the tumor associated antigen- binding domains can share a common light chain.

[0094] **FIG. 2** is a representation of a heterodimeric, multi-specific antibody. Either the NKG2D-binding domain or the tumor associated antigen-binding domain can take the scFv format (right arm).

[0095] **FIG. 3** are line graphs demonstrating the binding affinity of NKG2D-binding domains (listed as clones) to human recombinant NKG2D in an ELISA assay.

[0096] **FIG. 4** are line graphs demonstrating the binding affinity of NKG2D-binding domains (listed as clones) to cynomolgus recombinant NKG2D in an ELISA assay.

[0097] **FIG. 5** are line graphs demonstrating the binding affinity of NKG2D-binding domains (listed as clones) to mouse recombinant NKG2D in an ELISA assay.

[0098] **FIG. 6** are bar graphs demonstrating the binding of NKG2D-binding domains (listed as clones) to EL4 cells expressing human NKG2D by flow cytometry showing mean fluorescence intensity (MFI) fold over background (FOB).

[0099] **FIG. 7** are bar graphs demonstrating the binding of NKG2D-binding domains (listed as clones) to EL4 cells expressing mouse NKG2D by flow cytometry showing mean fluorescence intensity (MFI) fold over background (FOB).

[0100] **FIG. 8** are line graphs demonstrating specific binding affinity of NKG2D-binding domains (listed as clones) to recombinant human NKG2D-Fc by competing with natural ligand ULBP-6.

[0101] **FIG. 9** are line graphs demonstrating specific binding affinity of NKG2D-binding domains (listed as clones) to recombinant human NKG2D-Fc by competing with natural ligand MICA.

[0102] **FIG. 10** are line graphs demonstrating specific binding affinity of NKG2D-binding domains (listed as clones) to recombinant mouse NKG2D-Fc by competing with natural ligand Rae-1 delta.

[0103] **FIG. 11** are bar graphs showing activation of human NKG2D by NKG2D-binding domains (listed as clones) by quantifying the percentage of TNF-α positive cells, which express human NKG2D-CD3 zeta fusion proteins.

[0104] **FIG. 12** are bar graphs showing activation of mouse NKG2D by NKG2D-binding domains (listed as clones) by quantifying the percentage of TNF-α positive cells, which express mouse NKG2D-CD3 zeta fusion proteins.

[0105] **FIG. 13** are bar graphs showing activation of human NK cells by NKG2D-binding domains (listed as clones).

[0106] **FIG. 14** are bar graphs showing activation of human NK cells by NKG2D-binding domains (listed as clones).

[0107] **FIG. 15** are bar graphs showing activation of mouse NK cells by NKG2D-binding domains (listed as clones).

[0108] **FIG. 16** are bar graphs showing activation of mouse NK cells by NKG2D-binding domains (listed as clones).

[0109] **FIG. 17** are bar graphs showing the cytotoxic effect of NKG2D-binding domains (listed as clones) on tumor cells.

[0110] **FIG. 18** are bar graphs showing the melting temperature of NKG2D-binding domains (listed as clones) measured by differential scanning fluorimetry.

[0111] **FIGs. 19A-19C** are bar graphs of synergistic activation of NK cells using CD16 and NKG2D-binding. FIG. 19A demonstrates levels of CD107a; FIG. 19B demonstrates levels of IFN-γ; FIG. 19C demonstrates levels of CD107a and IFN-γ. Graphs indicate the mean (n = 2) ± SD. Data are representative of five independent experiments using five different healthy donors.

[0112] **FIG. 20** is a representation of a trispecific binding protein (TriNKET) in the Triomab form, which is a trifunctional, bispecific antibody that maintains an IgG-like shape. This chimera consists of two half antibodies, each with one light and one heavy chain, that originate from two parental antibodies. Triomab form may be a heterodimeric construct containing 1/2 of rat antibody and 1/2 of mouse antibody.

[0113] **FIG. 21** is a representation of a TriNKET in the KiH Common Light Chain form, which involves the knobs-into-holes (KIHs) technology. KiH is a heterodimer containing 2 Fab fragments binding to target 1 and 2, and an Fc stabilized by heterodimerization mutations. TriNKET in the KiH format may be a heterodimeric construct with 2 Fab fragments binding to target 1 and target 2, containing two different heavy chains and a common light chain that pairs with both heavy chains.

[0114] **FIG. 22** is a representation of a TriNKET in the dual-variable domain immunoglobulin (DVD-Ig™) form, which combines the target-binding domains of two monoclonal antibodies via flexible naturally occurring linkers, and yields a tetravalent IgG-like molecule. DVD-Ig™ is a homodimeric construct where variable domain targeting antigen 2 is fused to the N-terminus of a variable domain of Fab fragment targeting antigen 1. DVD-Ig™ form contains normal Fc.

[0115] **FIG. 23** is a representation of a TriNKET in the Orthogonal Fab interface (Ortho-Fab) form, which is a heterodimeric construct that contains 2 Fab fragments binding to target 1 and target 2 fused to Fc. Light chain (LC)-heavy chain (HC) pairing is ensured by orthogonal interface. Heterodimerization is ensured by mutations in the Fc.

[0116] **FIG. 24** is a representation of a TriNKET in the 2-in-1 Ig format.

[0117] **FIG. 25** is a representation of a TriNKET in the ES form, which is a heterodimeric construct containing two different Fab fragments binding to target 1 and target 2 fused to the Fc. Heterodimerization is ensured by electrostatic steering mutations in the Fc.

[0118] **FIG. 26** is a representation of a TriNKET in the Fab fragment Arm Exchange form: antibodies that exchange Fab arms by swapping a heavy chain and attached light chain (half-molecule) with a heavy-light chain pair from another molecule, resulting in bispecific antibodies. Fab Arm Exchange form (cFae) is a heterodimer containing 2 Fab fragments binding to target 1 and 2, and an Fc stabilized by heterodimerization mutations.

[0119] **FIG. 27** is a representation of a TriNKET in the SEED Body form, which is a heterodimer containing 2 Fab fragments binding to target 1 and 2, and an Fc stabilized by heterodimerization mutations.

[0120] **FIG. 28** is a representation of a TriNKET in the LuZ-Y form, in which a leucine zipper is used to induce heterodimerization of two different HCs. The LuZ-Y form is a heterodimer containing two different scFabs binding to target 1 and 2, fused to Fc. Heterodimerization is ensured through leucine zipper motifs fused to C-terminus of Fc.

[0121] **FIG. 29** is a representation of a TriNKET in the Cov-X-Body form.

[0122] **FIGs. 30A and 30B** are representations of TriNKETs in the κλ-Body forms, which are heterodimeric constructs with two different Fab fragments fused to Fc stabilized by heterodimerization mutations: one Fab fragment targeting antigen 1 contains kappa LC, and the second Fab fragment targeting antigen 2 contains lambda LC. FIG. 30A is an exemplary representation of one form of a κλ-Body; FIG. 30B is an exemplary representation of another κλ-Body.

[0123] **FIG. 31** is an Oasc-Fab heterodimeric construct that includes Fab fragment binding to target 1 and scFab binding to target 2, both of which are fused to the Fc domain. Heterodimerization is ensured by mutations in the Fc domain.

[0124] **FIG. 32** is a DuetMab, which is a heterodimeric construct containing two different Fab fragments binding to antigens 1 and 2, and an Fc that is stabilized by heterodimerization mutations. Fab fragments 1 and 2 contain differential S-S bridges that ensure correct light chain and heavy chain pairing.

[0125] **FIG. 33** is a CrossmAb, which is a heterodimeric construct with two different Fab fragments binding to targets 1 and 2, and an Fc stabilized by heterodimerization mutations. CL and CH1 domains, and VH and VL domains are switched, *e.g.*, CH1 is fused in-line with VL, while CL is fused in-line with VH.

[0126] **FIG. 34** is a Fit-Ig, which is a homodimeric construct where Fab fragment binding to antigen 2 is fused to the N-terminus of HC of Fab fragment that binds to antigen 1. The construct contains wild-type Fc.

[0127] **FIG. 35** shows data from a FACS showing expression of CXCR4 on human B cell lymphoma cell line Raji (Black = Isotype control; Empty = CXCR4 staining).

[0128] **FIG. 36** are line graphs showing that CXCR4-TriNKETs mediate KHYG-1 killing of Raji target cells.

[0129] **FIG. 37** is a bar graph showing that CXCR4-targeted TrINKETs mediate human NK cell killing of Raji target cells.

DETAILED DESCRIPTION

[0130] The invention provides multi-specific binding proteins that bind CXCR4 on a cancer cell and the NKG2D receptor and CD16 receptor on natural killer cells to activate the natural killer cells, pharmaceutical compositions comprising such multi-specific binding proteins, and therapeutic methods using such multi-specific proteins and pharmaceutical compositions, including for the treatment of cancer. Various aspects of the invention are set forth below in sections; however, aspects of the invention described in one particular section are not to be limited to any particular section.

[0131] To facilitate an understanding of the present invention, a number of terms and phrases are defined below.

[0132] The terms “a” and “an” as used herein mean “one or more” and include the plural unless the context is inappropriate.

[0133] As used herein, the term "antigen-binding site" refers to the part of the immunoglobulin molecule that participates in antigen binding. In human antibodies, the antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable regions" which are

interposed between more conserved flanking stretches known as "framework regions," or "FR". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In a human antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs." In certain animals, such as camels and cartilaginous fish, the antigen-binding site is formed by a single antibody chain providing a "single domain antibody." Antigen-binding sites can exist in an intact antibody, in an antigen-binding fragment of an antibody that retains the antigen-binding surface, or in a recombinant polypeptide such as an scFv, using a peptide linker to connect the heavy chain variable domain to the light chain variable domain in a single polypeptide.

[0134] The term "tumor associated antigen" as used herein means any antigen including but not limited to a protein, glycoprotein, ganglioside, carbohydrate, lipid that is associated with cancer. Such antigen can be expressed on malignant cells or in the tumor microenvironment such as on tumor-associated blood vessels, extracellular matrix, mesenchymal stroma, or immune infiltrates.

[0135] As used herein, the terms "subject" and "patient" refer to an organism to be treated by the methods and compositions described herein. Such organisms preferably include, but are not limited to, mammals (*e.g.*, murines, simians, equines, bovines, porcines, canines, felines, and the like), and more preferably include humans.

[0136] As used herein, the term "effective amount" refers to the amount of a compound (*e.g.*, a compound of the present invention) sufficient to effect beneficial or desired results. An effective amount can be administered in one or more administrations, applications or dosages and is not intended to be limited to a particular formulation or administration route. As used herein, the term "treating" includes any effect, *e.g.*, lessening, reducing, modulating, ameliorating or eliminating, that results in the improvement of the condition, disease, disorder, and the like, or ameliorating a symptom thereof.

[0137] As used herein, the term "pharmaceutical composition" refers to the combination of an active agent with a carrier, inert or active, making the composition especially suitable for diagnostic or therapeutic use *in vivo* or *ex vivo*.

[0138] As used herein, the term "pharmaceutically acceptable carrier" refers to any of the standard pharmaceutical carriers, such as a phosphate buffered saline solution, water, emulsions (*e.g.*, such as an oil/water or water/oil emulsions), and various types of wetting agents. The compositions also can include stabilizers and preservatives. For examples of carriers, stabilizers and adjuvants, s*ee e.g.*, Martin, Remington's Pharmaceutical Sciences, 15th Ed., Mack Publ. Co., Easton, PA [1975].

[0139] As used herein, the term "pharmaceutically acceptable salt" refers to any pharmaceutically acceptable salt (*e.g.*, acid or base) of a compound of the present invention which, upon administration to a subject, is capable of providing a compound of this invention or an active metabolite or residue thereof. As is known to those of skill in the art, "salts" of the compounds of the present invention may be derived from inorganic or organic acids and bases. Exemplary acids include, but are not limited to, hydrochloric, hydrobromic, sulfuric, nitric, perchloric, fumaric, maleic, phosphoric, glycolic, lactic, salicylic, succinic, toluene-p-sulfonic, tartaric, acetic, citric, methanesulfonic, ethanesulfonic, formic, benzoic, malonic, naphthalene-2-sulfonic, benzenesulfonic acid, and the like. Other acids, such as oxalic, while not in themselves pharmaceutically acceptable, may be employed in the preparation of salts useful as intermediates in obtaining the compounds of the invention and their pharmaceutically acceptable acid addition salts.

[0140] Exemplary bases include, but are not limited to, alkali metal (*e.g.*, sodium) hydroxides, alkaline earth metal (*e.g.*, magnesium) hydroxides, ammonia, and compounds of formula NW_4^+, wherein W is C_{1-4} alkyl, and the like.

[0141] Exemplary salts include, but are not limited to: acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, flucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethanesulfonate, lactate, maleate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, palmoate, pectinate, persulfate, phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, undecanoate, and the like. Other examples of salts include anions of the compounds

of the present invention compounded with a suitable cation such as Na^+, NH_4^+, and NW_4^+ (wherein W is a C_{1-4} alkyl group), and the like.

[0142] For therapeutic use, salts of the compounds of the present invention are contemplated as being pharmaceutically acceptable. However, salts of acids and bases that are non-pharmaceutically acceptable may also find use, for example, in the preparation or purification of a pharmaceutically acceptable compound.

[0143] Throughout the description, where compositions are described as having, including, or comprising specific components, or where processes and methods are described as having, including, or comprising specific steps, it is contemplated that, additionally, there are compositions of the present invention that consist essentially of, or consist of, the recited components, and that there are processes and methods according to the present invention that consist essentially of, or consist of, the recited processing steps.

[0144] As a general matter, compositions specifying a percentage are by weight unless otherwise specified. Further, if a variable is not accompanied by a definition, then the previous definition of the variable controls.

I. PROTEINS

[0145] The invention provides multi-specific binding proteins that bind to the NKG2D receptor and CD16 receptor on natural killer cells, and the tumor-associated antigen selected from any one of the antigens provided in Table 15. The multi-specific binding proteins are useful in the pharmaceutical compositions and therapeutic methods described herein. Binding of the multi-specific binding proteins to the NKG2D receptor and CD16 receptor on a natural killer cell enhances the activity of the natural killer cell toward destruction of tumor cells expressing the tumor-associated antigen selected from any one of the antigens provided in Table 15. Binding of the multi-specific binding proteins to tumor-associated antigen-expressing cells brings the cancer cells into proximity with the natural killer cell, which facilitates direct and indirect destruction of the cancer cells by the natural killer cell. Further description of some exemplary multi-specific binding proteins is provided below.

[0146] The first component of the multi-specific binding proteins binds to NKG2D receptor-expressing cells, which can include but are not limited to NK cells, γδ T cells and $CD8^+$ αβ T cells. Upon NKG2D binding, the multi-specific binding proteins may block natural ligands, such as ULBP6 (UL16 binding protein 6) and MICA (Major

Histocompatibility Complex Class I Chain-Related A), from binding to NKG2D and activating NKG2D receptors.

[0147] The second component of the multi-specific binding proteins binds a tumor-associated antigen selected from any one of the antigens provided in Table 15. The tumor-associated antigen-expressing cells, which may be found in leukemias such as, for example, acute myeloid leukemia and T-cell leukemia.

[0148] The third component for the multi-specific binding proteins binds to cells expressing CD16, an Fc receptor on the surface of leukocytes including natural killer cells, macrophages, neutrophils, eosinophils, mast cells, and follicular dendritic cells.

[0149] The multi-specific binding proteins described herein can take various formats. For example, one format is a heterodimeric, multi-specific antibody including a first immunoglobulin heavy chain, a first immunoglobulin light chain, a second immunoglobulin heavy chain and a second immunoglobulin light chain (FIG. 1). The first immunoglobulin heavy chain includes a first Fc (hinge-CH2-CH3) domain, a first heavy chain variable domain and optionally a first CH1 heavy chain domain. The first immunoglobulin light chain includes a first light chain variable domain and a first light chain constant domain. The first immunoglobulin light chain, together with the first immunoglobulin heavy chain, forms an antigen-binding site that binds NKG2D. The second immunoglobulin heavy chain comprises a second Fc (hinge-CH2-CH3) domain, a second heavy chain variable domain and optionally a second CH1 heavy chain domain. The second immunoglobulin light chain includes a second light chain variable domain and a second light chain constant domain. The second immunoglobulin light chain, together with the second immunoglobulin heavy chain, forms an antigen-binding site that binds a tumor-associated antigen selected from any one of the antigens provided in Table 15. The first Fc domain and second Fc domain together are able to bind to CD16 (FIG. 1). In some embodiments, the first immunoglobulin light chain is identical to the second immunoglobulin light chain.

[0150] Another exemplary format involves a heterodimeric, multi-specific antibody including a first immunoglobulin heavy chain, a second immunoglobulin heavy chain and an immunoglobulin light chain (FIG. 2). The first immunoglobulin heavy chain includes a first Fc (hinge-CH2-CH3) domain fused via either a linker or an antibody hinge to a single-chain variable fragment (scFv) composed of a heavy chain variable domain and light chain variable domain which pair and bind NKG2D, or bind a tumor-associated antigen selected from any

one of the antigens provided in Table 15. The second immunoglobulin heavy chain includes a second Fc (hinge-CH2-CH3) domain, a second heavy chain variable domain and optionally a CH1 heavy chain domain. The immunoglobulin light chain includes a light chain variable domain and a light chain constant domain. The second immunoglobulin heavy chain pairs with the immunoglobulin light chain and binds to NKG2D or binds a tumor-associated antigen selected from any one of the antigens provided in Table 15. The first Fc domain and the second Fc domain together are able to bind to CD16 (FIG. 2).

[0151] One or more additional binding motifs may be fused to the C-terminus of the constant region CH3 domain, optionally via a linker sequence. In certain embodiments, the antigen-binding motif is a single-chain or disulfide-stabilized variable region (scFv) forming a tetravalent or trivalent molecule.

[0152] In some embodiments, the multi-specific binding protein is in the Triomab form, which is a trifunctional, bispecific antibody that maintains an IgG-like shape. This chimera consists of two half antibodies, each with one light and one heavy chain, that originate from two parental antibodies.

[0153] In some embodiments, the multi-specific binding protein is the KiH Common Light Chain (LC) form, which involves the knobs-into-holes (KIHs) technology. The KIH involves engineering C_H3 domains to create either a "knob" or a "hole" in each heavy chain to promote heterodimerization. The concept behind the "Knobs-into-Holes (KiH)" Fc technology was to introduce a "knob" in one CH3 domain (CH3A) by substitution of a small residue with a bulky one (*e.g.*, $T366W_{CH3A}$ in EU numbering). To accommodate the "knob," a complementary "hole" surface was created on the other CH3 domain (CH3B) by replacing the closest neighboring residues to the knob with smaller ones (*e.g.*, $T366S/L368A/Y407V_{CH3B}$). The "hole" mutation was optimized by structured-guided phage library screening (Atwell S, Ridgway JB, Wells JA, Carter P., Stable heterodimers from remodeling the domain interface of a homodimer using a phage display library, *J. Mol. Biol.* (1997) 270(1):26–35). X-ray crystal structures of KiH Fc variants (Elliott JM, Ultsch M, Lee J, Tong R, Takeda K, Spiess C, *et al.*, Antiparallel conformation of knob and hole aglycosylated half-antibody homodimers is mediated by a CH2-CH3 hydrophobic interaction. *J. Mol. Biol.* (2014) 426(9):1947–57; Mimoto F, Kadono S, Katada H, Igawa T, Kamikawa T, Hattori K. Crystal structure of a novel asymmetrically engineered Fc variant with improved affinity for FcγRs. *Mol. Immunol.* (2014) 58(1):132–8) demonstrated that heterodimerization is thermodynamically favored by hydrophobic interactions driven by

steric complementarity at the inter-CH3 domain core interface, whereas the knob–knob and the hole–hole interfaces do not favor homodimerization owing to steric hindrance and disruption of the favorable interactions, respectively.

[0154] In some embodiments, the multi-specific binding protein is in the dual-variable domain immunoglobulin (DVD-Ig™) form, which combines the target binding domains of two monoclonal antibodies via flexible naturally occurring linkers, and yields a tetravalent IgG-like molecule.

[0155] In some embodiments, the multi-specific binding protein is in the Orthogonal Fab interface (Ortho-Fab) form. In the ortho-Fab IgG approach (Lewis SM, Wu X, Pustilnik A, Sereno A, Huang F, Rick HL, *et al.*, Generation of bispecific IgG antibodies by structure-based design of an orthogonal Fab interface. *Nat. Biotechnol.* (2014) 32(2):191–8), structure-based regional design introduces complementary mutations at the LC and $HC_{VH\text{-}CH1}$ interface in only one Fab fragment, without any changes being made to the other Fab fragment.

[0156] In some embodiments, the multi-specific binding protein is in the 2-in-1 Ig format. In some embodiments, the multi-specific binding protein is in the ES form, which is a heterodimeric construct containing two different Fab fragments binding to targets 1 and target 2 fused to the Fc. Heterodimerization is ensured by electrostatic steering mutations in the Fc.

[0157] In some embodiments, the multi-specific binding protein is in the κλ-Body form, which is a heterodimeric construct with two different Fab fragments fused to Fc stabilized by heterodimerization mutations: Fab fragment1 targeting antigen 1 contains kappa LC, while second Fab fragment targeting antigen 2 contains lambda LC. FIG. 30A is an exemplary representation of one form of a κλ-Body; FIG. 30B is an exemplary representation of another κλ-Body.

[0158] In some embodiments, the multi-specific binding protein is in Fab Arm Exchange form (antibodies that exchange Fab arms by swapping a heavy chain and attached light chain (half-molecule) with a heavy-light chain pair from another molecule, which results in bispecific antibodies).

[0159] In some embodiments, the multi-specific binding protein is in the SEED Body form. The strand-exchange engineered domain (SEED) platform was designed to generate asymmetric and bispecific antibody-like molecules, a capability that expands therapeutic applications of natural antibodies. This protein engineered platform is based on exchanging structurally related sequences of immunoglobulin within the conserved CH3 domains. The

SEED design allows efficient generation of AG/GA heterodimers, while disfavoring homodimerization of AG and GA SEED CH3 domains. (Muda M. *et al.*, *Protein Eng. Des. Sel.* (2011, 24(5):447-54)).

[0160] In some embodiments, the multi-specific binding protein is in the LuZ-Y form, in which a leucine zipper is used to induce heterodimerization of two different HCs. (Wranik, BJ. *et al.*, *J. Biol. Chem.* (2012), 287:43331-9).

[0161] In some embodiments, the multi-specific binding protein is in the Cov-X-Body form. In bispecific CovX-Bodies, two different peptides are joined together using a branched azetidinone linker and fused to the scaffold antibody under mild conditions in a site-specific manner. Whereas the pharmacophores are responsible for functional activities, the antibody scaffold imparts long half-life and Ig-like distribution. The pharmacophores can be chemically optimized or replaced with other pharmacophores to generate optimized or unique bispecific antibodies. (Doppalapudi VR *et al.*, *PNAS* (2010), 107(52);22611-22616).

[0162] In some embodiments, the multi-specific binding protein is in an Oasc-Fab heterodimeric form that includes Fab fragment binding to target 1, and scFab binding to target 2 fused to Fc. Heterodimerization is ensured by mutations in the Fc.

[0163] In some embodiments, the multi-specific binding protein is in a DuetMab form, which is a heterodimeric construct containing two different Fab fragments binding to antigens 1 and 2, and Fc stabilized by heterodimerization mutations. Fab fragments 1 and 2 contain differential S-S bridges that ensure correct LC and HC pairing.

[0164] In some embodiments, the multi-specific binding protein is in a CrossmAb form, which is a heterodimeric construct with two different Fab fragments binding to targets 1 and 2, fused to Fc stabilized by heterodimerization. CL and CH1 domains and VH and VL domains are switched, *e.g.*, CH1 is fused in-line with VL, while CL is fused in-line with VH.

[0165] In some embodiments, the multi-specific binding protein is in a Fit-Ig form, which is a homodimeric construct where Fab fragment binding to antigen 2 is fused to the N terminus of HC of Fab fragment that binds to antigen 1. The construct contains wild-type Fc.

[0166] Table 1 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination, can bind to NKG2D. The NKG2D binding domains can vary in their binding affinity to NKG2D, nevertheless, they all activate human NKG2D and NK cells.

Table 1		
Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
ADI-27705	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:1) CDR1 (SEQ ID NO:105) – GSFSGYYWS CDR2 (SEQ ID NO:106) – EIDHSGSTNYNPSLKS CDR3 (SEQ ID NO:107) – ARARGPWSFDP	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYNSYPITFGGGTKVEIK (SEQ ID NO:2)
ADI-27724	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:3)	EIVLTQSPGTLSLSPGERATLS CRASQSVSSSYLAWYQQKPG QAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAV YYCQQYGSSPITFGGGTKVEI K (SEQ ID NO:4)
ADI-27740 (A40)	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:5)	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYHSFYTFGGGTKVEIK (SEQ ID NO:6)
ADI-27741	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQSNSYYTFGGGTKVEIK

	(SEQ ID NO:7)	(SEQ ID NO:8)
ADI-27743	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:9)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYNSYPTFGGGTKVEIK (SEQ ID NO:10)
ADI-28153	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWGFDPWGQGTLVTVSS (SEQ ID NO:11)	ELQMTQSPSSLSASVGDRVTIT CRTSQSISSYLNWYQQKPGQP PKLLIYWASTRESGVPDRFSGS GSGTDFTLTISSLQPEDSATYY CQQSYDIPYTFGQGTKLEIK (SEQ ID NO:12)
ADI-28226 (C26)	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:13)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYGSFPITFGGGTKVEIK (SEQ ID NO:14)
ADI-28154	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:15)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTDFTLTISSLQPDDFATY YCQQSKEVPWTFGQGTKVEIK (SEQ ID NO:16)
ADI-29399	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:17)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYNSFPTFGGGTKVEIK (SEQ ID NO:18)
ADI-29401	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGK

	GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:19)	APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYDIYPTFGGGTKVEIK (SEQ ID NO:20)
ADI- 29403	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:21)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYDSYPTFGGGTKVEIK (SEQ ID NO:22)
ADI- 29405	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:23)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYGSFPTFGGGTKVEIK (SEQ ID NO:24)
ADI- 29407	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:25)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYQSFPTFGGGTKVEIK (SEQ ID NO:26)
ADI- 29419	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:27)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYSSFSTFGGGTKVEIK (SEQ ID NO:28)
ADI- 29421	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYESYSTFGGGTKVEIK

	(SEQ ID NO:29)	(SEQ ID NO:30)
ADI-29424	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:31)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYDSFITFGGGTKVEIK (SEQ ID NO:32)
ADI-29425	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:33)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYQSYPTFGGGTKVEIK (SEQ ID NO:34)
ADI-29426	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:35)	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYHSFPTFGGGTKVEIK (SEQ ID NO:36)
ADI-29429	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:37)	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYELYSYTFGGGTKVEIK (SEQ ID NO:38)
ADI-29447 (F47)	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:39)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCQQYDTFITFGGGTKVEIK (SEQ ID NO:40)
ADI-27727	QVQLVQSGAEVKKPGSSVKVSCKA SGGTFSSYAISWVRQAPGQGLEWM	DIVMTQSPDSLAVSLGERATIN CKSSQSVLYSSNNKNYLAWY

	GGIIPIFGTANYAQKFQGRVTITADE STSTAYMELSSLRSEDTAVYYCAR GDSSIRHAYYYYGMDVWGQGTTV TVSS (SEQ ID NO:41) CDR1 (SEQ ID NO:43) – GTFSSYAIS CDR2 (SEQ ID NO:44) – GIIPIFGTANYAQKFQG CDR3 (SEQ ID NO:45) – ARGDSSIRHAYYYYGMDV	QQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTISSLQ AEDVAVYYCQQYYSTPITFGG GTKVEIK (SEQ ID NO:42) CDR1 (SEQ ID NO:46) – KSSQSVLYSSNNKNYLA CDR2 (SEQ ID NO:47) – WASTRES CDR3 (SEQ ID NO:48) – QQYYSTPIT
ADI- 29443 (F43)	QLQLQESGPGLVKPSETLSLTCTVS GGSISSSSYYWGWIRQPPGKGLEWI GSIYYSGSTYYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARG SDRFHPYFDYWGQGTLVTVSS (SEQ ID NO:49) CDR1 (SEQ ID NO:51) – GSISSSSYYWG CDR2 (SEQ ID NO:52) – SIYYSGSTYYNPSLKS CDR3 (SEQ ID NO:53) – ARGSDRFHPYFDY	EIVLTQSPATLSLSPGERATLS CRASQSVSRYLAWYQQKPGQ APRLLIYDASNRATGIPARFSG SGSGTDFTLTISSLEPEDFAVY YCQQFDTWPPTFGGGTKVEIK (SEQ ID NO:50) CDR1 (SEQ ID NO:54) – RASQSVSRYLA CDR2 (SEQ ID NO:55) – DASNRAT CDR3 (SEQ ID NO:56) – QQFDTWPPT
ADI- 29404 (F04)	QVQLQQWGAGLLKPSETLSLTCAV YGGSFSGYYWSWIRQPPGKGLEWI GEIDHSGSTNYNPSLKSRVTISVDTS KNQFSLKLSSVTAADTAVYYCARA RGPWSFDPWGQGTLVTVSS (SEQ ID NO:57)	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGK APKLLIYKASSLESGVPSRFSG SGSGTEFTLTISSLQPDDFATY YCEQYDSYPTFGGGTKVEIK (SEQ ID NO:58)
ADI- 28200	QVQLVQSGAEVKKPGSSVKVSCKA SGGTFSSYAISWVRQAPGQGLEWM GGIIPIFGTANYAQKFQGRVTITADE	DIVMTQSPDSLAVSLGERATIN CESSQSLLNSGNQKNYLTWY QQKPGQPPKPLIYWASTRESG

	STSTAYMELSSLRSEDTAVYYCAR RGRKASGSFYYYYGMDVWGQGTT VTVSS (SEQ ID NO:59) CDR1 (SEQ ID NO:517) – GTFSSYAIS CDR2 (SEQ ID NO:518) – GIIPIFGTANYAQKFQG CDR3 (SEQ ID NO:519) – ARRGRKASGSFYYYYGMDV	VPDRFSGSGSGTDFTLTISSLQ AEDVAVYYCQNDYSYPYTFG QGTKLEIK (SEQ ID NO:60) CDR1 (SEQ ID NO:520) – ESSQSLLNSGNQKNYLT CDR2 (SEQ ID NO:521) – WASTRES CDR3 (SEQ ID NO:355) – QNDYSYPYT
ADI-29379 (E79)	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTSYYMHWVRQAPGQGLE WMGIINPSGGSTSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYY CARGAPNYGDTTHDYYYMDVWG KGTTVTVSS (SEQ ID NO:61) CDR1 (SEQ ID NO:63) - YTFTSYYMH CDR2 (SEQ ID NO:64) - IINPSGGSTSYAQKFQG CDR3 (SEQ ID NO:65) - ARGAPNYGDTTHDYYYMDV	EIVMTQSPATLSVSPGERATLS CRASQSVSSNLAWYQQKPGQ APRLLIYGASTRATGIPARFSG SGSGTEFTLTISSLQSEDFAVY YCQQYDDWPFTFGGGTKVEI K (SEQ ID NO:62) CDR1 (SEQ ID NO:66) - RASQSVSSNLA CDR2 (SEQ ID NO:67) - GASTRAT CDR3 (SEQ ID NO:68) - QQYDDWPFT
ADI-29463 (F63)	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTGYYMHWVRQAPGQGLE WMGWINPNSGGTNYAQKFQGRVT MTRDTSISTAYMELSRLRSDDTAV YYCARDTGEYYDTDDHGMDVWG QGTTVTVSS (SEQ ID NO:69) CDR1 (SEQ ID NO:71) - YTFTGYYMH	EIVLTQSPGTLSLSPGERATLS CRASQSVSSNLAWYQQKPGQ APRLLIYGASTRATGIPARFSG SGSGTEFTLTISSLQSEDFAVY YCQQDDYWPPTFGGGTKVEI K (SEQ ID NO:70) CDR1 (SEQ ID NO:74) - RASQSVSSNLA

	CDR2 (SEQ ID NO:72) - WINPNSGGTNYAQKFQG CDR3 (SEQ ID NO:73) - ARDTGEYYDTDDHGMDV	CDR2 (SEQ ID NO:75) - GASTRAT CDR3 (SEQ ID NO:76) - QQDDYWPPT
ADI-27744 (A44)	EVQLLESGGGLVQPGGSLRLSCAAS GFTFSSYAMSWVRQAPGKGLEWV SAISGSGGSTYYADSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYC AKDGGYYDSGAGDYWGQGTLVTV SS (SEQ ID NO:77) CDR1 (SEQ ID NO:79) - FTFSSYAMS CDR2 (SEQ ID NO:80) - AISGSGGSTYYADSVKG CDR3 (SEQ ID NO:81) - AKDGGYYDSGAGDY	DIQMTQSPSSVSASVGDRVTIT CRASQGIDSWLAWYQQKPGK APKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATY YCQQGVSYPRTFGGGTKVEIK (SEQ ID NO:78) CDR1 (SEQ ID NO:82) - RASQGIDSWLA CDR2 (SEQ ID NO:83) - AASSLQS CDR3 (SEQ ID NO:84) - QQGVSYPRT
ADI-27749 (A49)	EVQLVESGGGLVKPGGSLRLSCAA SGFTFSSYSMNWVRQAPGKGLEW VSSISSSSSYIYYADSVKGRFTISRD NAKNSLYLQMNSLRAEDTAVYYC ARGAPMGAAAGWFDPWGQGTLVT VSS (SEQ ID NO:85) CDR1 (SEQ ID NO:87) - FTFSSYSMN CDR2 (SEQ ID NO:88) - SISSSSSYIYYADSVKG CDR3 (SEQ ID NO:89) - ARGAPMGAAAGWFDP	DIQMTQSPSSVSASVGDRVTIT CRASQGISSWLAWYQQKPGK APKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATY YCQQGVSFPRTFGGGTKVEIK (SEQ ID NO:86) CDR1 (SEQ ID NO:90) - RASQGISSWLA CDR2 (SEQ ID NO:91) - AASSLQS CDR3 (SEQ ID NO:92) - QQGVSFPRT
ADI-29378 (E78)	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTSYYMHWVRQAPGQGLE WMGIINPSGGSTSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYY CAREGAGFAYGMDYYYMDVWGK	EIVLTQSPATLSLSPGERATLS CRASQSVSSYLAWYQQKPGQ APRLLIYDASNRATGIPARFSG SGSGTDFTLTISSLEPEDFAVY YCQQSDNWPFTFGGGTKVEIK

	GTTVTVSS (SEQ ID NO:93) CDR1 (SEQ ID NO:95) - YTFTSYYMH CDR2 (SEQ ID NO:96) - IINPSGGSTSYAQKFQG CDR3 (SEQ ID NO:97) - AREGAGFAYGMDYYYMDV	(SEQ ID NO:94) CDR1 (SEQ ID NO:98) - RASQSVSSYLA CDR2 (SEQ ID NO:99) - DASNRAT CDR3 (SEQ ID NO:100) - QQSDNWPFT

[0167] Alternatively, a heavy chain variable domain represented by SEQ ID NO:101 can be paired with a light chain variable domain represented by SEQ ID NO:102 to form an antigen-binding site that can bind to NKG2D, as illustrated in US 9,273,136.

SEQ ID NO:101

QVQLVESGGGLVKPGGSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAFI
RYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDRGL
GDGTYFDYWGQGTTVTVSS

SEQ ID NO:102

QSALTQPASVSGSPGQSITISCSGSSSNIGNNAVNWYQQLPGKAPKLLIYYDDL
LPSGVSDRFSGSKSGTSAFLAISGLQSEDEADYYCAAWDDSLNGPVFGGGTK
LTVL

[0168] Alternatively, a heavy chain variable domain represented by SEQ ID NO:103 can be paired with a light chain variable domain represented by SEQ ID NO:104 to form an antigen-binding site that can bind to NKG2D, as illustrated in US 7,879,985.

SEQ ID NO:103

QVHLQESGPGLVKPSETLSLTCTVSDDSISSYYWSWIRQPPGKGLEWIGHISYS
GSANYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCANWDDAFNIWG
QGTMVTVSS

SEQ ID NO:104

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASS
RATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

[0169] Table 2 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination, can bind to CXCR4.

Table 2		
Clones	Heavy chain variable domain amino acid sequence	Light chain variable domain amino acid sequence
Ulocuplumab	EVQLVESGGGLVQPGGSLRL SCAAAGFTFSSYSMNWVRQ APGKGLEWVSYISSRSRTIYY ADSVKGRFTISRDNAKNSLY LQMNSLRDEDTAVYYCARD YGGQPPYYYYYGMDVWGQ GTTVTVSSA (SEQ ID NO:109) CDR1 (SEQ ID NO:111) - GFTFSSY CDR2 (SEQ ID NO:112) - SSRSRT CDR3 (SEQ ID NO:113) - DYGGQPPYYYYYGMDV	DIQMTQSPSSLSASVGDRVT ITCRASQGISSWLAWYQQK PEKAPKSLIYAASSLQSGVP SRFSGSGSGTDFTLTISSLQP EDFVTYYCQQYNSYPRTFG QGTKVEIKR (SEQ ID NO:110) CDR1(SEQ ID NO:114) - QGISSWLA CDR2 (SEQ ID NO:115) - AASSLQS CDR3 (SEQ ID NO:116) - QQYNSYPRT
anti-CXCR4 (U.S. Patent No. 8,329,178)	QVQLVQSGAEVKKPGASVK VSCKASGYTFTSYGISWVRQ APGQGLEWMGWISAYNGNT NYAQKLQGRVTMTTDTSTS TAYMELRSLRSDDTAVYYC ARDTPGIAARRYYYYGMDV WGQGTTVTVSS (SEQ ID NO:117) CDR1 (SEQ ID NO:119) - GFTFSSY CDR2 (SEQ ID NO:120) - SAYNGN	SSELTQDPAVSVALGQTVRI TCQGDSLRKFFASWYQQKP GQAPVLVIYGKNSRPSGIPD RFSGSNSRNTASLTITGAQA EDEGDYYCNSRDSRDNHQ VFGAGTKVTVLS (SEQ ID NO:118) CDR1 (SEQ ID NO:122) - SLRKFFAS CDR2 (SEQ ID NO:123) - GKNSRPS CDR3 (SEQ ID NO:124) -

	CDR3 (SEQ ID NO:121) - DTPGIAARRYYYYGMDV	NSRDSRDNHQV
anti-CXCR4 (WO2009140124)	EVQLVESGGGLVQPGGSLRLSCAASGFTSTDYYFSWVRQAPGKGLEWVGFIRTKSKGYTTEYSGSVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCAREPITTDPRDYWGQGTLVTVSS (SEQ ID NO:125) CDR1 (SEQ ID NO:127) - GFTSTDYYFS CDR2 (SEQ ID NO:128) - FIRTKSKGYTTEYSGSVKG CDR3 (SEQ ID NO:129) - EPITTDPRDY	DIVMTQSPDSLAVSLGERATINCKSSQSLFNSRTRKKYLAWYQQKPGQPPKLLIYWASKRKSGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSRFLRAFGQGTKLEIK (SEQ ID NO:126) CDR1 (SEQ ID NO:130) - KSSQSLFNSRTRKKYL CDR2 (SEQ ID NO:131) - WASKRKS CDR3 (SEQ ID NO:132) - KQSRFLRA
US 2011/0020218 A1	EVQLVESGGGLVQPGRSLRLSCTASGFTFTDNYMSWVRQAPGKGLEWVGFIRNKANGYTTEYAASVKGRFTISRDNSKSIAYLQMNSLKTEDTAVYYCARDVGSNYFDYWGQGTLVTVSS (SEQ ID NO:522) CDR1 (SEQ ID NO:523): FTFTDNYMS CDR2 (SEQ ID NO:524): FIRNKANGYTTEYAASV CDR3 (SEQ ID NO:525): ARDVGSNYFDY	DIVMTQSPSSLAVSLGERATMSCKSSQSLFNSRTRKNYLAWYQQKPGQSPKLLIYWASARDSGVPARFTGSGSETYFTLTISRVQAEDLAVYYCMQSFNLRTFGQGTKVEIK (SEQ ID NO:526) CDR1 (SEQ ID NO:527): KSSQSLFNSRTRKNYLA CDR2 (SEQ ID NO:528): WASARDS CRD3 (SEQ ID NO:529): MQSFNLRT

[0170] Alternatively, novel antigen-binding sites that can bind to CXCR4 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:133.

SEQ ID NO:133

MEGISIYTSDNYTEEMGSGDYDSMKEPCFREENANFNKIFLPTIYSIIFLTGIVGNGLVI
LVMGYQKKLRSMTDKYRLHLSVADLLFVITLPFWAVDAVANWYFGNFLCKAVHVI
YTVNLYSSVLILAFISLDRYLAIVHATNSQRPRKLLAEKVVYVGVWIPALLLTIPDFIF
ANVSEADDRYICDRFYPNDLWVVVFQFQHIMVGLILPGIVILSCYCIIISKLSHSKGHQ
KRKALKTTVILILAFFACWLPYYIGISIDSFILLEIIKQGCEFENTVHKWISITEALAFFH
CCLNPILYAFLGAKFKTSAQHALTSVSRGSSLKILSKGKRGGHSSVSTESESSSFHSS

[0171] Table 3 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination, can bind to CD25.

Table 3		
Clones	Heavy chain variable domain amino acid sequence	Light chain variable domain amino acid sequence
Daclizumab	QVQLVQSGAEVKKPGSSVKVS CKASGYTFTSYRMHWVRQAP GQGLEWIGYINPSTGYTEYNQK FKDKATITADESTNTAYMELSS LRSEDTAVYYCARGGGVFDY WGQGTLVTVSSA (SEQ ID NO:134) CDR1 (SEQ ID NO:136) - GYTFTSY CDR2 (SEQ ID NO:137) - NPSTGY CDR3 (SEQ ID NO:138) - GGGVFDY	DIQMTQSPSTLSASVGDRVTI TCSASSSISYMHWYQQKPGK APKLLIYTTSNLASGVPARFS GSGSGTEFTLTISSLQPDDFA TYYCHQRSTYPLTFGQGTKV EVKR (SEQ ID NO:135) CDR1(SEQ ID NO:139) - SSISYMH CDR2 (SEQ ID NO:140) - TTSNLAS CDR3 (SEQ ID NO:141) - HQRSTYPLT
Basiliximab	QLQQSGTVLARPGASVKMSCK ASGYSFTRYWMHWIKQRPGQ GLEWIGAIYPGNSDTSYNQKFE	QIVSTQSPAIMSASPGEKVT MTCSASSSRSYMQWYQQKP GTSPKRWIYDTSKLASGVPA

	GKAKLTAVTSASTAYMELSSL THEDSAVYYCSRDYGYYFDFW GQGTTLTVSSA (SEQ ID NO:142) CDR1 (SEQ ID NO:144) - GYSFTRY CDR2 (SEQ ID NO:145) - YPGNSD CDR3 (SEQ ID NO:146) - DYGYYFDF	RFSGSGSGTSYSLTISSMEAE DAATYYCHQRSSYTFGGGT KLEIKR (SEQ ID NO:143) CDR1 (SEQ ID NO:147) - SSRSYMQ CDR2 (SEQ ID NO:148) - DTSKLAS CDR3 (SEQ ID NO:149) - HQRSSYT
Camidanlumab	QVQLVQSGAEVKKPGSSVKVS CKASGGTFSRYIINWVRQAPGQ GLEWMGRIIPILGVENYAQKFQ GRVTITADKSTSTAYMELSSLR SEDTAVYYCARKDWFDYWGQ GTLVTVSSA (SEQ ID NO:150) CDR1 (SEQ ID NO:152) - GGTFSRYIIN CDR2 (SEQ ID NO:153) - RIIPILGVENYAQKFQG CDR3 (SEQ ID NO:154) - KDWFDY	EIVLTQSPGTLSLSPGERATL SCRASQSVSSYLAWYQQKP GQAPRLLIYGASSRATGIPDR FSGSGSGTDFTLTISRLEPEDF AVYYCQQYGSSPLTFGGGT KVEIKR (SEQ ID NO:151) CDR1 (SEQ ID NO:155) - CRASQSVSSYLA CDR2 (SEQ ID NO:156) - GASSRAT CDR3 (SEQ ID NO:157) - QQYGSSPLT

[0172] Alternatively, novel antigen-binding sites that can bind to CD25 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:158.

SEQ ID NO:158

[0173] MDSYLLMWGLLTFIMVPGCQAELCDDDPPEIPHATFKAMAYKEGTMLNC ECKRGFRRIKSGSLYMLCTGNSSHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKT TEMQSPMQPVDQASLPGHCREPPPWENEATERIYHFVVGQMVYYQCVQGYRALHR GPAESVCKMTHGKTRWTQPQLICTGEMETSQFPGEEKPQASPEGRPESETSCLVTTT DFQIQTEMAATMETSIFTTEYQVAVAGCVFLLISVLLLSGLTWQRRQRKSRRTI

[0174] Antigen-binding sites that can bind to tumor associated antigen VLA4 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:159 or SEQ ID NO:160.

SEQ ID NO:159

MAWEARREPGPRRAAVRETVMLLLCLGVPTGRPYNVDTESALLYQGPHNTLFGYS
VVLHSHGANRWLLVGAPTANWLANASVINPGAIYRCRIGKNPGQTCEQLQLGSPNG
EPCGKTCLEERDNQWLGVTLSRQPGENGSIVTCGHRWKNIFYIKNENKLPTGGCYGV
PPDLRTELSKRIAPCYQDYVKKFGENFASCQAGISSFYTKDLIVMGAPGSSYWTGSLF
VYNITTNKYKAFLDKQNQVKFGSYLGYSVGAGHFRSQHTTEVVGGAPQHEQIGKAY
IFSIDEKELNILHEMKGKKLGSYFGASVCAVDLNADGFSDLLVGAPMQSTIREEGRVF
VYINSGSGAVMNAMETNLVGSDKYAARFGESIVNLGDIDNDGFEDVAIGAPQEDDL
QGAIYIYNGRADGISSTFSQRIEGLQISKSLSMFGQSISGQIDADNNGYVDVAVGAFRS
DSAVLLRTRPVVIVDASLSHPESVNRTKFDCVENGWPSVCIDLTLCFSYKGKEVPGYI
VLFYNMSLDVNRKAESPPRFYFSSNGTSDVITGSIQVSSREANCRTHQAFMRKDVRDI
LTPIQIEAAYHLGPHVISKRSTEEFPPLQPILQQKKEKDIMKKTINFARFCAHENCSAD
LQVSAKIGFLKPHENKTYLAVGSMKTLMLNVSLFNAGDDAYETTLHVKLPVGLYFI
KILELEEKQINCEVTDNSGVVQLDCSIGYIYVDHLSRIDISFLLDVSSLSRAEEDLSITV
HATCENEEEMDNLKHSRVTVAIPLKYEVKLTVHGFVNPTSFVYGSNDENEPETCMV
EKMNLTFHVINTGNSMAPNVSVEIMVPNSFSPQTDKLFNILDVQTTTGECHFENYQR
VCALEQQKSAMQTLKGIVRFLSKTDKRLLYCIKADPHCLNFLCNFGKMESGKEASV
HIQLEGRPSILEMDETSALKFEIRATGFPEPNPRVIELNKDENVAHVLLEGLHHQRPKR
YFTIVIISSSLLLGLIVLLLISYVMWKAGFFKRQYKSILQEENRRDSWSYINSKSNDD

SEQ ID NO:160

MNLQPIFWIGLISSVCCVFAQTDENRCLKANAKSCGECIQAGPNCGWCTNSTFLQEG
MPTSARCDDLEALKKKGCPPDDIENPRGSKDIKKNKNVTNRSKGTAEKLKPEDITQI
QPQQLVLRLRSGEPQTFTLKFKRAEDYPIDLYYLMDLSYSMKDDLENVKSLGTDLM
NEMRRITSDFRIGFGSFVEKTVMPYISTTPAKLRNPCTSEQNCTSPFSYKNVLSLTNKG
EVFNELVGKQRISGNLDSPEGGFDAIMQVAVCGSLIGWRNVTRLLVFSTDAGFHFAG
DGKLGGIVLPNDGQCHLENNMYTMSHYYDYPSIAHLVQKLSENNIQTIFAVTEEFQP
VYKELKNLIPKSAVGTLSANSSNVIQLIIDAYNSLSSEVILENGKLSEGVTISYKSYCK
NGVNGTGENGRKCSNISIGDEVQFEISITSNKCPKKDSDSFKIRPLGFTEEVEVILQYIC
ECECQSEGIPESPKCHEGNGTFECGACRCNEGRVGRHCECSTDEVNSEDMDAYCRK
ENSSEICSNNGECVCGQCVCRKRDNTNEIYSGKFCECDNFNCDRSNGLICGGNGVCK

CRVCECNPNYTGSACDCSLDTSTCEASNGQICNGRGICECGVCKCTDPKFQGQTCEM
CQTCLGVCAEHKECVQCRAFNKGEKKDTCTQECSYFNITKVESRDKLPQPVQPDPVS
HCKEKDVDDCWFYFTYSVNGNNEVMVHVVENPECPTGPDIIPIVAGVVAGIVLIGLA
LLLIWKLLMIIHDRREFAKFEKEKMNAKWDTGENPIYKSAVTTVVNPKYEGK

[0175] Antigen-binding sites that can bind to tumor associated antigen CD44 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:161.

SEQ ID NO:161

MDKFWWHAAWGLCLVPLSLAQIDLNITCRFAGVFHVEKNGRYSISRTEAADLCKAF
NSTLPTMAQMEKALSIGFETCRYGFIEGHVVIPRIHPNSICAANNTGVYILTSNTSQYD
TYCFNASAPPEEDCTSVTDLPNAFDGPITITIVNRDGTRYVQKGEYRTNPEDIYPSNPT
DDDVSSGSSSERSSTSGGYIFYTFSTVHPIPDEDSPWITDSTDRIPATTLMSTSATATET
ATKRQETWDWFSWLFLPSESKNHLHTTTQMAGTSSNTISAGWEPNEENEDERDRHL
SFSGSGIDDDEDFISSTISTTPRAFDHTKQNQDWTQWNPSHSNPEVLLQTTTRMTDVD
RNGTTAYEGNWNPEAHPPLIHHEHHEEEETPHSTSTIQATPSSTTEETATQKEQWFGN
RWHEGYRQTPKEDSHSTTGTAAASAHTSHPMQGRTTPSPEDSSWTDFFNPISHPMGR
GHQAGRRMDMDSSHSITLQPTANPNTGLVEDLDRTGPLSMTTQQSNSQSFSTSHEGL
EEDKDHPTTSTLTSSNRNDVTGGRRDPNHSEGSTTLLEGYTSHYPHTKESRTFIPVTS
AKTGSFGVTAVTVGDSNSNVNRSLSGDQDTFHPSGGSHTTHGSESDGHSHGSQEGG
ANTTSGPIRTPQIPEWLIILASLLALALILAVCIAVNSRRRCGQKKKLVINSGNGAVED
RKPSGLNGEASKSQEMVHLVNKESSETPDQFMTADETRNLQNVDMKIGV

[0176] Antigen-binding sites that can bind to tumor associated antigen CD13 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:162.

SEQ ID NO:162

MAKGFYISKSLGILGILLGVAAVCTIIALSVVYSQEKNKNANSSPVASTTPSASATTNP
ASATTLDQSKAWNRYRLPNTLKPDSYRVTLRPYLTPNDRGLYVFKGSSTVRFTCKE
ATDVIIIHSKKLNYTLSQGHRVVLRGVGGSQPPDIDKTELVEPTEYLVVHLKGSLVKD
SQYEMDSEFEGELADDLAGFYRSEYMEGNVRKVVATTQMQAADARKSFPCFDEPA
MKAEFNITLIHPKDLTALSNMLPKGPSTPLPEDPNWNVTEFHTTPKMSTYLLAFIVSE
FDYVEKQASNGVLIRIWARPSAIAAGHGDYALNVTGPILNFFAGHYDTPYPLPKSDQI
GLPDFNAGAMENWGLVTYRENSLLFDPLSSSSSNKERVVTVIAHELAHQWFGNLVTI
EWWNDLWLNEGFASYVEYLGADYAEPTWNLKDLMVLNDVYRVMAVDALASSHP
LSTPASEINTPAQISELFDAISYSKGASVLRMLSSFLSEDVFKQGLASYLHTFAYQNTI

YLNLWDHLQEAVNNRSIQLPTTVRDIMNRWTLQMGFPVITVDTSTGTLSQEHFLLDP
DSNVTRPSEFNYVWIVPITSIRDGRQQQDYWLIDVRAQNDLFSTSGNEWVLLNLNVT
GYYRVNYDEENWRKIQTQLQRDHSAIPVINRAQIINDAFNLASAHKVPVTLALNNTL
FLIEERQYMPWEAALSSLSYFKLMFDRSEVYGPMKNYLKKQVTPLFIHFRNNTNNW
REIPENLMDQYSEVNAISTACSNGVPECEEMVSGLFKQWMENPNNNPIHPNLRSTVY
CNAIAQGGEEEWDFAWEQFRNATLVNEADKLRAALACSKELWILNRYLSYTLNPDL
IRKQDATSTIISITNNVIGQGLVWDFVQSNWKKLFNDYGGGSFSFSNLIQAVTRRFSTE
YELQQLEQFKKDNEETGFGSGTRALEQALEKTKANIKWVKENKEVVLQWFTENSK

[0177] Antigen-binding sites that can bind to tumor associated antigen CD15 can be identified by screening for binding to 3-fucosyl-N-acetyl-lactosamine.

[0178] Antigen-binding sites that can bind to tumor associated antigen CD47 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:163.

SEQ ID NO:163

MWPLVAALLLGSACCGSAQLLFNKTKSVEFTFCNDTVVIPCFVTNMEAQNTTEVYV
KWKFKGRDIYTFDGALNKSTVPTDFSSAKIEVSQLLKGDASLKMDKSDAVSHTGNY
TCEVTELTREGETIIELKYRVVSWFSPNENILIVIFPIFAILLFWGQFGIKTLKYRSGGM
DEKTIALLVAGLVITVIVIVGAILFVPGEYSLKNATGLGLIVTSTGILILLHYYVFSTAIG
LTSFVIAILVIQVIAYILAVVGLSLCIAACIPMHGPLLISGLSILALAQLLGLVYMKFVA
SNQKTIQPPRKAVEEPLNAFKESKGMMNDE

[0179] Antigen-binding sites that can bind to tumor associated antigen CD81 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:165.

SEQ ID NO:165

MGVEGCTKCIKYLLFVFNFVFWLAGGVILGVALWLRHDPQTTNLLYLELGDKPAPN
TFYVGIYILIAVGAVMMFVGFLGCYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFV
NKDQIAKDVKQFYDQALQQAVVDDDANNAKAVVKTFHETLDCCGSSTLTALTTSV
LKNNLCPSGSNIISNLFKEDCHQKIDDLFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCG
IRNSSVY

[0180] Alternatively, Table 4 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination, can bind to VLA4 (Natalizumab), CD44 (Bivatuzumab), or CD47.

Table 4		
Clones	Heavy chain variable domain amino acid sequence	Light chain variable domain amino acid sequence
Natalizumab	VKLQQSGAELVKPGASVKLF CTASGFNIKDTYMHWVKQR PQQGLEWIGRIDPASGDTKY DPKFQVKATITADTSSNTAW LQLSSLTSEDTAVYYCADGM WVSTGYALDFWGQGTTVTV SS (SEQ ID NO:166) CDR1 (SEQ ID NO:168) - GFNIKDT CDR2 (SEQ ID NO:169) - DPASGD CDR3 (SEQ ID NO:170) - GMWVSTGYALDF	SIVMTQTPKFLLVSAGDRVTITCK ASQSVTNDVAWYQQKPGQSPKL LIYYASNRYTGVPDRFTGSGYGT DFTFTISTVQAEDLAVYFCQQDYS SPYTFGGGTKLEI (SEQ ID NO:167) CDR1(SEQ ID NO:171) - QSVTNDVA CDR2 (SEQ ID NO:172) - YASNRYT CDR3 (SEQ ID NO:173) - QQDYSSPYT
Bivatuzumab	EVQLVESGGGLVKPGGSLRL SCAASGFTFSSYDMSWVRQ APGKGLEWVSTISSGGSYTY YLDSIKGRFTISRDNAKNSLY LQMNSLRAEDTAVYYCARQ GLDYWGRGTLVTVSSA (SEQ ID NO:174) CDR1 (SEQ ID NO:176) - GFTFSSY CDR2 (SEQ ID NO:177) - SSGGSY CDR3 (SEQ ID NO:178) - QGLDY	EIVLTQSPATLSLSPGERATLSCSA SSSINYIYWYQQKPGQAPRLLIYL TSNLASGVPARFSGSGSGTDFTLT ISSLEPEDFAVYYCLQWSSNPLTF GGGTKVEIKR (SEQ ID NO:175) CDR1 (SEQ ID NO:179) - SSINYIY CDR2 (SEQ ID NO:180) - LTSNLAS CDR3 (SEQ ID NO:181) - LQWSSNPLT
Anti-CD47 (WO	QVQLVQSGAEVKKPGASVK VSCKASGYTFTNYNMHWVR	DIVMTQSPLSLPVTPGEPASISCRS SQSIVYSNGNTYLGWYLQKPGQS

2011143624)	QAPGQRLEWMGTIYPGNDD TSYNQKFKDRVTITADTSAS TAYMELSSLRSEDTAVYYCA RGGYRAMDYWGQGTLVTV SS (SEQ ID NO:182) CDR1 (SEQ ID NO:184) - GYTFTNYNMH CDR2 (SEQ ID NO:185) - TIYPGNDDTSYNQKFKD CDR3 (SEQ ID NO:186) - GGYRAMDY	PQLLIYKVSNRFSGVPDRFSGSGS GTDFTLKISRVEAEDVGVYYCFQ GSHVPYTFGQGTKLEIK (SEQ ID NO:183) CDR1 (SEQ ID NO:187) - RSSQSIVYSNGNTYLG CDR2 (SEQ ID NO:188) - KVSNRFS CDR3 (SEQ ID NO:189) - FQGSHVPYT

[0181] Antigen-binding sites that can bind to tumor associated antigen CD23 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:190.

SEQ ID NO:190

MEEGQYSEIEELPRRRCCRRGTQIVLLGLVTAALWAGLLTLLLLWHWDTTQSLKQL
EERAARNVSQVSKNLESHHGDQMAQKSQSTQISQELEELRAEQQRLKSQDLELSWN
LNGLQADLSSFKSQELNERNEASDLLERLREEVTKLRMELQVSSGFVCNTCPEKWIN
FQRKCYYFGKGTKQWVHARYACDDMEGQLVSIHSPEEQDFLTKHASHTGSWIGLR
NLDLKGEFIWVDGSHVDYSNWAPGEPTSRSQGEDCVMMRGSGRWNDAFCDRKLG
AWVCDRLATCTPPASEGSAESMGPDSRPDPDGRLPTPSAPLHS

[0182] Antigen-binding sites that can bind to tumor associated antigen CD40 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:191.

SEQ ID NO:191

MVRLPLQCVLWGCLLTAVHPEPPTACREKQYLINSQCCSLCQPGQKLVSDCTEFTET
ECLPCGESEFLDTWNRETHCHQHKYCDPNLGLRVQQKGTSETDTICTCEEGWHCTSE
ACESCVLHRSCSPGFGVKQIATGVSDTICEPCPVGFFSNVSSAFEKCHPWTSCETKDL
VVQQAGTNKTDVVCGPQDRLRALVVIPIIFGILFAILLVLVFIKKVAKKPTNKAPHPK
QEPQEINFPDDLPGSNTAAPVQETLHGCQPVTQEDGKESRISVQERQ

[0183] Antigen-binding sites that can bind to tumor associated antigen CD70 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:192.

SEQ ID NO:192

MPEEGSGCSVRRRPYGCVLRAALVPLVAGLVICLVVCIQRFAQAQQQLPLESLGWD
VAELQLNHTGPQQDPRLYWQGGPALGRSFLHGPELDKGQLRIHRDGIYMVHIQVTL
AICSSTTASRHHPTTLAVGICSPASRSISLLRLSFHQGCTIASQRLTPLARGDTLCTNLT
GTLLPSRNTDETFFGVQWVRP

[0184] Antigen-binding sites that can bind to tumor associated antigen CD79a can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:193.

SEQ ID NO:193

MPGGPGVLQALPATIFLLFLLSAVYLGPGCQALWMHKVPASLMVSLGEDAHFQCPH
NSSNNANVTWWRVLHGNYTWPPEFLGPGEDPNGTLIIQNVNKSHGGIYVCRVQEGN
ESYQQSCGTYLRVRQPPPRPFLDMGEGTKNRIITAEGIILLFCAVVPGTLLLFRKRWQ
NEKLGLDAGDEYEDENLYEGLNLDDCSMYEDISRGLQGTYQDVGSLNIGDVQLEKP

[0185] Antigen-binding sites that can bind to tumor associated antigen CD79b can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:194.

SEQ ID NO:194

MARLALSPVPSHWMVALLLLLSAEPVPAARSEDRYRNPKGSACSRIWQSPRFIARKR
GFTVKMHCYMNSASGNVSWLWKQEMDENPQQLKLEKGRMEESQNESLATLTIQGI
RFEDNGIYFCQQKCNNTSEVYQGCGTELRVMGFSTLAQLKQRNTLKDGIIMIQTLLII
LFIIVPIFLLLDKDDSKAGMEEDHTYEGLDIDQTATYEDIVTLRTGEVKWSVGEHPGQ
E

[0186] Antigen-binding sites that can bind to tumor associated antigen CD80 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:195.

SEQ ID NO:195

MGHTRRQGTSPSKCPYLNFFQLLVLAGLSHFCSGVIHVTKEVKEVATLSCGHNVSVE
ELAQTRIYWQKEKKMVLTMMSGDMNIWPEYKNRTIFDITNNLSIVILALRPSDEGTY
ECVVLKYEKDAFKREHLAEVTLSVKADFPTPSISDFEIPTSNIRRIICSTSGGFPEPHLS
WLENGEELNAINTTVSQDPETELYAVSSKLDFNMTTNHSFMCLIKYGHLRVNQTFN
WNTTKQEHFPDNLLPSWAITLISVNGIFVICCLTYCFAPRCRERRRNERLRRESVRPV

[0187] Antigen-binding sites that can bind to tumor associated antigen CRLF2 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:196.

SEQ ID NO:196

MGRLVLLWGAAVFLLGGWMALGQGGAAEGVQIQIIYFNLETVQVTWNASKYSRTN
LTFHYRFNGDEAYDQCTNYLLQEGHTSGCLLDAEQRDDILYFSIRNGTHPVFTASRW
MVYYLKPSSPKHVRFSWHQDAVTVTCSDLSYGDLLYEVQYRSPFDTEWQSKQENT
CNVTIEGLDAEKCYSFWVRVKAMEDVYGPDTYPSDWSEVTCWQRGEIRDACAETPT
PPKPKLSKFILISSLAILLMVSLLLLSLWKLWRVKKFLIPSVPDPKSIFPGLFEIHQGNFQ
EWITDTQNVAHLHKMAGAEQESGPEEPLVVQLAKTEAESPRMLDPQTEEKEASGGS
LQLPHQPLQGGDVVTIGGFTFVMNDRSYVAL

[0188] Alternatively, table 5 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination, can bind to CD23 (lumiliximab), CD40 (dacetuzumab, selicrelumab, lucatumumab, bleselumab), CD70 (vorsetuzumab), CD79b (polatuzumab), CD80 (galiximab), or CRLF2 (US20160046720).

Table 5		
Clones	Heavy chain variable domain amino acid sequence	Light chain variable domain amino acid sequence
lumiliximab	EVQLVESGGGLAKPGGSLRLSC AASGFRFTFNNYYMDWVRQA PGQGLEWVSRISSSGDPTWYA DSVKGRFTISRENANNTLFLQM NSLRAEDTAVYYCASLTTGSDS WGQGVLVTVSS (SEQ ID NO:197) CDR1 (SEQ ID NO:199) - GFRFTFNNY CDR2 (SEQ ID NO:200) - SSSGDP CDR3 (SEQ ID NO:201) – LTTGSDS	DIQMTQSPSSLSASVGDRVTI TCRASQDIRYYLNWYQQKP GKAPKLLIYVASSLQSGVPS RFSGSGSGTEFTLTVSSLQPE DFATYYCLQVYSTPRTFGQG TKVEIK (SEQ ID NO:198) CDR1(SEQ ID NO:202) - QDIRYYLN CDR2 (SEQ ID NO:203) - VASSLQS CDR3 (SEQ ID NO:204) - LQVYSTPRT
dacetuzumab	EVQLVESGGGLVQPGGSLRLSC AASGYSFTGYYIHWVRQAPGK GLEWVARVIPNAGGTSYNQKF	DIQMTQSPSSLSASVGDRVTI TCRSSQSLVHSNGNTFLHW YQQKPGKAPKLLIYTVSNRF

	KGRFTLSVDNSKNTAYLQMNS LRAEDTAVYYCAREGIYWWG QGTLVTVSSA (SEQ ID NO:205) CDR1 (SEQ ID NO:207) - GYSFTGY CDR2 (SEQ ID NO:208) - IPNAGG CDR3 (SEQ ID NO:209) – EGIYW	SGVPSRFSGSGSGTDFTLTIS SLQPEDFATYFCSQTTHVPW TFGQGTKVEIKR (SEQ ID NO:206) CDR1 (SEQ ID NO:210) - QSLVHSNGNTFLH CDR2 (SEQ ID NO:211) - TVSNRFS CDR3 (SEQ ID NO:212) – SQTTHVPWT
selicrelumab	QVQLVQSGAEVKKPGASVKVS CKASGYTFTGYYMHWVRQAP GQGLEWMGWINPDSGGTNYA QKFQGRVTMTRDTSISTAYME LNRLRSDDTAVYYCARDQPLG YCTNGVCSYFDYWGQGTLVT VSSA (SEQ ID NO:213) CDR1 (SEQ ID NO:215) - GYTFTGY CDR2 (SEQ ID NO:216) - NPDSGG CDR3 (SEQ ID NO:217) - DQPLGYCTNGVCSYFDY	DIQMTQSPSSVSASVGDRVT ITCRASQGIYSWLAWYQQK PGKAPNLLIYTASTLQSGVPS RFSGSGSGTDFTLTISSLQPE DFATYYCQQANIFPLTFGGG TKVEIKR (SEQ ID NO:214) CDR1 (SEQ ID NO:218) - QGIYSWLA CDR2 (SEQ ID NO:219) - TASTLQS CDR3 (SEQ ID NO:220) - QQANIFPLT
lucatumumab	QVQLVESGGGVVQPGRSLRLS CAASGFTFSSYGMHWVRQAPG KGLEWVAVISYEESNRYHADS VKGRFTISRDNSKITLYLQMNS LRTEDTAVYYCARDGGIAAPG PDYWGQGTLVTVSSA (SEQ ID NO:221) CDR1 (SEQ ID NO:223) - GFTFSSY	DIVMTQSPLSLTVTPGEPASI SCRSSQSLLYSNGYNYLDW YLQKPGQSPQVLISLGSNRA SGVPDRFSGSGSGTDFTLKIS RVEAEDVGVYYCMQARQTP FTFGPGTKVDIRR (SEQ ID NO:222) CDR1(SEQ ID NO:226) - QSLLYSNGYNYLD

	CDR2 (SEQ ID NO:224) - SYEESN CDR3 (SEQ ID NO:225) - DGGIAAPGPDY	CDR2 (SEQ ID NO:227) - LGSNRAS CDR3 (SEQ ID NO:228) - MQARQTPFT
Bleselumab ASKP1240	QVQLQQSGPGLVKPSQTLSLTC AISGDSVSSNSATWNWIRQSPS RDLEWLGRTYYRSKWYRDYV GSVKSRIIINPDTSNNQFSLQLN SVTPEDTAIYYCTRAQWLGGD YPYYYSMDVWGQGTTVTVSS (SEQ ID NO:229) CDR1 (SEQ ID NO:231) - GDSVSSNSA CDR2 (SEQ ID NO:232) - YYRSKWY CDR3 (SEQ ID NO:233) - AQWLGGDYPYYYSMDV	EIVLTQSPATLSLSPGERATL SCRASQSVSSYLAWYQQKP GQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPE DFAVYYCQQRSNTFGPGTK VDIK (SEQ ID NO:230) CDR1 (SEQ ID NO:234) - QSVSSYLA CDR2 (SEQ ID NO:235) - DASNRAT CDR3 (SEQ ID NO:236) - QQRSNT
vorsetuzumab	QVQLVQSGAEVKKPGASVKVS CKASGYTFTNYGMNWVRQAP GQGLKWMGWINTYTGEPTYA DAFKGRVTMTRDTSISTAYME LSRLRSDDTAVYYCARDYGDY GMDYWGQGTTVTVSSA (SEQ ID NO:237) CDR1 (SEQ ID NO:239) - GYTFTNY CDR2 (SEQ ID NO:240) - NTYTGE CDR3 (SEQ ID NO:241) - DYGDYGMDY	DIVMTQSPDSLAVSLGERAT INCRASKSVSTSGYSFMHWY QQKPGQPPKLLIYLASNLES GVPDRFSGSGSGTDFTLTISS LQAEDVAVYYCQHSREVPW TFGQGTKVEIKR (SEQ ID NO:238) CDR1 (SEQ ID NO:242) - KSVSTSGYSFMH CDR2 (SEQ ID NO:243) - LASNLES CDR3 (SEQ ID NO:244) – QHSREVPWT
polatuzumab	EVQLVESGGGLVQPGGSLRLSC AASGYTFSSYWIEWVRQAPGK	DIQLTQSPSSLSASVGDRVTI TCKASQSVDYEGDSFLNWY

	GLEWIGEILPGGGDTNYNEIFK GRATFSADTSKNTAYLQMNSL RAEDTAVYYCTRRVPIRLDYW GQGTLVTVSSA (SEQ ID NO:245) CDR1 (SEQ ID NO:247) - GYTFSSY CDR2 (SEQ ID NO:248) - LPGGGD CDR3 (SEQ ID NO:249) - RVPIRLDY	QQKPGKAPKLLIYAASNLES GVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQSNEDPLT FGQGTKVEIKR (SEQ ID NO:246) CDR1 (SEQ ID NO:250) - QSVDYEGDSFLN CDR2 (SEQ ID NO:251) - AASNLES CDR3 (SEQ ID NO:252) - QQSNEDPLT
galiximab	QVQLQESGPGLVKPSETLSLTC AVSGGSISGGYGWGWIRQPPG KGLEWIGSFYSSSGNTYYNPSL KSQVTISTDTSKNQFSLKLNSM TAADTAVYYCVRDRLFSVVG MVYNNWFDVWGPGVLVTVSS A (SEQ ID NO:253) CDR1 (SEQ ID NO:255) - GGSISGGY CDR2 (SEQ ID NO:256) - YSSSGN CDR3 (SEQ ID NO:257) - DRLFSVVGMVYNNWFDV	ESALTQPPSVSGAPGQKVTIS CTGSTSNIGGYDLHWYQQL PGTAPKLLIYDINKRPSGISD RFSGSKSGTAASLAITGLQTE DEADYYCQSYDSSLNAQVF GGGTRLTVLG (SEQ ID NO:254) CDR1 (SEQ ID NO:258) - TSNIGGYDLH CDR2 (SEQ ID NO:259) - DINKRPS CDR3 (SEQ ID NO:260) - QSYDSSLNAQV
US20160046720	EVQLLESGGGLVQPGGSLRLSC AASGFTFRSSAMHWVRQAPGK GLKWVSSVSGSGAGTYYADSV KGRFTISRDNPKNTLYLQMNSL RAEDTAVYYCVKEGGSRGFDY WGQGTLVTVSS (SEQ ID NO:261) CDR1 (SEQ ID NO:263) -	DIQMTQSPSSLSASVGDRVTI TCRASQDISNYLAWFQQKP GKAPKSLIYTASSLQSGVPS KFSGSGSGTDFTLTISSLQPE DFATYYCQQYNLYPPTFGQ GTKVEIKR (SEQ ID NO:262) CDR1 (SEQ ID NO:266) -

	GFTFRSS CDR2 (SEQ ID NO:264) - SVSGSGAGTYYADSVKG CDR3 (SEQ ID NO:265) - EGGSRGFDY	QDISNYLA CDR2 (SEQ ID NO:267) - YTASSLQSGVPSKFS CDR3 (SEQ ID NO:268) - QQYNLYPPT

[0189] Antigen-binding sites that can bind to tumor associated antigen SLAMF7 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:269.

SEQ ID NO:269

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNT
TPLVTIQPEGGTIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPS
TQEYVLHVYEHLSKPKVTMGLQSNKNGTCVTNLTCCMEHGEEDVIYTWKALGQAA
NESHNGSILPISWRWGESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLL
CLLLVPLLLSLFVLGLFLWFLKRERQEEYIEEKKRVDICRETPNICPHSGENTEYDTIP
HTNRTILKEDPANTVYSTVEIPKKMENPHSLLTMPDTPRLFAYENVI

[0190] Antigen-binding sites that can bind to tumor associated antigen CD38 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:270.

SEQ ID NO:270

MANCEFSPVSGDKPCCRLSRRAQLCLGVSILVLILVVVLAVVVPRWRQQWSGPGTT
KRFPETVLARCVKYTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLG
TQTVPCNKILLWSRIKDLAHQFTQVQRDMFTLEDTLLGYLADDLTWCGEFNTSKINY
QSCPDWRKDCSNNPVSVFWKTVSRRFAEAACDVVHVMLNGSRSKIFDKNSTFGSVE
VHNLQPEKVQTLEAWVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCKNIYRPDKFL
QCVKNPEDSSCTSEI

[0191] Antigen-binding sites that can bind to tumor associated antigen CD138 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:271.

SEQ ID NO:271

MRRAALWLWLCALALSLQPALPQIVATNLPPEDQDGSGDDSDNFSGSGAGALQDIT
LSQQTPSTWKDTQLLTAIPTSPEPTGLEATAASTSTLPAGEGPKEGEAVVLPEVEPGLT
AREQEATPRPRETTQLPTTHLASTTTATTAQEPATSHPHRDMQPGHHETSTPAGPSQ
ADLHTPHTEDGGPSATERAAEDGASSQLPAAEGSGEQDFTFETSGENTAVVAVEPDR

RNQSPVDQGATGASQGLLDRKEVLGGVIAGGLVGLIFAVCLVGFMLYRMKKKDEG SYSLEEPKQANGGAYQKPTKQEEFYA

[0192] Alternatively, Table 6 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination, can bind to SLAMF7 (elotuzumab, azintuxizumab), CD138 (indatuximab), or CD38 (daratumumab, MOR202).

Table 6		
Clones	Heavy chain variable domain amino acid sequence	Light chain variable domain amino acid sequence
elotuzumab	EVQLVESGGGLVQPGGSLRLS CAASGFDFSRYWMSWVRQAP GKGLEWIGEINPDSSTINYAPS LKDKFIISRDNAKNSLYLQMN SLRAEDTAVYYCARPDGNYW YFDVWGQGTLVTVSSA (SEQ ID NO:272) CDR1 (SEQ ID NO:274) - GFDFSRY CDR2 (SEQ ID NO:275) - NPDSST CDR3 (SEQ ID NO:276) - PDGNYWYFDV	DIQMTQSPSSLSASVGDRVTITC KASQDVGIAVAWYQQKPGKVP KLLIYWASTRHTGVPDRFSGSG SGTDFTLTISSLQPEDVATYYCQ QYSSYPYTFGQGTKVEIKR (SEQ ID NO:273) CDR1(SEQ ID NO:277) - QDVGIAVA CDR2 (SEQ ID NO:278) - WASTRHT CDR3 (SEQ ID NO:279) - QQYSSYPYT
azintuxizumab	EVQLVESGGGLVQPGGSLRLS CAASGFTFSDYYMAWVRQAP GKGLEWVASINYDGSSTYYV DSVKGRFTISRDNAKNSLYLQ MNSLRAEDTAVYYCARDRGY YFDYWGQGTTVTVSSA (SEQ ID NO:280) CDR1 (SEQ ID NO:282) - GFTFSDYYMA	DVVMTQTPLSLSVTPGQPASISC RSSQSLVHSNGNTYLHWYLQK PGQSPQLLIYKVSNRFSGVPDRF SGSGSGTDFTLKISRVEAEDVG VYFCSQSTHVPPFTFGGGTKVEI KR (SEQ ID NO:281) CDR1 (SEQ ID NO:285) - CRSSQSLVHSNGNTYLH

	CDR2 (SEQ ID NO:283) - SINYDGSSTYYVDSVKGRFTIS RDNA CDR3 (SEQ ID NO:284) - DRGYYFDY	CDR2 (SEQ ID NO:286) - KVSNRFS CDR3 (SEQ ID NO:287) - SQSTHVPPFT
indatuximab	QVQLQQSGSELMMPGASVKIS CKATGYTFSNYWIEWVKQRP GHGLEWIGEILPGTGRTIYNEK FKGKATFTADISSNTVQMQLS SLTSEDSAVYYCARRDYYGNF YYAMDYWGQGTSVTVSSA (SEQ ID NO:288) CDR1 (SEQ ID NO:290) - GYTFSNY CDR2 (SEQ ID NO:291) - LPGTGR CDR3 (SEQ ID NO:292) - RDYYGNFYYAMDY	DIQMTQSTSSLSASLGDRVTISC SASQGINNYLNWYQQKPDGTV ELLIYYTSTLQSGVPSRFSGSGS GTDYSLTISNLEPEDIGTYYCQQ YSKLPRTFGGGTKLEIKR (SEQ ID NO:289) CDR1(SEQ ID NO:293) - QGINNYLN CDR2 (SEQ ID NO:294) - YTSTLQS CDR3 (SEQ ID NO:295) - QQYSKLPRT
daratumumab	EVQLLESGGGLVQPGGSLRLS CAVSGFTFNSFAMSWVRQAP GKGLEWVSAISGSGGGTYYA DSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYFCAKDKIL WFGEPVFDYWGQGTLVTVSS A (SEQ ID NO:296) CDR1 (SEQ ID NO:298) - GFTFNSF CDR2 (SEQ ID NO:299) - SGSGGG CDR3 (SEQ ID NO:300) - DKILWFGEPVFDY	EIVLTQSPATLSLSPGERATLSC RASQSVSSYLAWYQQKPGQAP RLLIYDASNRATGIPARFSGSGS GTDFTLTISSLEPEDFAVYYCQQ RSNWPPTFGQGTKVEIKR (SEQ ID NO:297) CDR1 (SEQ ID NO:301) - QSVSSYLA CDR2 (SEQ ID NO:302) - DASNRAT CDR3 (SEQ ID NO:303) - QQRSNWPPT

MOR202	QVQLVESGGGLVQPGGSLRLS CAASGFTFSSYYMNWVRQAP GKGLEWVSGISGDPSNTYYAD SVKGRFTISRDNSKNTLYLQM NSLRAEDTAVYYCARDLPLV YTGFAYWGQGTLVTVSS (SEQ ID NO:304) CDR1 (SEQ ID NO:306) - GFTFSSYYMN CDR2 (SEQ ID NO:307) - GISGDPSNTYYADSVKGRFTIS RDNS CDR3 (SEQ ID NO:308) - DLPLVYTGFAY	DIELTQPPSVSVAPGQTARISCS GDNLRHYYWWYQQKPGQAPV LVIYGDSKRPSGIPERFSGSNSG NTATLTISGTQAEDEADYYCQT YTGGASLVFGGGTKLTVLGQ (SEQ ID NO:305) CDR1 (SEQ ID NO:309) - SGDNLRHYYW CDR2 (SEQ ID NO:310) - GDSKRPS CDR3 (SEQ ID NO:311) - QTYTGGASLV

[0193] Antigen-binding sites that can bind to tumor associated antigen TRBC1 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:312.

SEQ ID NO:312

EDLNKVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGKEVHSGVS TDPQPLKEQPALNDSRYCLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWTQDR AKPVTQIVSAEAWGRADCGFTSVSYQQGVLSATILYEILLGKATLYAVLVSALVLMA MVKRKDF

[0194] Antigen-binding sites that can bind to tumor associated antigen TRBC2 can be identified by screening for binding to the amino acid sequence defined by SEQ ID NO:313.

SEQ ID NO:313

DLKNVFPPEVAVFEPSEAEISHTQKATLVCLATGFYPDHVELSWWVNGKEVHSGVST DPQPLKEQPALNDSRYCLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWTQDRA KPVTQIVSAEAWGRADCGFTSESYQQGVLSATILYEILLGKATLYAVLVSALVLMAM VKRKDSRG

[0195] Antigen-binding sites that bind to different tumor associated antigens can be routinely identified by screening for binding to the amino acid sequence of each antigen. For example, antigen-binding sites that bind to LILRB2 can be routinely identified by screening for binding to the amino acid sequence of LILRB2 as defined by SEQ ID NO:314.

SEQ ID NO:314

MTPIVTVLICLGLSLGPRTHVQTGTIPKPTLWAEPDSVITQGSPVTLSCQGSLEAQEYR
LYREKKSASWITRIRPELVKNGQFHIPSITWEHTGRYGCQYYSRARWSELSDPLVLV
MTGAYPKPTLSAQPSPVVTSGGRVTLQCESQVAFGGFILCKEGEEEHPQCLNSQPHA
RGSSRAIFSVGPVSPNRRWSHRCYGYDLNSPYVWSSPSDLLELLVPGVSKKPSLSVQP
GPVVAPGESLTLQCVSDVGYDRFVLYKEGERDLRQLPGRQPQAGLSQANFTLGPVS
RSYGGQYRCYGAHNLSSECSAPSDPLDILITGQIRGTPFISVQPGPTVASGENVTLLCQ
SWRQFHTFLLTKAGAADAPLRLRSIHEYPKYQAEFPMSPVTSAHAGTYRCYGSLNSD
PYLLSHPSEPLELVVSGPSMGSSPPPTGPISTPAGPEDQPLTPTGSDPQSGLGRHLGVVI
GILVAVVLLLLLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWR
SSPAADAQEENLYAAVKDTQPEDGVEMDTRAAASEAPQDVTYAQLHSLTLRRKATE
PPPSQEREPPAEPSIYATLAIH

[0196] Antigen-binding sites that bind to LILRB1 can be routinely identified by screening for binding to the amino acid sequence of LILRB1 as defined by SEQ ID NO:315.

SEQ ID NO:315

MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVITQGSPVTLRCQGGQETQEY
RLYREKKTALWITRIPQELVKKGQFPIPSITWEHAGRYRCYYGSDTAGRSESSDPLEL
VVTGAYIKPTLSAQPSPVVNSGGNVILQCDSQVAFDGFSLCKEGEDEHPQCLNSQPH
ARGSSRAIFSVGPVSPSRRWWYRCYAYDSNSPYEWSLPSDLLELLVLGVSKKPSLSV
QPGPIVAPEETLTLQCGSDAGYNRFVLYKDGERDFLQLAGAQPQAGLSQANFTLGPV
SRSYGGQYRCYGAHNLSSEWSAPSDPLDILIAGQFYDRVSLSVQPGPTVASGENVTL
LCQSQGWMQTFLLTKEGAADDPWRLRSTYQSQKYQAEFPMGPVTSAHAGTYRCYG
SQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRH
LGVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRG
LQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPR
REMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATE
PPPSQEGPSPAVPSIYATLAIH

[0197] Antigen-binding sites that bind to LILRB3 can be routinely identified by screening for binding to the amino acid sequence of LILRB3 as defined by SEQ ID NO:316.

SEQ ID NO:316

MTPALTALLCLGLSLGPRTRVQAGPFPKPTLWAEPGSVISWGSPVTIWCQGSQEAQE
YRLHKEGSPEPLDRNNPLEPKNKARFSIPSMTEHHAGRYRCHYYSSAGWSEPSDPLE
MVMTGAYSKPTLSALPSPVVASGGNMTLRCGSQKGYHHFVLMKEGEHQLPRTLDS
QQLHSRGFQALFPVGPVTPSHRWRFTCYYYYTNTPWVWSHPSDPLEILPSGVSRKPS
LLTLQGPVLAPGQSLTLQCGSDVGYNRFVLYKEGERDFLQRPGQQPQAGLSQANFT
LGPVSPSNGGQYRCYGAHNLSSEWSAPSDPLNILMAGQIYDTVSLSAQPGPTVASGE
NVTLLCQSWWQFDTFLLTKEGAAHPPLRLRSMYGAHKYQAEFPMSPVTSAHAGTY
RCYGSYSSNPHLLSHPSEPLELVVSGHSGGSSLPPTGPPSTPGLGRYLEVLIGVSVAFV
LLLFLLLFLLLRRQRHSKHRTSDQRKTDFQRPAGAAETEPKDRGLLRRSSPAADVQE

ENLYAAVKDTQSEDRVELDSQSPHDEDPQAVTYAPVKHSSPRREMASPPSSLSGEFL
DTKDRQVEEDRQMDTEAAASEASQDVTYAQLHSLTLRRKATEPPPSQEGEPPAEPSI
YATLAIH

[0198] Antigen-binding sites that bind to LILRB4 can be routinely identified by screening for binding to the amino acid sequence of LILRB4 as defined by SEQ ID NO:317.

SEQ ID NO:317

MIPTFTALLCLGLSLGPRTHMQAGPLPKPTLWAEPGSVISWGNSVTIWCQGTLEARE
YRLDKEESPAPWDRQNPLEPKNKARFSIPSMTEDYAGRYRCYYRSPVGWSQPSDPLE
LVMTGAYSKPTLSALPSPLVTSGKSVTLLCQSRSPMDTFLLIKERAAHPLLHLRSEHG
AQQHQAEFPMSPVTSVHGGTYRCFSSHGFSHYLLSHPSDPLELIVSGSLEDPRPSPTRS
VSTAAGPEDQPLMPTGSVPHSGLRRHWEVLIGVLVVSILLLSLLLFLLLQHWRQGKH
RTLAQRQADFQRPPGAAEPEPKDGGLQRRSSPAADVQGENFCAAVKNTQPEDGVE
MDTRQSPHDEDPQAVTYAKVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDT
EAAASEAPQDVTYAQLHSFTLRQKATEPPPSQEGASPAEPSVYATLAIH

[0199] Antigen-binding sites that bind to LILRB5 can be routinely identified by screening for binding to the amino acid sequence of LILRB5 as defined by SEQ ID NO:318.

SEQ ID NO:318

MTLTLSVLICLGLSVGPRTCVQAGTLPKPTLWAEPASVIARGKPVTLWCQGPLETEE
YRLDKEGLPWARKRQNPLEPGAKAKFHIPSTVYDSAGRYRCYYETPAGWSEPSDPL
ELVATGFYAEPTLLALPSPVVASGGNVTLQCDTLDGLLTFVLVEEEQKLPRTLYSQK
LPKGPSQALFPVGPVTPSCRWRFRCYYYYRKNPQVWSNPSDLLEILVPGVSRKPSLLI
PQGSVVARGGSLTLQCRSDVGYDIFVLYKEGEHDLVQGSGQQPQAGLSQANFTLGP
VSRSHGGQYRCYGAHNLSPRWSAPSDPLDILIAGLIPDIPALSVQPGPKVASGENVTL
LCQSWHQIDTFFLTKEGAAHPPLCLKSKYQSYRHQAEFSMSPVTSAQGGTYRCYSAI
RSYPYLLSSPSYPQELVVSGPSGDPSLSPTGSTPTPGPEDQPLTPTGLDPQSGLGRHLG
VVTGVSVAFVLLLFLLLFLLLRHRHQSKHRTSAHFYRPAGAAGPEPKDQGLQKRASP
VADIQEEILNAAVKDTQPKDGVEMDARAAASEAPQDVTYAQLHSLTLRREATEPPPS
QEREPPAEPSIYAPLAIH

[0200] Antigen-binding sites that bind to LILRA1 can be routinely identified by screening for binding to the amino acid sequence of LILRA1 as defined by SEQ ID NO:319.

SEQ ID NO:319

MTPIVTVLICLRLSLGPRTHVQAGTLPKPTLWAEPGSVITQGSPVTLWCQGILETQEY
RLYREKKTAPWITRIPQEIVKKGQFPIPSITWEHTGRYRCFYGSHTAGWSEPSDPLELV
VTGAYIKPTLSALPSPVVTSGGNVTLHCVSQVAFGSFILCKEGEDEHPQCLNSQPRTH
GWSRAIFSVGPVSPSRRWSYRCYAYDSNSPHVWSLPSDLLELLVLGVSKKPSLSVQP
GPIVAPGESLTLQCVSDVSYDRFVLYKEGERDFLQLPGPQPQAGLSQANFTLGPVSRS
YGGQYRCSGAYNLSSEWSAPSDPLDILIAGQFRGRPFISVHPGPTVASGENVTLLCQS
WGPFHTFLLTKAGAADAPLRLRSIHEYPKYQAEFPMSPVTSAHSGTYRCYGSLSSNP
YLLSHPSDSLELMVSGAAETLSPPQNKSDSKAGAANTLSPSQNKTASHPQDYTVENL
IRMGIAGLVLVVLGILLFEAQHSQRSL

[0201] Antigen-binding sites that bind to LILRA2 can be routinely identified by screening for binding to the amino acid sequence of LILRA2 as defined by SEQ ID NO:320.

SEQ ID NO:320

MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVIIQGSPVTLRCQGSLQAEEY
HLYRENKSASWVRRIQEPGKNGQFPIPSITWEHAGRYHCQYYSHNHSSEYSDPLELV
VTGAYSKPTLSALPSPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHPQRLNSHSHA
RGWSWAIFSVGPVSPSRRWSYRCYAYDSNSPYVWSLPSDLLELLVPGVSKKPSLSVQ
PGPMVAPGESLTLQCVSDVGYDRFVLYKEGERDFLQRPGWQPQAGLSQANFTLGPV
SPSHGGQYRCYSAHNLSSEWSAPSDPLDILITGQFYDRPSLSVQPVPTVAPGKNVTLL
CQSRGQFHTFLLTKEGAGHPPLHLRSEHQAQQNQAEFRMGPVTSAHVGTYRCYSSL
SSNPYLLSLPSDPLELVVSEAAETLSPSQNKTDSTTTSLGQHPQDYTVENLIRMGVAG
LVLVVLGILLFEAQHSQRSLQDAAGR

[0202] Antigen-binding sites that bind to LILRA3 can be routinely identified by screening for binding to the amino acid sequence of LILRA3 as defined by SEQ ID NO:321.

SEQ ID NO:321

MTPILTVLICLGLSLDPRTHVQAGPLPKPTLWAEPGSVITQGSPVTLRCQGSLETQEY
HLYREKKTALWITRIPQELVKKGQFPILSITWEHAGRYCCIYGSHTAGLSESSDPLELV
VTGAYSKPTLSALPSPVVTSGGNVTIQCDSQVAFDGFILCKEGEDEHPQCLNSHSHAR
GSSRAIFSVGPVSPSRRWSYRCYGYDSRAPYVWSLPSDLLGLLVPGVSKKPSLSVQP
GPVVAPGEKLTFQCGSDAGYDRFVLYKEWGRDFLQRPGRQPQAGLSQANFTLGPVS
RSYGGQYTCSGAYNLSSEWSAPSDPLDILITGQIRARPFLSVRPGPTVASGENVTLLC
QSQGGMHTFLLTKEGAADSPLRLKSKRQSHKYQAEFPMSPVTSAHAGTYRCYGSLS
SNPYLLTHPSDPLELVVSGAAETLSPPQNKSDSKAGE

[0203] Antigen-binding sites that bind to LILRA4 can be routinely identified by screening for binding to the amino acid sequence of LILRA4 as defined by SEQ ID NO:322.

SEQ ID NO:322

MTLILTSLLFFGLSLGPRTRVQAENLPKPILWAEPGPVITWHNPVTIWCQGTLEAQGY
RLDKEGNSMSRHILKTLESENKVKLSIPSMMWEHAGRYHCYYQSPAGWSEPSDPLE
LVVTAYSRPTLSALPSPVVTSGVNVTLRCASRLGLGRFTLIEEGDHRLSWTLNSHQH
NHGKFQALFPMGPLTFSNRGTFRCYGYENNTPYVWSEPSDPLQLLVSGVSRKPSLLT
LQGPVVTPGENLTLQCGSDVGYIRYTLYKEGADGLPQRPGRQPQAGLSQANFTLSPV
SRSYGGQYRCYGAHNVSSEWSAPSDPLDILIAGQISDRPSLSVQPGPTVTSGEKVTLL
CQSWDPMFTFLLTKEGAAHPPLRLRSMYGAHKYQAEFPMSPVTSAHAGTYRCYGSR
SSNPYLLSHPSEPLELVVSGATETLNPAQKKSDSKTAPHLQDYTVENLIRMGVAGLV
LLFLGILLFEAQHSQRSPPRCSQEANSRKDNAPFRVVEPWEQI

[0204] Antigen-binding sites that bind to LILRA5 can be routinely identified by screening for binding to the amino acid sequence of LILRA5 as defined by SEQ ID NO:323.

SEQ ID NO:323

MAPWSHPSAQLQPVGGDAVSPALMVLLCLGLSLGPRTHVQAGNLSKATLWAEPGS
VISRGNSVTIRCQGTLEAQEYRLVKEGSPEPWDTQNPLEPKNKARFSIPSMTEHHAGR
YRCYYYSPAGWSEPSDPLELVVTGFYNKPTLSALPSPVVTSGENVTLQCGSRLRFDR
FILTEEGDHKLSWTLDSQLTPSGQFQALFPVGPVTPSHRWMLRCYGSRRHILQVWSE
PSDLLEIPVSGAADNLSPSQNKSDSGTASHLQDYAVENLIRMGMAGLILVVLGILIFQ
DWHSQRSPQAAAGR

[0205] Antigen-binding sites that bind to LILRA6 can be routinely identified by screening for binding to the amino acid sequence of LILRA6 as defined by SEQ ID NO:324.

SEQ ID NO:324

MTPALTALLCLGLSLGPRTRVQAGPFPKPTLWAEPGSVISWGSPVTIWCQGSLEAQE
YQLDKEGSPEPLDRNNPLEPKNKARFSIPSMTQHHAGRYRCHYYSSAGWSEPSDPLE
LVMTGFYNKPTLSALPSPVVASGGNMTLRCGSQKGYHHFVLMKEGEHQLPRTLDSQ
QLHSGGFQALFPVGPVTPSHRWRFTCYYYYTNTPRVWSHPSDPLEILPSGVSRKPSLL
TLQGPVLAPGQSLTLQCGSDVGYDRFVLYKEGERDFLQRPGQQPQAGLSQANFTLG
PVSPSHGGQYRCYGAHNLSSEWSAPSDPLNILMAGQIYDTVSLSAQPGPTVASGENV
TLLCQSRGYFDTFLLTKEGAAHPPLRLRSMYGAHKYQAEFPMSPVTSAHAGTYRCY
GSYSSNPHLLSFPSEPLELMVSGHSGGSSLPPTGPPSTPASHAKDYTVENLIRMGMAG
LVLVFLGILLFEAQHSQRNPQDAAGR

[0206] Table 7 lists examples of peptide sequences of heavy chain variable domains that by itself or in combination with light chain variable domains, can bind to each of T_{reg} associated antigens.

Table 7		
Examples*	Heavy chain variable domain amino acid sequence	Light chain variable domain amino acid sequence
Anti-CD7 (US20170226204A1)	MDVQLQESGGGSVQAGGSLR LSCPASGYTFSHYCMGWNRQ APGKEREEVATIDTDDTPTYA DSVMGRFTISRDNANNALYL QMNDLKPEDTSMYYCAIWM KLRGSCHDRRLEVRGQGTQV TVSIN (SEQ ID NO:325) CDR1 (SEQ ID NO:326) - GYTFSHYCM	

	CDR2 (SEQ ID NO:327) - TIDTDDTPT CDR3 (SEQ ID NO:328) - AIWMKLRGSCHDRRLE	
Anti-CD7 (US20170226204A1)	MDVQLQESGGGSVQAGGSLR LSCAASGYTHSSYCMAWFRQ APGREREGVASIDSDGTTSYA DSVKGRFTISQDNAKNTLYL QMNSLKPEDTAMYYCAARF GPMGCVDLSTLSFGHWGQGT QVTVSIT (SEQ ID NO:329) CDR1 (SEQ ID NO:330) - GYTHSSYCM CDR2 (SEQ ID NO:331) - SIDSDGTTS CDR3 (SEQ ID NO:332) - AARFGPMGCVDLSTLSFGH	
Anti-CTLA4 (ipilimumab)	QVQLVESGGGVVQPGRSLRL SCAASGFTFSSYTMHWVRQA PGKGLEWVTFISYDGNNKYY ADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAIYYCARTGW LGPFDYWGQGTLVTVSS (SEQ ID NO:333) CDR1 (SEQ ID NO:335) - GFTFSSY CDR2 (SEQ ID NO:336) - SYDGNN CDR3 (SEQ ID NO:337) - TGWLGPFDY	EIVLTQSPGTLSLSPGERATL SCRASQSVGSSYLAWYQQK PGQAPRLLIYGAFSRATGIP DRFSGSGSGTDFTLTISRLEP EDFAVYYCQQYGSSPWTFG QGTKVEIK (SEQ ID NO:334) CDR1 (SEQ ID NO:338) - QSVGSSYLA CDR2 (SEQ ID NO:339) - GAFSRAT CDR3 (SEQ ID NO:340) - QQYGSSPWT
Anti-CTLA4 (tremelimumab)	QVQLVESGGGVVQPGRSLRL SCAASGFTFSSYGMHWVRQA	DIQMTQSPSSLSASVGDRVT ITCRASQSINSYLDWYQQKP

	PGKGLEWVAVIWYDGSNKY YADSVKGRFTISRDNSKNTLY LQMNSLRAEDTAVYYCARDP RGATLYYYYYGMDVWGQGT TVTVSSASTKGPSVFPLAPCS RSTSESTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSNFG TQTYTCNVDHKPSNTKVDKT VERKCCVECPPCPAPPVAGPS VFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVQFNWYV DGVEVHNAKTKPREEQFNST FRVVSVLTVVHQDWLNGKE YKCKVSNKGLPAPIEKTISKT KGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPMLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKS LSLSPGK (SEQ ID NO:341) CDR1 (SEQ ID NO:343) - GFTFSSY CDR2 (SEQ ID NO:344) - WYDGSN CDR3 (SEQ ID NO:345) - DPRGATLYYYYYGMDV	GKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPE DFATYYCQQYYSTPFTFGP GTKVEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGN SQESVTEQDSKDSTYSLSST LTLSKADYEKHKVYACEVT HQGLSSPVTKSFNRGEC (SEQ ID NO:342) CDR1 (SEQ ID NO:346) - QSINSYLD CDR2 (SEQ ID NO:347) - AASSLQS CDR3 (SEQ ID NO:348) - QQYYSTPFT
Anti-CX3CR1 (WO2013130381A1)	EVQLVESGGGSVQAGESLRL SCAASGSIFSSNAMAWYRQA PGKQRDLVAGINSVGITKYA DSVKGRFTISRDNAKNTVYL QMNSLKPEDTAVYYCTSDPR	

	RGWDTRYWGQGTQVTVSS (SEQ ID NO:349) CDR1 (SEQ ID NO:350) - GSIFSSNAMA CDR2 (SEQ ID NO:351) - AINSVGVTK CDR3 (SEQ ID NO:352) - DPRRGWDTRY	
Anti-CX3CR1 (WO2013130381A1)	VQLVESGGGLVQPGGSLRLS CAASGSIFSSTAMAWYRQAP GKRRDLVAAISSVGVTKYAD SVKGRFTISRDNSKNTVYLQ MNSLRPEDTAVYYCTSDPRR GWDTRYWGQGTLVTVSS (SEQ ID NO:353) CDR1 (SEQ ID NO:354) - GSIFSSTAMA CDR2 (SEQ ID NO:356) - AISSVGVTK CDR3 (SEQ ID NO:357) - DPRRGWDTRY	
Anti-ENTPD1 (WO2016073845A1)	EVQLVESGGDLVKPGGSLKL SCAAFGFTFSRYGMSWVRQT PDKRLEWVATITSGGIYTYYP DSVKGRFTISRDNAKNTLYLQ MSSLKSEETAMYYCARHGQF GDYYGMDYWGQGTSVTVSS (SEQ ID NO:358) CDR1 (SEQ ID NO:360) - GFTFSRYGMS CDR2 (SEQ ID NO:361) - TITSGGIYTYYPDSVKG CDR3 (SEQ ID NO:362) -	DVVMTQTPLSLPVSLGDQA SISCRSSQSLLHSNGNTYLH WYLQKPGQSPKLLIYKVSN RFSGVPDRFSGSGSGTDFTL KISRVEAEDLGVYFCSQSTH VPYTFGGGTKLEIK (SEQ ID NO:359) CDR1 (SEQ ID NO:363) - RSSQSLLHSNGNTYLH CDR2 (SEQ ID NO:364) - KVSNRFS CDR3 (SEQ ID NO:365) -

	HGQFGDYYGMDY	SQSTHVPYT
Anti-ENTPD1 (WO2017157948A1)	QVQLVQSGSELKKPGASVKV SCKASGYTFTHYGMNWVRQ APGQGLKWMGWINTYTGEP TYADDFKGRFVFSLDTSVSTA YLQISSLKAEDTAVYYCARR RYEGNYVFYYFDYWGQGTT VTVSS (SEQ ID NO:366) CDR1 (SEQ ID NO:368) - GYTFTHYG CDR2 (SEQ ID NO:369) - NTYTGEP CDR3 (SEQ ID NO:370) - ARRRYEGNYVFYYFDY	DIQMTQSPSSLSASVGDRVT ITCRASENIYSYFSWYQQKP GKAPKLLIYTAKTLAEGVPS RFSGSGSGTDFTLTISSLQPE DFATYYCQHHYVTPYTFGG GTKVEIK (SEQ ID NO:367) CDR1 (SEQ ID NO:371) - RASENIYSYFS CDR2 (SEQ ID NO:372) - TAKTLAE CDR3 (SEQ ID NO:373) - QHHYVTPYT
Anti-HAVCR2 (WO2016161270A1)	EVQLLESGGGLVQPGGSLRLS CAAASGFTFSSYDMSWVRQA PGKGLDWVSTISGGGTYTYY QDSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCASMD YWGQGTTVTVSSA (SEQ ID NO:374) CDR1 (SEQ ID NO:376) - SGFTFSSYD CDR2 (SEQ ID NO:377) - SGGGTYT CDR3 (SEQ ID NO:378) - ASMDY	DIQMTQSPSSLSASVGDRVT ITCRASQSIRRYLNWYHQKP GKAPKLLIYGASTLQSGVPS RFSGSGSGTDFTLTISSLQPE DFAVYYCQQSHSAPLTFGG GTKVEIKR (SEQ ID NO:375) CDR1 (SEQ ID NO:379) - RASQSIRRYLN CDR2 (SEQ ID NO:380) - GASTLQS CDR3 (SEQ ID NO:381) - QQSHSAPLT
Anti-HAVCR2 (US20170190777A1)	QVQLQQPGAELVKPGASVK MSCKASGYTFTSYNMHWIKQ TPGQGLEWIGDIYPGNGDTSY NQKFKGKATLTADKSSSTVY MQLSSLTSEDSAVYYCARVG GAFPMDYWGQGTSVTVSS	DIVLTQSPASLAVSLGQRAT ISCRASESVEYYGTSLMQW YQQKPGQPPKLLIYAASNV ESGVPARFSGSGSGTDFSLN IHPVEEDDIAIYFCQQSRKD PSTFGGGTKLEIK (SEQ ID

	(SEQ ID NO:382) CDR1 (SEQ ID NO:384) - SYNMH CDR2 (SEQ ID NO:385) - DIYPGNGDTSYNQKFKG CDR3 (SEQ ID NO:386) - VGGAFPMDY	NO:383) CDR1 (SEQ ID NO:387) - RASESVEYYGTSLMQ CDR2 (SEQ ID NO:388) - AASNVES CDR3 (SEQ ID NO:389) - QQSRKDPST
Anti-PDCD1LG2 (US20160137731A1)	QVQLVQSGAEVKKPGASVKV SCKASGYTFTGYTMHWVRQ APGQGLEWIGYINPRSGYTEY NQKFKDRTTLTADKSTSTAY MELSSLRSEDTAVYYCARPW FAYWGQGTLVTVSS (SEQ ID NO:390) CDR1 (SEQ ID NO:392) - GYTFTGYT CDR2 (SEQ ID NO:393) - NPRSGYT CDR3 (SEQ ID NO:394) - ARPWFAY	DIVMTQSPAFLSVTPGEKVT ITCKSSQSLLNSGNQKNYLT WYQQKPGQPPKLLIYWAST RESGVPDRFSGSGSGTDFTL TISSLQAEDVAVYYCQNDY SYPLTFGQGTKLEIK (SEQ ID NO:391) CDR1 (SEQ ID NO:395) - KSSQSLLNSGNQKNYLT CDR2 (SEQ ID NO:396) - WASTRES CDR3 (SEQ ID NO:397) - QNDYSYPLT
Anti-PDCD1LG2 (WO2017053250A1)	MNFGLSLIFLALILKGVQCEV QLVESGGDLVKSGGSLKLSC AASGFIFSSFGMSWVRQTPDK RLEWVATISSGGRNIYYLDSV KGRFTISRDNVKNILYLQMSG LKSEDSAMYYCAREGHYALD YCGQGTSVTVSS (SEQ ID NO:398) CDR1 (SEQ ID NO:400) - SFGMS CDR2 (SEQ ID NO:401) - TISSGGRNIYYLDSVKG CDR3 (SEQ ID NO:402) -	DIVMTQSPSSLATSVGQRVT MSCKSSQNLLYSTDQKNYL AWFQQKPGQSPKLLLYFASI RESGVPDRFIGSGSGTDFTL TISSVQAEDLADYFCQQHY NTPPTFGGGTRLEIK (SEQ ID NO:399) CDR1 (SEQ ID NO:403) - KSSQNLLYSTDQKNYLA CDR2 (SEQ ID NO:404) - FASIRES CDR3 (SEQ ID NO:405) - QQHYNTPPT

	EGHYALDY	
Anti-TIGIT (US20170088613A1)	EVQLVQSGSDLKKPGASVRV SCKASGYTFTSYPMNWVRQA PGHGLEWMGWINTNTGNPT YVQGFTGRFVFSLDTSVNTA YLQISSLKAEDTAVYFCARTG GHTYDSYAFDVWGQGTMVT VSS (SEQ ID NO:406) CDR1 (SEQ ID NO:408) - SYPMN CDR2 (SEQ ID NO:409) - WINTNTGNPTYVQGFTG CDR3 (SEQ ID NO:410) - TGGHTYDSYAFDV	DIQLTQSPTFLSASVGDRVTI TCRASQVISSSLAWYQQNP GKAPKLLIYAASTLQSGVPS RFSGSGSGTEFTLTISSLQPE DFVTYYCQHLHGYPSNFGQ GTKVEIK (SEQ ID NO:407) CDR1 (SEQ ID NO:411) - RASQVISSSLA CDR2 (SEQ ID NO:412) - AASTLQS CDR3 (SEQ ID NO:413) - QHLHGYPSN
Anti-TIGIT (US20160376365A1)	DVQLQESGPGLVKPSQSLSLT CTVTGYSITSDYAWNWVRQF PGNKLEWMGYISYSGSTSYN PSLRSRISITRDTSKNQFFLQL NSVTTEDTATYYCARRQVGL GFAYWGQGTLVTVSS (SEQ ID NO:414) CDR1 (SEQ ID NO:416) - TSDYAWN CDR2 (SEQ ID NO:417) - YISYSGSTSYNPSLRS CDR3 (SEQ ID NO:418) - ARRQVGLGFAY	DIVMTQSHKFMSTSVGDRV SITCKASQDVSTAVAWYQQ KPGQSPKLLIYSASYRYTGV PDRFTGSGSGTDFTFTISSVQ AEDLAVYYCQQHYSTPWTF G (SEQ ID NO:415) CDR1 (SEQ ID NO:419) - KASQDVSTAVA CDR2 (SEQ ID NO:420) - SASYRYT CDR3 (SEQ ID NO:421) - QQHYSTP
Anti-TNFRSF4 (pogalizumab)	EVQLVQSGAEVKKPGASVKV SCKASGYTFTDSYMSWVRQA PGQGLEWIGDMYPDNGDSSY NQKFRERVTITRDTSTSTAYL ELSSLRSEDTAVYYCVLAPR WYFSVWGQGTLVTVSSASTK	DIQMTQSPSSLSASVGDRVT ITCRASQDISNYLNWYQQK PGKAPKLLIYYTSRLRSGVP SRFSGSGSGTDFTLTISSLQP EDFATYYCQQGHTLPPTFG QGTKVEIKRTVAAPSVFIFP

	GPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLS SVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTH TCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVS HEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQ PENNYKTTPPVLDSDGSFFLY SKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK (SEQ ID NO:422) CDR1 (SEQ ID NO:424) - GYTFTDSY CDR2 (SEQ ID NO:425) - DNGDS CDR3 (SEQ ID NO:426) - VLAPRWYFSV	PSDEQLKSGTASVVCLLNN FYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLS STLTLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC (SEQ ID NO:423) CDR1 (SEQ ID NO:427) - RASQDISNYLN CDR2 (SEQ ID NO:428) - TSRLRS CDR3 (SEQ ID NO:429) - QQGHTLPPT
Anti-TNFRSF4 (tavolixizumab)	QVQLQESGPGLVKPSQTLSLT CAVYGGSFSSGYWNWIRKHP GKGLEYIGYISYNGITYHNPS LKSRITINRDTSKNQYSLQLN SVTPEDTAVYYCARYKYDYD GGHAMDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLY	DIQMTQSPSSLSASVGDRVT ITCRASQDISNYLNWYQQK PGKAPKLLIYYTSKLHSGVP SRFSGSGSGTDYTLTISSLQP EDFATYYCQQGSALPWTFG QGTKVEIKRTVAAPSVFIFP PSDEQLKSGTASVVCLLNN FYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLS

	SLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKRVEPKSCDK THTCPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSL TCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPG K (SEQ ID NO:430) CDR1 (SEQ ID NO:432) - GGSFSSGY CDR2 (SEQ ID NO:433) - SYNGITYH CDR3 (SEQ ID NO:434) - ARYKYDYDGGHAMDY	STLTLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC (SEQ ID NO:431) CDR1 (SEQ ID NO:435) - RASQDISNYLN CDR2 (SEQ ID NO:436) - TSKLH CDR3 (SEQ ID NO:437) - QQGSALPWT
Anti-TNFRSF8 (brentuximab vedotin)	QIQLQQSGPEVVKPGASVKIS CKASGYTFTDYYITWVKQKP GQGLEWIGWIYPGSGNTKYN EKFKGKATLTVDTSSSTAFM QLSSLTSEDTAVYFCANYGN YWFAYWGQGTQVTVSAAST KGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKT HTCPPCPAPELLGGPSVFLFPP	DIVLTQSPASLAVSLGQRAT ISCKASQSVDFDGDSYMNW YQQKPGQPPKVLIYAASNL ESGIPARFSGSGSGTDFTLNI HPVEEEDAATYYCQQSNED PWTFGGGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVV CLLNNFYPREAKVQWKVD NALQSGNSQESVTEQDSKD STYSLSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSF NRGEC (SEQ ID NO:439)

	KPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPR EPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPG (SEQ ID NO:438) CDR1 (SEQ ID NO:440) - GYTFTDYY CDR2 (SEQ ID NO:441) - YPGSGNT CDR3 (SEQ ID NO:442) - ANYGNYWFAY	 CDR1 (SEQ ID NO:443) - KASQSVDFDGDSYMN CDR2 (SEQ ID NO:444) - AASNLES CDR3 (SEQ ID NO:445) - QQSNEDPWT
Anti-TNFRSF8 (US20100239571A1)	QVQLVQSGAEVKKPGASVKV SCKASGYTFTDYYITWVRQA PGQGLEWMGWIYPGSGNTK YNEKFKGRVTMTVDTSISTA YMELSRLRSDDTAVYFCANY GNYWFAYWGQGTLVTVSS (SEQ ID NO:446) CDR1 (SEQ ID NO:448) - GYTFTDYY CDR2 (SEQ ID NO:449) - YPGSGNT CDR3 (SEQ ID NO:450) - ANYGNYWFAY	DIVMTQSPDSLAVSLGERAT INCKASQSVDFDGDSYMN WYQQKPGQPPKLLIYAASN LESGVPDRFSGSGSGTDFTL TISSLQAEDVAVYYCQQSN EDPWTFGQGTKVEIK (SEQ ID NO:447) CDR1 (SEQ ID NO:451) - KASQSVDFDGDSYMN CDR2 (SEQ ID NO:452) - AASNLES CDR3 (SEQ ID NO:453) - QQSNEDPWT
Anti-TNFRSF9	QVQLQQWGAGLLKPSETLSL	EIVLTQSPATLSLSPGERATL

(urelumab)	TCAVYGGSFSGYYWSWIRQS PEKGLEWIGEINHGGYVTYNP SLESRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDYGPG NYDWYFDLWGRGTLVTVSS ASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTKTYTCN VDHKPSNTKVDKRVESKYGP PCPPCPAPEFLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVS QEDPEVQFNWYVDGVEVHN AKTKPREEQFNSTYRVVSVLT VLHQDWLNGKEYKCKVSNK GLPSSIEKTISKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSRL TVDKSRWQEGNVFSCSVMHE ALHNHYTQKSLSLSLGK (SEQ ID NO:454) CDR1 (SEQ ID NO:456) - GGSFSGYY CDR2 (SEQ ID NO:457) - NHGGYV CDR3 (SEQ ID NO:458) - ARDYGPGNYDWYFDL	SCRASQSVSSYLAWYQQKP GQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPE DFAVYYCQQRSNWPPALTF CGGTKVEIKRTVAAPSVFIF PPSDEQLKSGTASVVCLLN NFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSL SSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC (SEQ ID NO:455) CDR1 (SEQ ID NO:459) - RASQSVSSYLA CDR2 (SEQ ID NO:460) - DASNRATGI CDR3 (SEQ ID NO:461) - QQRSNWPPALT
Anti-TNFRSF9 (utomilumab)	EVQLVQSGAEVKKPGESLRIS CKGSGYSFSTYWISWVRQMP GKGLEWMGKIYPGDSYTNYS PSFQGQVTISADKSISTAYLQ	SYELTQPPSVSVSPGQTASIT CSGDNIGDQYAHWYQQKP GQSPVLVIYQDKNRPSGIPE RFSGSNSGNTATLTISGTQA

	WSSLKASDTAMYYCARGYGI FDYWGQGTLVTVSSASTKGP SVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNVDHK PSNTKVDKTVERKCCVECPP CPAPPVAGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDP EVQFNWYVDGVEVHNAKTK PREEQFNSTFRVVSVLTVVHQ DWLNGKEYKCKVSNKGLPA PIEKTISKTKGQPREPQVYTLP PSREEMTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYK TTPPMLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK (SEQ ID NO:462) CDR1 (SEQ ID NO:464) - GYSFSTYW CDR2 (SEQ ID NO:465) - YPGDSYT CDR3 (SEQ ID NO:466) - ARGYGIFDY	MDEADYYCATYTGFGSLA VFGGGTKLTVLGQPKAAPS VTLFPPSSEELQANKATLVC LISDFYPGAVTVAWKADSS PVKAGVETTTPSKQSNNKY AASSYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVAPTE CS (SEQ ID NO:463) CDR1 (SEQ ID NO:467) - SGDNIGDQYAH CDR2 (SEQ ID NO:468) - QDKNRPS CDR3 (SEQ ID NO:469) - ATYTGFGSLAV
Anti-NST5 (oleclumab)	EVQLLESGGGLVQPGGSLRLS CAASGFTFSSYAYSWVRQAP GKGLEWVSAISGSGGRTYYA DSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARLGY GRVDEWGRGTLVTVSSASTK GPSVFPLAPSSKSTSGGTAAL	QSVLTQPPSASGTPGQRVTI SCSGSLSNIGRNPVNWYQQ LPGTAPKLLIYLDNLRLSGV PDRFSGSKSGTSASLAISGL QSEDEADYYCATWDDSHP GWTFGGGTKLTVLGQPKA APSVTLFPPSSEELQANKAT

	GCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLS SVVTVPSSSLGTQTYICNVNH KPSNTKVDKRVEPKSCDKTH TCPPCPAPEFEGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVS HEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSN KALPASIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQ PENNYKTTPPVLDSDGSFFLY SKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK (SEQ ID NO:470) CDR1 (SEQ ID NO:472) - GFTFSSYA CDR2 (SEQ ID NO:473) - SGSGGRT CDR3 (SEQ ID NO:474) - ARLGYGRVDE	LVCLISDFYPGAVTVAWKA DSSPVKAGVETTTPSKQSN NKYAASSYLSLTPEQWKSH RSYSCQVTHEGSTVEKTVA PTECS (SEQ ID NO:471) CDR1 (SEQ ID NO:475) - SGSLSNIGRNPVN CDR2 (SEQ ID NO:476) - LDNLRLS CDR3 (SEQ ID NO:477) - ATWDDSHPGWT
Anti-NST5 (US20170253665A1)	QVQLVESGGGVVQPGRSLRL SCAASGFTFSNYGMHWVRQ APGKGLEWVAVILYDGSNKY YPDSVKGRFTISRDNSKNTLY LQMNSLRAEDTAVYYCARG GSSWYPDSFDIWGQGTMVTV SS (SEQ ID NO:478) CDR1 (SEQ ID NO:480) - NYGMH	EIVLTQSPATLSLSPGERATL SCRASQGVSSYLAWYQQKP GQAPRLLIYDASNRATGIPA RFSGSGPGTDFTLTISSLEPE DFAVYYCQQRSNWHLTFG GGTKVEIK (SEQ ID NO:479) CDR1 (SEQ ID NO:483) - RASQGVSSYLA CDR2 (SEQ ID NO:484) -

	CDR2 (SEQ ID NO:481) - VILYDGSNKYYPDSVK CDR3 (SEQ ID NO:482) - GGSSWYPDSFDI	DASNRAT CDR3 (SEQ ID NO:485) - QQRSNWHLT
Anti-TNFRSF18 (US20170253665A1)	QVQLVESGGGVVQPGRSLRL SCAASGFTFSSYAMHWVRQA PGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCARGIA AAGPPYYYYYYYMDVWGK GTTVTVSS (SEQ ID NO:486) CDR1 (SEQ ID NO:488) - GFTFSSY CDR2 (SEQ ID NO:489) - SYDGSN CDR3 (SEQ ID NO:490) - GIAAAGPPYYYYYYYMDV	DIQMTQSPSSLSASVGDRVT ITCRASQTIYNYLNWYQQK PGKAPKLLIYAASSLQSGVP SRFGGRGYGTDFTLTINSLQ PEDFATYFCQQSYTSPLTFG QGTKVDIK (SEQ ID NO:487) CDR1 (SEQ ID NO:491) - QTIYNYLN CDR2 (SEQ ID NO:492) - AASSLQS CDR3 (SEQ ID NO:493) - QQSYTSPLT
Anti-TNFRSF18 (US9701751 B2)	QVQLVESGGGVVQPGRSLRL SCAASGFTFSSYAMSWVRQA PGKGLEWVASISSGGTTYYPD SVKGRFTISRDNSKNTLYLQM NSLRAEDTAVYYCARVGGY YDSMDYWGQGTLVTVSS (SEQ ID NO:494) CDR1 (SEQ ID NO:496) - GFTFSSYA CDR2 (SEQ ID NO:497) - SSGGTT CDR3 (SEQ ID NO:498) - ARVGGYYDSMDY	EIVLTQSPGTLSLSPGERATL SCRASESVDXYGVSFMNW YQQKPGQAPRLLIYAASXQ GSGIPDRFSGSGSGTDFTLTI SRLEPEDFAVYYCQQTKEV TWTFGQGTKVEIKR (SEQ ID NO:495) CDR1 (SEQ ID NO:499) - RASESVDXYGVSFMN CDR2 (SEQ ID NO:500) - AASXQGS CDR3 (SEQ ID NO:501) - QQTKEVTWT

*References in parenthesis indicate the sources of peptide sequences.

[0207] Alternatively, antigen-binding sites that bind to each of T_{reg} associated antigens can be routinely identified by screening for binding to the amino acid sequence of each antigen. For example, antigen-binding sites that bind to CCR8 can be routinely identified by screening for binding to the amino acid sequence of CCR8 is defined by SEQ ID NO:502.

SEQ ID NO:502

MDYTLDLSVTTVTDYYYPDIFSSPCDAELIQTNGKLLLAVFYCLLFVFSLLGNSLVIL
VLVVCKKLRSITDVYLLNLALSDLLFVFSFPFQTYYLLDQWVFGTVMCKVVSGFYYI
GFYSSMFFITLMSVDRYLAVVHAVYALKVRTIRMGTTLCLAVWLTAIMATIPLLVFY
QVASEDGVLQCYSFYNQQTLKWKIFTNFKMNILGLLIPFTIFMFCYIKILHQLKRCQN
HNKTKAIRLVLIVVIASLLFWVPFNVVLFLTSLHSMHILDGCSISQQLTYATHVTEIISF
THCCVNPVIYAFVGEKFKKHLSEIFQKSCSQIFNYLGRQMPRESCEKSSSCQQHSSRSS
SVDYILLILRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE
NLYAAVKDTQPEDGVEMDTRAAASEAPQDVTYAQLHSLTLRRKATEPPPSQEREPP
AEPSIYATLAIH

[0208] Antigen-binding sites that bind to CD7 can be routinely identified by screening for binding to the amino acid sequence of CD7 is defined by SEQ ID NO:503.

SEQ ID NO:503

MAGPPRLLLLPLLLALARGLPGALAAQEVQQSPHCTTVPVGASVNITCSTSGGLRGIY
LRQLGPQPQDIIYYEDGVVPTTDRRFRGRIDFSGSQDNLTITMHRLQLSDTGTYTCQA
ITEVNVYGSGTLVLVTEEQSQGWHRCSDAPPRASALPAPPTGSALPDPQTASALPDPP
AASALPAALAVISFLLGLGLGVACVLARTQIKKLCSWRDKNSAACVVYEDMSHSRC
NTLSSPNQYQ

[0209] Antigen-binding sites that bind to CTLA4 can be routinely identified by screening for binding to the amino acid sequence of CTLA4 is defined by SEQ ID NO:504.

SEQ ID NO:504

MACLGFQRHKAQLNLATRTWPCTLLFFLLFIPVFCKAMHVAQPAVVLASSRGIASFV
CEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVN
LTIQGLRAMDTGLYICKVELMYPPPYYLGIGNGTQIYVIDPEPCPDSDFLLWILAAVSS
GLFFYSFLLTAVSLSKMLKKRSPLTTGVYVKMPPTEPECEKQFQPYFIPIN

[0210] Antigen-binding sites that bind to CX3CR1 can be routinely identified by screening for binding to the amino acid sequence of CX3CR1 is defined by SEQ ID NO:505.

SEQ ID NO:505

MREPLEAFKLADLDFRKSSLASGWRMASGAFTMDQFPESVTENFEYDDLAEACYIG
DIVVFGTVFLSIFYSVIFAIGLVGNLLVVFALTNSKKPKSVTDIYLLNLALSDLLFVATL
PFWTHYLINEKGLHNAMCKFTTAFFFIGFFGSIFFITVISIDRYLAIVLAANSMNNRTV
QHGVTISLGVWAAAILVAAPQFMFTKQKENECLGDYPEVLQEIWPVLRNVETNFLGF
LLPLLIMSYCYFRIIQTLFSCKNHKKAKAIKLILLVVIVFFLFWTPYNVMIFLETLKLYD
FFPSCDMRKDLRLALSVTETVAFSHCCLNPLIYAFAGEKFRRYLYHLYGKCLAVLCG
RSVHVDFSSSESQRSRHGSVLSSNFTYHTSDGDALLLL

[0211] Antigen-binding sites that bind to ENTPD1 can be routinely identified by screening for binding to the amino acid sequence of LILRB2 is defined by SEQ ID NO:506.

SEQ ID NO:506

MGREELFLTFSFSSGFQESNVKTFCSKNILAILGFSSIIAVIALLAVGLTQNKALPENVK
YGIVLDAGSSHTSLYIYKWPAEKENDTGVVHQVEECRVKGPGISKFVQKVNEIGIYL
TDCMERAREVIPRSQHQETPVYLGATAGMRLLRMESEELADRVLDVVERSLSNYPF
DFQGARIITGQEEGAYGWITINYLLGKFSQKTRWFSIVPYETNNQETFGALDLGGAST
QVTFVPQNQTIESPDNALQFRLYGKDYNVYTHSFLCYGKDQALWQKLAKDIQVASN
EILRDPCFHPGYKKVVNVSDLYKTPCTKRFEMTLPFQQFEIQGIGNYQQCHQSILELF
NTSYCPYSQCAFNGIFLPPLQGDFGAFSAFYFVMKFLNLTSEKVSQEKVTEMMKKFC
AQPWEEIKTSYAGVKEKYLSEYCFSGTYILSLLLQGYHFTADSWEHIHFIGKIQGSDA
GWTLGYMLNLTNMIPAEQPLSTPLSHSTYVFLMVLFSLVLFTVAIIGLLIFHKPSYFW
KDMV

[0212] Antigen-binding sites that bind to HAVCR2 can be routinely identified by screening for binding to the amino acid sequence of HAVCR2 is defined by SEQ ID NO:507.

SEQ ID NO:507

MFSHLPFDCVLLLLLLLLTRSSEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGKG
ACPVFECGNVVLRTDERDVNYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRI
QIPGIMNDEKFNLKLVIKPAKVTPAPTRQRDFTAAFPRMLTTRGHGPAETQTLGSLPD
INLTQISTLANELRDSRLANDLRDSGATIRIGIYIGAGICAGLALALIFGALIFKWYSHS
KEKIQNLSLISLANLPPSGLANAVAEGIRSEENIYTIEENVYEVEEPNEYYCYVSSRQQ
PSQPLGCRFAMP

[0213] Antigen-binding sites that bind to IL1R2 can be routinely identified by screening for binding to the amino acid sequence of IL1R2 is defined by SEQ ID NO:508.

SEQ ID NO:508

MLRLYVLVMGVSAFTLQPAAHTGAARSCRFRGRHYKREFRLEGEPVALRCPQVPY
WLWASVSPRINLTWHKNDSARTVPGEEETRMWAQDGALWLLPALQEDSGTYVCTT
RNASYCDKMSIELRVFENTDAFLPFISYPQILTLSTSGVLVCPDLSEFTRDKTDVKIQW
YKDSLLLDKDNEKFLSVRGTTHLLVHDVALEDAGYYRCVLTFAHEGQQYNITRSIEL
RIKKKKEETIPVIISPLKTISASLGSRLTIPCKVFLGTGTPLTTMLWWTANDTHIESAYP
GGRVTEGPRQEYSENNENYIEVPLIFDPVTREDLHMDFKCVVHNTLSFQTLRTTVKE
ASSTFSWGIVLAPLSLAFLVLGGIWMHRRCKHRTGKADGLTVLWPHHQDFQSYPK

[0214] Antigen-binding sites that bind to PDCD1LG2 can be routinely identified by screening for binding to the amino acid sequence of PDCD1LG2 is defined by SEQ ID NO:509.

SEQ ID NO:509

MIFLLLMLSLELQLHQIAALFTVTVPKELYIIEHGSNVTLECNFDTGSHVNLGAITASL
QKVENDTSPHRERATLLEEQLPLGKASFHIPQVQVRDEGQYQCIIIYGVAWDYKYLT
LKVKASYRKINTHILKVPETDEVELTCQATGYPLAEVSWPNVSVPANTSHSRTPEGL
YQVTSVLRLKPPPGRNFSCVFWNTHVRELTLASIDLQSQMEPRTHPTWLLHIFIPFCII
AFIFIATVIALRKQLCQKLYSSKDTTKRPVTTTKREVNSAI

[0215] Antigen-binding sites that bind to TIGIT can be routinely identified by screening for binding to the amino acid sequence of TIGIT is defined by SEQ ID NO:510.

SEQ ID NO:510

MRWCLLLIWAQGLRQAPLASGMMTGTIETTGNISAEKGGSIILQCHLSSTTAQVTQV
NWEQQDQLLAICNADLGWHISPSFKDRVAPGPGLGLTLQSLTVNDTGEYFCIYHTYP
DGTYTGRIFLEVLESSVAEHGARFQIPLLGAMAATLVVICTAVIVVVALTRKKKALRI
HSVEGDLRRKSAGQEEWSPSAPSPPGSCVQAEAAPAGLCGEQRGEDCAELHDYFNV
LSYRSLGNCSFFTETG

[0216] Antigen-binding sites that bind to TNFRSF4 can be routinely identified by screening for binding to the amino acid sequence of TNFRSF4 is defined by SEQ ID NO:511.

SEQ ID NO:511

MCVGARRLGRGPCAALLLLGLGLSTVTGLHCVGDTYPSNDRCCHECRPGNGMVSR
CSRSQNTVCRPCGPGFYNDVVSSKPCKPCTWCNLRSGSERKQLCTATQDTVCRCRA
GTQPLDSYKPGVDCAPCPPGHFSPGDNQACKPWTNCTLAGKHTLQPASNSSDAICED

RDPPATQPQETQGPPARPITVQPTEAWPRTSQGPSTRPVEVPGGRAVAAILGLGLVLG
LLGPLAILLALYLLRRDQRLPPDAHKPPGGGSFRTPIQEEQADAHSTLAKI

[0217] Antigen-binding sites that bind to TNFRSF8 can be routinely identified by screening for binding to the amino acid sequence of TNFRSF8 is defined by SEQ ID NO:512.

SEQ ID NO:512

MRVLLAALGLLFLGALRAFPQDRPFEDTCHGNPSHYYDKAVRRCCYRCPMGLFPTQ
QCPQRPTDCRKQCEPDYYLDEADRCTACVTCSRDDLVEKTPCAWNSSRVCECRPGM
FCSTSAVNSCARCFFHSVCPAGMIVKFPGTAQKNTVCEPASPGVSPACASPENCKEPS
SGTIPQAKPTPVSPATSSASTMPVRGGTRLAQEAASKLTRAPDSPSSVGRPSSDPGLSP
TQPCPEGSGDCRKQCEPDYYLDEAGRCTACVSCSRDDLVEKTPCAWNSSRTCECRP
GMICATSATNSCARCVPYPICAAETVTKPQDMAEKDTTFEAPPLGTQPDCNPTPENG
EAPASTSPTQSLLVDSQASKTLPIPTSAPVALSSTGKPVLDAGPVLFWVILVLVVVVG
SSAFLLCHRRACRKRIRQKLHLCYPVQTSQPKLELVDSRPRRSSTQLRSGASVTEPVA
EERGLMSQPLMETCHSVGAAYLESLPLQDASPAGGPSSPRDLPEPRVSTEHTNNKIEK
IYIMKADTVIVGTVKAELPEGRGLAGPAEPELEEELEADHTPHYPEQETEPPLGSCSD
VMLSVEEEGKEDPLPTAASGK

[0218] Antigen-binding sites that bind to TNFRSF9 can be routinely identified by screening for binding to the amino acid sequence of TNFRSF9 is defined by SEQ ID NO:513.

SEQ ID NO:513

MGNSCYNIVATLLLVLNFERTRSLQDPCSNCPAGTFCDNNRNQICSPCPPNSFSSAGG
QRTCDICRQCKGVFRTRKECSSTSNAECDCTPGFHCLGAGCSMCEQDCKQGQELTK
KGCKDCCFGTFNDQKRGICRPWTNCSLDGKSVLVNGTKERDVVCGPSPADLSPGAS
SVTPPAPAREPGHSPQIISFFLALTSTALLFLLFFLTLRFSVVKRGRKKLLYIFKQPFMR
PVQTTQEEDGCSCRFPEEEEGGCEL

[0219] Antigen-binding sites that bind to GEM can be routinely identified by screening for binding to the amino acid sequence of GEM is defined by SEQ ID NO:514.

SEQ ID NO:514

MTLNNVTMRQGTVGMQPQQQRWSIPADGRHLMVQKEPHQYSHRNRHSATPEDHC
RRSWSSDSTDSVISSESGNTYYRVVLIGEQGVGKSTLANIFAGVHDSMDSDCEVLGE
DTYERTLMVDGESATIILLDMWENKGENEWLHDHCMQVGDAYLIVYSITDRASFEK

ASELRIQLRRARQTEDIPIILVGNKSDLVRCREVSVSEGRACAVVFDCKFIETSAAVQH
NVKELFEGIVRQVRLRRDSKEKNERRLAYQKRKESMPRKARRFWGKIVAKNNKNM
AFKLKSKSCHDLSVL

[0220] Antigen-binding sites that bind to NT5E can be routinely identified by screening for binding to the amino acid sequence of NT5E is defined by SEQ ID NO:515.

SEQ ID NO:515

MCPRAARAPATLLLALGAVLWPAAGAWELTILHTNDVHSRLEQTSEDSSKCVNASR
CMGGVARLFTKVQQIRRAEPNVLLLDAGDQYQGTIWFTVYKGAEVAHFMNALRYD
AMALGNHEFDNGVEGLIEPLLKEAKFPILSANIKAKGPLASQISGLYLPYKVLPVGDE
VVGIVGYTSKETPFLSNPGTNLVFEDEITALQPEVDKLKTLNVNKIIALGHSGFEMDK
LIAQKVRGVDVVVGGHSNTFLYTGNPPSKEVPAGKYPFIVTSDDGRKVPVVQAYAF
GKYLGYLKIEFDERGNVISSHGNPILLNSSIPEDPSIKADINKWRIKLDNYSTQELGKTI
VYLDGSSQSCRFRECNMGNLICDAMINNNLRHTDEMFWNHVSMCILNGGGIRSPIDE
RNNGTITWENLAAVLPFGGTFDLVQLKGSTLKKAFEHSVHRYGQSTGEFLQVGGIHV
VYDLSRKPGDRVVKLDVLCTKCRVPSYDPLKMDEVYKVILPNFLANGGDGFQMIKD
ELLRHDSGDQDINVVSTYISKMKVIYPAVEGRIKFSTGSHCHGSFSLIFLSLWAVIFVL
YQ

[0221] Antigen-binding sites that bind to TNFRSF18 can be routinely identified by screening for binding to the amino acid sequence of TNFRSF18 is defined by SEQ ID NO:516.

SEQ ID NO:516

MAQHGAMGAFRALCGLALLCALSLGQRPTGGPGCGPGRLLLGTGTDARCCRVHTT
RCCRDYPGEECCSEWDCMCVQPEFHCGDPCCTTCRHHPCPPGQGVQSQGKFSFGFQ
CIDCASGTFSGGHEGHCKPWTDCCWRCRRRPKTPEAASSPRKSGASDRQRRRGGWE
TCGCEPGRPPGPPTAASPSPGAPQAAGALRSALGRALLPWQQKWVQEGGSDQRPGP
CSSAAAAGPCRRERETQSWPPSSLAGPDGVGS

[0222] Within the Fc domain, CD16 binding is mediated by the hinge region and the CH2 domain. For example, within human IgG1, the interaction with CD16 is primarily focused on amino acid residues Asp 265 – Glu 269, Asn 297 – Thr 299, Ala 327 – Ile 332, Leu 234 – Ser 239, and carbohydrate residue N-acetyl-D-glucosamine in the CH2 domain (see, Sondermann *et al.*, Nature, 406 (6793):267-273). Based on the known domains, mutations can be selected to enhance or reduce the binding affinity to CD16, such as by using phage-displayed libraries

or yeast surface-displayed cDNA libraries, or can be designed based on the known three-dimensional structure of the interaction.

[0223] The assembly of heterodimeric antibody heavy chains can be accomplished by expressing two different antibody heavy chain sequences in the same cell, which may lead to the assembly of homodimers of each antibody heavy chain as well as assembly of heterodimers. Promoting the preferential assembly of heterodimers can be accomplished by incorporating different mutations in the CH3 domain of each antibody heavy chain constant region as shown in US13/494870, US16/028850, US11/533709, US12/875015, US13/289934, US14/773418, US12/811207, US13/866756, US14/647480, and US14/830336. For example, mutations can be made in the CH3 domain based on human IgG1 and incorporating distinct pairs of amino acid substitutions within a first polypeptide and a second polypeptide that allow these two chains to selectively heterodimerize with each other. The positions of amino acid substitutions illustrated below are all numbered according to the EU index as in Kabat.

[0224] In one scenario, an amino acid substitution in the first polypeptide replaces the original amino acid with a larger amino acid, selected from arginine (R), phenylalanine (F), tyrosine (Y) or tryptophan (W), and at least one amino acid substitution in the second polypeptide replaces the original amino acid(s) with a smaller amino acid(s), chosen from alanine (A), serine (S), threonine (T), or valine (V), such that the larger amino acid substitution (a protuberance) fits into the surface of the smaller amino acid substitutions (a cavity). For example, one polypeptide can incorporate a T366W substitution, and the other can incorporate three substitutions including T366S, L368A, and Y407V.

[0225] An antibody heavy chain variable domain of the invention can optionally be coupled to an amino acid sequence at least 90% identical to an antibody constant region, such as an IgG constant region including hinge, CH2 and CH3 domains with or without CH1 domain. In some embodiments, the amino acid sequence of the constant region is at least 90% identical to a human antibody constant region, such as an human IgG1 constant region, an IgG2 constant region, IgG3 constant region, or IgG4 constant region. In some other embodiments, the amino acid sequence of the constant region is at least 90% identical to an antibody constant region from another mammal, such as rabbit, dog, cat, mouse, or horse. One or more mutations can be incorporated into the constant region as compared to human IgG1 constant region, for example at Q347, Y349, L351, S354, E356, E357, K360, Q362, S364, T366, L368, K370, N390, K392, T394, D399, S400, D401, F405, Y407, K409, T411

and/or K439. Exemplary substitutions include, for example, Q347E, Q347R, Y349S, Y349K, Y349T, Y349D, Y349E, Y349C, T350V, L351K, L351D, L351Y, S354C, E356K, E357Q, E357L, E357W, K360E, K360W, Q362E, S364K, S364E, S364H, S364D, T366V, T366I, T366L, T366M, T366K, T366W, T366S, L368E, L368A, L368D, K370S, N390D, N390E, K392L, K392M, K392V, K392F, K392D, K392E, T394F, T394W, D399R, D399K, D399V, S400K, S400R, D401K, F405A, F405T, Y407A, Y407I , Y407V, K409F, K409W, K409D, T411D, T411E, K439D, and K439E.

[0226] In certain embodiments, mutations that can be incorporated into the CH1 of a human IgG1 constant region may be at amino acid V125, F126, P127, T135, T139, A140, F170, P171, and/or V173. In certain embodiments, mutations that can be incorporated into the Cκ of a human IgG1 constant region may be at amino acid E123, F116, S176, V163, S174, and/or T164.

[0227] Alternatively, amino acid substitutions could be selected from the following sets of substitutions shown in Table 8.

Table 8		
	First Polypeptide	Second Polypeptide
Set 1	S364E/F405A	Y349K/T394F
Set 2	S364H/D401K	Y349T/T411E
Set 3	S364H/T394F	Y349T/F405A
Set 4	S364E/T394F	Y349K/F405A
Set 5	S364E/T411E	Y349K/D401K
Set 6	S364D/T394F	Y349K/F405A
Set 7	S364H/F405A	Y349T/T394F
Set 8	S364K/E357Q	L368D/K370S
Set 9	L368D/K370S	S364K
Set 10	L368E/K370S	S364K
Set 11	K360E/Q362E	D401K
Set 12	L368D/K370S	S364K/E357L
Set 13	K370S	S364K/E357Q
Set 14	F405L	K409R
Set 15	K409R	F405L

[0228] Alternatively, amino acid substitutions could be selected from the following sets of substitutions shown in Table 9.

Table 9		
	First Polypeptide	Second Polypeptide
Set 1	K409W	D399V/F405T
Set 2	Y349S	E357W
Set 3	K360E	Q347R
Set 4	K360E/K409W	Q347R/D399V/F405T
Set 5	Q347E/K360E/K409W	Q347R/D399V/F405T
Set 6	Y349S/K409W	E357W/D399V/F405T

[0229] Alternatively, amino acid substitutions could be selected from the following set of substitutions shown in Table 10.

Table 10		
	First Polypeptide	Second Polypeptide
Set 1	T366K/L351K	L351D/L368E
Set 2	T366K/L351K	L351D/Y349E
Set 3	T366K/L351K	L351D/Y349D
Set 4	T366K/L351K	L351D/Y349E/L368E
Set 5	T366K/L351K	L351D/Y349D/L368E
Set 6	E356K/D399K	K392D/K409D

[0230] Alternatively, at least one amino acid substitution in each polypeptide chain could be selected from Table 11.

Table 11	
First Polypeptide	Second Polypeptide
L351Y, D399R, D399K, S400K, S400R, Y407A, Y407I, Y407V	T366V, T366I, T366L, T366M, N390D, N390E, K392L, K392M, K392V, K392F K392D, K392E, K409F, K409W, T411D and T411E

[0231] Alternatively, at least one amino acid substitutions could be selected from the following set of substitutions in Table 12, where the position(s) indicated in the First Polypeptide column is replaced by any known negatively-charged amino acid, and the position(s) indicated in the Second Polypeptide Column is replaced by any known positively-charged amino acid.

Table 12	
First Polypeptide	Second Polypeptide
K392, K370, K409, or K439	D399, E356, or E357

[0232] Alternatively, at least one amino acid substitutions could be selected from the following set of in Table 13, where the position(s) indicated in the First Polypeptide column is replaced by any known positively-charged amino acid, and the position(s) indicated in the Second Polypeptide Column is replaced by any known negatively-charged amino acid.

Table 13	
First Polypeptide	Second Polypeptide
D399, E356, or E357	K409, K439, K370, or K392

[0233] Alternatively, amino acid substitutions could be selected from the following set in Table 14.

Table 14	
First Polypeptide	Second Polypeptide
T350V, L351Y, F405A, and Y407V	T350V, T366L, K392L, and T394W

[0234] Alternatively, or in addition, the structural stability of a hetero-multimeric protein may be increased by introducing S354C on either of the first or second polypeptide chain, and Y349C on the opposing polypeptide chain, which forms an artificial disulfide bridge within the interface of the two polypeptides.

[0235] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at position T366, and wherein the amino acid sequence of the other polypeptide chain of the

antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of T366, L368 and Y407.

[0236] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of T366, L368 and Y407, and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at position T366.

[0237] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of E357, K360, Q362, S364, L368, K370, T394, D401, F405, and T411 and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Y349, E357, S364, L368, K370, T394, D401, F405 and T411.

[0238] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Y349, E357, S364, L368, K370, T394, D401, F405 and T411 and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of E357, K360, Q362, S364, L368, K370, T394, D401, F405, and T411.

[0239] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of L351, D399, S400 and Y407 and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of T366, N390, K392, K409 and T411.

[0240] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of T366, N390, K392, K409 and T411 and wherein the amino acid sequence of the other polypeptide chain of the antibody

constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of L351, D399, S400 and Y407.

[0241] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Q347, Y349, K360, and K409, and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Q347, E357, D399 and F405.

[0242] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Q347, E357, D399 and F405, and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Y349, K360, Q347 and K409.

[0243] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of K370, K392, K409 and K439, and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of D356, E357 and D399.

[0244] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of D356, E357 and D399, and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of K370, K392, K409 and K439.

[0245] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of L351, E356, T366 and D399, and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Y349, L351, L368, K392 and K409.

[0246] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of Y349, L351, L368, K392 and K409, and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region at one or more positions selected from the group consisting of L351, E356, T366 and D399.

[0247] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by an S354C substitution and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by a Y349C substitution.

[0248] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by a Y349C substitution and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by an S354C substitution.

[0249] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by K360E and K409W substitutions and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by O347R, D399V and F405T substitutions.

[0250] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by O347R, D399V and F405T substitutions and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by K360E and K409W substitutions.

[0251] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by a T366W substitutions and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by T366S, T368A, and Y407V substitutions.

[0252] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by T366S, T368A, and Y407V substitutions and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by a T366W substitution.

[0253] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by T350V, L351Y, F405A, and Y407V substitutions and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by T350V, T366L, K392L, and T394W substitutions.

[0254] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by T350V, T366L, K392L, and T394W substitutions and wherein the amino acid sequence of the other polypeptide chain of the antibody constant region differs from the amino acid sequence of an IgG1 constant region by T350V, L351Y, F405A, and Y407V substitutions.

[0255] In some embodiments, the amino acid sequence of one polypeptide chain of the antibody constant (human IgG1) region may be SEQ ID NO:164.

SEQ ID NO:164

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAP
ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK
TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFLLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

[0256] The multi-specific proteins described above can be made using recombinant DNA technology well known to a skilled person in the art. For example, a first nucleic acid sequence encoding the first immunoglobulin heavy chain can be cloned into a first expression vector; a second nucleic acid sequence encoding the second immunoglobulin heavy chain can be cloned into a second expression vector; a third nucleic acid sequence encoding the immunoglobulin light chain can be cloned into a third expression vector; and the first, second, and third expression vectors can be stably transfected together into host cells to produce the multimeric proteins.

[0257] To achieve the highest yield of the multi-specific protein, different ratios of the first, second, and third expression vector can be explored to determine the optimal ratio for transfection into the host cells. After transfection, single clones can be isolated for cell bank generation using methods known in the art, such as limited dilution, ELISA, FACS, microscopy, or Clonepix.

[0258] Clones can be cultured under conditions suitable for bio-reactor scale-up and maintained expression of the multi-specific protein. The multispecific proteins can be isolated and purified using methods known in the art including centrifugation, depth filtration, cell lysis, homogenization, freeze-thawing, affinity purification, gel filtration, ion exchange chromatography, hydrophobic interaction exchange chromatography, and mixed-mode chromatography.

II. CHARACTERISTICS OF THE MULTI-SPECIFIC PROTEINS

[0259] The multi-specific proteins described herein include an NKG2D-binding site, a CD16-binding site, and a tumor-associated antigen selected from any one of the antigens provided in Table 15. In some embodiments, the multi-specific proteins bind simultaneously to cells expressing NKG2D and/or CD16, such as NK cells, and to tumor cells expressing a tumor-associated antigen selected from any one of the antigens provided in Table 15. Binding of the multi-specific proteins to NK cells can enhance the activity of the NK cells toward destruction of the tumor cells.

Table 15

Type of Antigen	**Biological Name**
Chemokine receptor	CXCR4
Cell surface α chain of the IL-2 receptor	CD25
Adhesion molecule	Very late antigen-4 (VLA-4)
Transmembrane glycoprotein	CD44
Aminopeptidase N	CD13
3-fucosyl-N-acetyl-lactosamine	CD15
Integrin-associated protein	CD47
Cell surface glycoprotein	CD81
Type II integral membrane protein	CD23

Member of tumor necrosis factor receptors (TNFR)	CD40
Member of the tumor necrosis factor superfamily	CD70
Subunit of B-cell antigen receptor (BCR)	CD79a or CD79b
Member of the B7 family of immune coregulatory proteins	CD80
Type I cytokine receptor	CRLF2 (also known as thymic stromal lymphopoietin (TSLP) receptor (TSLPR)
Member of the signaling lymphocytic activation molecule (SLAM) family receptors	SLAMF7 (also named CD319)
Heparin sulphate proteoglycan	CD138
Multifunctional ectoenzyme that catalyzes the synthesis and hydrolysis of cyclic ADP-ribose (cADPR) from NAD^+ to ADP-ribose	CD38
T-cell associated tumor antigen	T-cell receptor beta-1 chain C region (TRBC1)
T-cell associated tumor antigen	T-cell receptor beta-2 chain C region (TRBC2)
Leukocyte immunoglobulin-like receptors (LILR)	LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, LILRA1, LILRA2, LILRA3, LILRA4, LILRA5, and LILRA6
Regulatory T cell expressing protein	CCR8, CD7, CTLA4, CX3CR1, ENTPD1, HAVCR2, IL-1R2, PDCD1LG2, TIGIT, TNFRSF4, TNFRSF8, TNFRSF9, GEM, NT5E, and TNFRSF18

[0260] In some embodiments, the multi-specific proteins bind to a tumor-associated antigen selected from any one of the antigens provided in Table 15 with a similar affinity to the corresponding monoclonal antibody (*i.e.,* a monoclonal antibody containing the same a tumor-associated antigen-binding site as the one incorporated in the multi-specific proteins (selected from any one of the antigens provided in Table 15)). In some embodiments, the multi-specific proteins are more effective in killing the tumor cells expressing a tumor-

associated antigen selected from any one of the antigens provided in Table 15 than the corresponding monoclonal antibodies.

[0261] In certain embodiments, the multi-specific proteins described herein, which include an NKG2D-binding site and a binding site for a tumor-associated antigen selected from any one of the antigens provided in Table 15, activate primary human NK cells when co-culturing with cells expressing the tumor-associated antigen. NK cell activation is marked by the increase in CD107a degranulation and IFN-γ cytokine production. Furthermore, compared to a corresponding monoclonal antibody for a tumor-associated antigen selected from any one of the antigens provided in Table 15, the multi-specific proteins may show superior activation of human NK cells in the presence of cells expressing the tumor-associated antigen.

[0262] In certain embodiments, the multi-specific proteins described herein, which include an NKG2D-binding site and a binding site for a tumor-associated antigen selected from any one of the antigens provided in Table 15, enhance the activity of rested and IL-2-activated human NK cells co-culturing with cells expressing the tumor-associated antigen.

[0263] In certain embodiments, compared to a corresponding monoclonal antibody that binds to a tumor-associated antigen selected from any one of the antigens provided in Table 15, the multi-specific proteins offer an advantage in targeting tumor cells that express medium and low levels of the tumor-associated antigen. The multi-specific binding proteins described herein may be more effective in reducing tumor growth and killing cancer cells. For example, TriNKETs A49-TriNKET-CXCR4-Hz515H7 (an NKG2D-binding domain from clone ADI-27749 and a CXCR4-binding domain derived from Hz515H7), A44-TriNKET-CXCR4-Hz515H7 (an NKG2D-binding domain from clone ADI-27744 and a CXCR4-binding domain derived from Hz515H7), and C26-TriNKET-CXCR4-Hz515H7 (an NKG2D-binding domain from clone ADI-28226 and a CXCR4-binding domain derived from Hz515H7) have enhanced potency and maximum lysis CXCR4-expressing target cells, compared to an anti-CXCR4 monoclonal antibody.

III. THERAPEUTIC APPLICATIONS

[0264] The invention provides methods for treating cancer using a multi-specific binding protein described herein and/or a pharmaceutical composition described herein. The methods may be used to treat a variety of cancers which express CXCR4 by administering to a patient

in need thereof a therapeutically effective amount of a multi-specific binding protein described herein.

[0265] The therapeutic method can be characterized according to the cancer to be treated. For example, in certain embodiments, the cancer is acute myeloid leukemia, multiple myeloma, diffuse large B cell lymphoma, thymoma, adenoid cystic carcinoma, gastrointestinal cancer, renal cancer, breast cancer, glioblastoma, lung cancer, ovarian cancer, brain cancer, prostate cancer, pancreatic cancer, or melanoma.

[0266] In certain other embodiments, the cancer is a solid tumor. In certain other embodiments, the cancer is colon cancer, bladder cancer, cervical cancer, endometrial cancer, esophageal cancer, leukemia, liver cancer, rectal cancer, stomach cancer, testicular cancer, or uterine cancer. In yet other embodiments, the cancer is a vascularized tumor, squamous cell carcinoma, adenocarcinoma, small cell carcinoma, melanoma, glioma, neuroblastoma, sarcoma (*e.g.*, an angiosarcoma or chondrosarcoma), larynx cancer, parotid cancer, bilary tract cancer, thyroid cancer, acral lentiginous melanoma, actinic keratoses, acute lymphocytic leukemia, acute myeloid leukemia, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal cancer, anal cancer, anorectum cancer, astrocytic tumor, bartholin gland carcinoma, basal cell carcinoma, biliary cancer, bone cancer, bone marrow cancer, bronchial cancer, bronchial gland carcinoma, carcinoid, cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, connective tissue cancer, cystadenoma, digestive system cancer, duodenum cancer, endocrine system cancer, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell cancer, ependymal cancer, epithelial cell cancer, Ewing's sarcoma, eye and orbit cancer, female genital cancer, focal nodular hyperplasia, gallbladder cancer, gastric antrum cancer, gastric fundus cancer, gastrinoma, glioblastoma, glucagonoma, heart cancer, hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary cancer, hepatocellular carcinoma, Hodgkin's disease, ileum cancer, insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct cancer, invasive squamous cell carcinoma, jejunum cancer, joint cancer, Kaposi's sarcoma, pelvic cancer, large cell carcinoma, large intestine cancer, leiomyosarcoma, lentigo maligna melanomas, lymphoma, male genital cancer, malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, meningeal cancer, mesothelial cancer, metastatic carcinoma, mouth cancer, mucoepidermoid carcinoma,

multiple myeloma, muscle cancer, nasal tract cancer, nervous system cancer, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin cancer, non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial cancer, oral cavity cancer, osteosarcoma, papillary serous adenocarcinoma, penile cancer, pharynx cancer, pituitary tumors, plasmacytoma, pseudosarcoma, pulmonary blastoma, rectal cancer, renal cell carcinoma, respiratory system cancer, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus cancer, skin cancer, small cell carcinoma, small intestine cancer, smooth muscle cancer, soft tissue cancer, somatostatin-secreting tumor, spine cancer, squamous cell carcinoma, striated muscle cancer, submesothelial cancer, superficial spreading melanoma, T cell leukemia, tongue cancer, undifferentiated carcinoma, ureter cancer, urethra cancer, urinary bladder cancer, urinary system cancer, uterine cervix cancer, uterine corpus cancer, uveal melanoma, vaginal cancer, verrucous carcinoma, VIPoma, vulva cancer, well differentiated carcinoma, or Wilms tumor.

[0267] In certain other embodiments, the cancer is non-Hodgkin's lymphoma, such as a B-cell lymphoma or a T-cell lymphoma. In certain embodiments, the non-Hodgkin's lymphoma is a B-cell lymphoma, such as a diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma, follicular lymphoma, small lymphocytic lymphoma, mantle cell lymphoma, marginal zone B-cell lymphoma, extranodal marginal zone B-cell lymphoma, nodal marginal zone B-cell lymphoma, splenic marginal zone B-cell lymphoma, Burkitt lymphoma, lymphoplasmacytic lymphoma, hairy cell leukemia, or primary central nervous system (CNS) lymphoma. In certain other embodiments, the non-Hodgkin's lymphoma is a T-cell lymphoma, such as a precursor T-lymphoblastic lymphoma, peripheral T-cell lymphoma, cutaneous T-cell lymphoma, angioimmunoblastic T-cell lymphoma, extranodal natural killer/T-cell lymphoma, enteropathy type T-cell lymphoma, subcutaneous panniculitis-like T-cell lymphoma, anaplastic large cell lymphoma, or peripheral T-cell lymphoma.

[0268] The cancer to be treated can be characterized according to the presence of a particular antigen expressed on the surface of the cancer cell. In certain embodiments, the cancer cell can express one or more of the following in addition to CXCR4: CD2, CD19, CD20, CD30, CD38, CD40, CD52, CD70, EGFR/ERBB1, IGF1R, HER3/ERBB3, HER4/ERBB4, MUC1, TROP2, cMET, SLAMF7, PSCA, MICA, MICB, TRAILR1, TRAILR2, MAGE-A3, B7.1, B7.2, CTLA4, and PD1.

[0269] In some other embodiments, when the second binding site binds CXCR4, the cancer to be treated is selected from acute myeloid leukemia, multiple myeloma, diffuse large

B cell lymphoma, thymoma, adenoid cystic carcinoma, gastrointestinal cancer, renal cancer, breast cancer, glioblastoma, lung cancer, ovarian cancer, brain cancer, prostate cancer, pancreatic cancer, and melanoma.

[0270] In some other embodiments, when the second binding site binds CD25, the cancer to be treated is selected from acute myeloid leukemia, chronic lymphocytic leukemia, glioblastoma, bladder cancer, colon cancer, germ cell tumors, lung cancer, osteosarcoma, melanoma, ovarian cancer, multiple myeloma, head and neck cancer, renal cell cancer, and breast cancer.

[0271] In some other embodiments, when the second binding site binds VLA4, CD44, CD13, CD15, CD47, or CD81, the cancer to be treated is selected from acute myeloid leukemia, multiple myeloma, chronic lymphocytic leukemia, B cell lymphoma, T cell lymphoma, Hodgkin lymphoma, breast cancer, glioblastoma, head and neck cancer, ovarian cancer, prostate cancer, melanoma, lung cancer, pancreatic cancer, liver cancer, gastric cancer, thyroid cancer, and brain cancer.

[0272] In some other embodiments, when the second binding site binds CD23, CD40, CD70, CD79a, CD79b, CD80, or CRLF2, the cancer to be treated is selected from B cell malignancies, Non-Hodgkin lymphoma, chronic lymphocytic leukemia, acute lymphoblastic leukemia, multiple myeloma, diffuse large B cell lymphoma, follicular lymphoma, T cell lymphoma, renal cancer, glioblastoma, head and neck cancer, nasopharyngeal carcinoma, bladder cancer, cervical cancer, kidney cancer, and ovarian cancer.

[0273] In some other embodiments, when the second binding site binds LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, LILRA1, LILRA2, LILRA3, LILRA4, LILRA5, or LILRA6, the cancer to be treated is selected from AML, B cell leukemia, B cell lymphoma, multiple myeloma, T cell leukemia, T cell lymphoma, lung cancer, gastric cancer, breast cancer, and pancreas cancer, wherein the method comprises administering an effective amount of protein according to any one of claims 1-24 or a formulation according to claim 25 to a patient.

IV. COMBINATION THERAPY

[0274] Another aspect of the invention provides for combination therapy. A multi-specific binding protein described herein can be used in combination with additional therapeutic agents to treat the cancer.

[0275] Exemplary therapeutic agents that may be used as part of a combination therapy in treating cancer, include, for example, radiation, mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetrorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma (IFN-γ), colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, luteinizing hormone releasing factor and variations of the aforementioned agents that may exhibit differential binding to its cognate receptor, and increased or decreased serum half-life.

[0276] An additional class of agents that may be used as part of a combination therapy in treating cancer is immune checkpoint inhibitors. Exemplary immune checkpoint inhibitors include agents that inhibit one or more of (i) cytotoxic T lymphocyte-associated antigen 4 (CTLA4), (ii) programmed cell death protein 1 (PD1), (iii) PDL1, (iv) LAG3, (v) B7-H3, (vi) B7-H4, and (vii) TIM3. The CTLA4 inhibitor ipilimumab has been approved by the United States Food and Drug Administration for treating melanoma.

[0277] Yet other agents that may be used as part of a combination therapy in treating cancer are monoclonal antibody agents that target non-checkpoint targets (*e.g.*, herceptin) and non-cytotoxic agents (*e.g.*, tyrosine-kinase inhibitors).

[0278] Yet other categories of anti-cancer agents include, for example: (i) an inhibitor selected from an ALK Inhibitor, an ATR Inhibitor, an A2A Antagonist, a Base Excision Repair Inhibitor, a Bcr-Abl Tyrosine Kinase Inhibitor, a Bruton's Tyrosine Kinase Inhibitor, a CDC7 Inhibitor, a CHK1 Inhibitor, a Cyclin-Dependent Kinase Inhibitor, a DNA-PK Inhibitor, an Inhibitor of both DNA-PK and mTOR, a DNMT1 Inhibitor, a DNMT1 Inhibitor plus 2-chloro-deoxyadenosine, an HDAC Inhibitor, a Hedgehog Signaling Pathway Inhibitor, an IDO Inhibitor, a JAK Inhibitor, a mTOR Inhibitor, a MEK Inhibitor, a MELK Inhibitor, a MTH1 Inhibitor, a PARP Inhibitor, a Phosphoinositide 3-Kinase Inhibitor, an Inhibitor of both PARP1 and DHODH, a Proteasome Inhibitor, a Topoisomerase-II Inhibitor, a Tyrosine Kinase Inhibitor, a VEGFR Inhibitor, and a WEE1 Inhibitor; (ii) an agonist of OX40, CD137,

CD40, GITR, CD27, HVEM, TNFRSF25, or ICOS; and (iii) a cytokine selected from IL-12, IL-15, GM-CSF, and G-CSF.

[0279] Proteins of the invention can also be used as an adjunct to surgical removal of the primary lesion.

[0280] The amount of multi-specific binding protein and additional therapeutic agent and the relative timing of administration may be selected in order to achieve a desired combined therapeutic effect. For example, when administering a combination therapy to a patient in need of such administration, the therapeutic agents in the combination, or a pharmaceutical composition or compositions comprising the therapeutic agents, may be administered in any order such as, for example, sequentially, concurrently, together, simultaneously and the like. Further, for example, a multi-specific binding protein may be administered during a time when the additional therapeutic agent(s) exerts its prophylactic or therapeutic effect, or *vice versa*.

V. PHARMACEUTICAL COMPOSITIONS

[0281] The present disclosure also features pharmaceutical compositions that contain a therapeutically effective amount of a protein described herein. The composition can be formulated for use in a variety of drug delivery systems. One or more physiologically acceptable excipients or carriers can also be included in the composition for proper formulation. Suitable formulations for use in the present disclosure are found in Remington's Pharmaceutical Sciences, Mack Publishing Company, Philadelphia, Pa., 17th ed., 1985. For a brief review of methods for drug delivery, *see, e.g.*, Langer (Science 249:1527-1533, 1990).

[0282] Pharmaceutical compositions can contain a therapeutically effective amount of a multi-specific binding protein comprising an antigen (listed in Table 15) site.

[0283] The intravenous drug delivery formulation of the present disclosure may be contained in a bag, a pen, or a syringe. In certain embodiments, the bag may be connected to a channel comprising a tube and/or a needle. In certain embodiments, the formulation may be a lyophilized formulation or a liquid formulation. In certain embodiments, the formulation may freeze-dried (lyophilized) and contained in about 12-60 vials. In certain embodiments, the formulation may be freeze-dried and 45 mg of the freeze-dried formulation may be contained in one vial. In certain embodiments, the about 40 mg – about 100 mg of freeze-dried formulation may be contained in one vial. In certain embodiments, freeze dried formulation from 12, 27, or 45 vials are combined to obtained a therapeutic dose of the

protein in the intravenous drug formulation. In certain embodiments, the formulation may be a liquid formulation and stored as about 250 mg/vial to about 1000 mg/vial. In certain embodiments, the formulation may be a liquid formulation and stored as about 600 mg/vial. In certain embodiments, the formulation may be a liquid formulation and stored as about 250 mg/vial.

[0284] The protein could exist in a liquid aqueous pharmaceutical formulation including a therapeutically effective amount of the protein in a buffered solution forming a formulation.

[0285] These compositions may be sterilized by conventional sterilization techniques, or may be sterile filtered. The resulting aqueous solutions may be packaged for use as-is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous carrier prior to administration. The pH of the preparations typically will be between 3 and 11, more preferably between 5 and 9 or between 6 and 8, and most preferably between 7 and 8, such as 7 to 7.5. The resulting compositions in solid form may be packaged in multiple single dose units, each containing a fixed amount of the above-mentioned agent or agents. The composition in solid form can also be packaged in a container for a flexible quantity.

[0286] In certain embodiments, the present disclosure provides a formulation with an extended shelf life including the protein of the present disclosure, in combination with mannitol, citric acid monohydrate, sodium citrate, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate, sodium chloride, polysorbate 80, water, and sodium hydroxide.

[0287] In certain embodiments, an aqueous formulation is prepared including the protein of the present disclosure in a pH-buffered solution. The buffer of this invention may have a pH ranging from about 4 to about 8, *e.g.*, from about 4.5 to about 6.0, or from about 4.8 to about 5.5, or may have a pH of about 5.0 to about 5.2. Ranges intermediate to the above recited pH's are also intended to be part of this disclosure. For example, ranges of values using a combination of any of the above recited values as upper and/or lower limits are intended to be included. Examples of buffers that will control the pH within this range include acetate (*e.g.*, sodium acetate), succinate (such as sodium succinate), gluconate, histidine, citrate and other organic acid buffers.

[0288] In certain embodiments, the formulation includes a buffer system which contains citrate and phosphate to maintain the pH in a range of about 4 to about 8. In certain embodiments the pH range may be from about 4.5 to about 6.0, or from about pH 4.8 to about

5.5, or in a pH range of about 5.0 to about 5.2. In certain embodiments, the buffer system includes citric acid monohydrate, sodium citrate, disodium phosphate dihydrate, and/or sodium dihydrogen phosphate dihydrate. In certain embodiments, the buffer system includes about 1.3 mg/mL of citric acid (*e.g.*, 1.305 mg/mL), about 0.3 mg/mL of sodium citrate (*e.g.*, 0.305 mg/mL), about 1.5 mg/mL of disodium phosphate dihydrate (*e.g.*, 1.53 mg/mL), about 0.9 mg/mL of sodium dihydrogen phosphate dihydrate (*e.g.*, 0.86), and about 6.2 mg/mL of sodium chloride (*e.g.*, 6.165 mg/mL). In certain embodiments, the buffer system includes 1-1.5 mg/mL of citric acid, 0.25 to 0.5 mg/mL of sodium citrate, 1.25 to 1.75 mg/mL of disodium phosphate dihydrate, 0.7 to 1.1 mg/mL of sodium dihydrogen phosphate dihydrate, and 6.0 to 6.4 mg/mL of sodium chloride. In certain embodiments, the pH of the formulation is adjusted with sodium hydroxide.

[0289] A polyol, which acts as a tonicifier and may stabilize the antibody, may also be included in the formulation. The polyol is added to the formulation in an amount which may vary with respect to the desired isotonicity of the formulation. In certain embodiments, the aqueous formulation may be isotonic. The amount of polyol added may also be altered with respect to the molecular weight of the polyol. For example, a lower amount of a monosaccharide (*e.g.*, mannitol) may be added, compared to a disaccharide (such as trehalose). In certain embodiments, the polyol which may be used in the formulation as a tonicity agent is mannitol. In certain embodiments, the mannitol concentration may be about 5 to about 20 mg/mL. In certain embodiments, the concentration of mannitol may be about 7.5 to 15 mg/mL. In certain embodiments, the concentration of mannitol may be about 10-14 mg/mL. In certain embodiments, the concentration of mannitol may be about 12 mg/mL. In certain embodiments, the polyol sorbitol may be included in the formulation.

[0290] A detergent or surfactant may also be added to the formulation. Exemplary detergents include nonionic detergents such as polysorbates (*e.g.*, polysorbates 20, 80 etc.) or poloxamers (*e.g.*, poloxamer 188). The amount of detergent added is such that it reduces aggregation of the formulated antibody and/or minimizes the formation of particulates in the formulation and/or reduces adsorption. In certain embodiments, the formulation may include a surfactant which is a polysorbate. In certain embodiments, the formulation may contain the detergent polysorbate 80 or Tween 80. Tween 80 is a term used to describe polyoxyethylene (20) sorbitanmonooleate (*see* Fiedler, Lexikon der Hifsstoffe, Editio Cantor Verlag Aulendorf, 4th ed., 1996). In certain embodiments, the formulation may contain between about 0.1 mg/mL and about 10 mg/mL of polysorbate 80, or between about 0.5 mg/mL and

about 5 mg/mL. In certain embodiments, about 0.1% polysorbate 80 may be added in the formulation.

[0291] In embodiments, the protein product of the present disclosure is formulated as a liquid formulation. The liquid formulation may be presented at a 10 mg/mL concentration in either a USP / Ph Eur type I 50R vial closed with a rubber stopper and sealed with an aluminum crimp seal closure. The stopper may be made of elastomer complying with USP and Ph Eur. In certain embodiments vials may be filled with 61.2 mL of the protein product solution in order to allow an extractable volume of 60 mL. In certain embodiments, the liquid formulation may be diluted with 0.9% saline solution.

[0292] In certain embodiments, the liquid formulation of the disclosure may be prepared as a 10 mg/mL concentration solution in combination with a sugar at stabilizing levels. In certain embodiments the liquid formulation may be prepared in an aqueous carrier. In certain embodiments, a stabilizer may be added in an amount no greater than that which may result in a viscosity undesirable or unsuitable for intravenous administration. In certain embodiments, the sugar may be disaccharides, *e.g.*, sucrose. In certain embodiments, the liquid formulation may also include one or more of a buffering agent, a surfactant, and a preservative.

[0293] In certain embodiments, the pH of the liquid formulation may be set by addition of a pharmaceutically acceptable acid and/or base. In certain embodiments, the pharmaceutically acceptable acid may be hydrochloric acid. In certain embodiments, the base may be sodium hydroxide.

[0294] In addition to aggregation, deamidation is a common product variant of peptides and proteins that may occur during fermentation, harvest/cell clarification, purification, drug substance/drug product storage and during sample analysis. Deamidation is the loss of NH_3 from a protein forming a succinimide intermediate that can undergo hydrolysis. The succinimide intermediate results in a 17 dalton mass decrease of the parent peptide. The subsequent hydrolysis results in an 18 dalton mass increase. Isolation of the succinimide intermediate is difficult due to instability under aqueous conditions. As such, deamidation is typically detectable as 1 dalton mass increase. Deamidation of an asparagine results in either aspartic or isoaspartic acid. The parameters affecting the rate of deamidation include pH, temperature, solvent dielectric constant, ionic strength, primary sequence, local polypeptide conformation and tertiary structure. The amino acid residues adjacent to Asn in the peptide

chain affect deamidation rates. Gly and Ser following an Asn in protein sequences results in a higher susceptibility to deamidation.

[0295] In certain embodiments, the liquid formulation of the present disclosure may be preserved under conditions of pH and humidity to prevent deamination of the protein product.

[0296] The aqueous carrier of interest herein is one which is pharmaceutically acceptable (safe and non-toxic for administration to a human) and is useful for the preparation of a liquid formulation. Illustrative carriers include sterile water for injection (SWFI), bacteriostatic water for injection (BWFI), a pH buffered solution (*e.g.*, phosphate-buffered saline), sterile saline solution, Ringer's solution or dextrose solution.

[0297] A preservative may be optionally added to the formulations herein to reduce bacterial action. The addition of a preservative may, for example, facilitate the production of a multi-use (multiple-dose) formulation.

[0298] Intravenous (IV) formulations may be the preferred administration route in particular instances, such as when a patient is in the hospital after transplantation receiving all drugs via the IV route. In certain embodiments, the liquid formulation is diluted with 0.9% Sodium Chloride solution before administration. In certain embodiments, the diluted drug product for injection is isotonic and suitable for administration by intravenous infusion.

[0299] In certain embodiments, a salt or buffer components may be added in an amount of 10 mM - 200 mM. The salts and/or buffers are pharmaceutically acceptable and are derived from various known acids (inorganic and organic) with "base forming" metals or amines. In certain embodiments, the buffer may be phosphate buffer. In certain embodiments, the buffer may be glycinate, carbonate, citrate buffers, in which case, sodium, potassium or ammonium ions can serve as counterion.

[0300] A preservative may be optionally added to the formulations herein to reduce bacterial action. The addition of a preservative may, for example, facilitate the production of a multi-use (multiple-dose) formulation.

[0301] The aqueous carrier of interest herein is one which is pharmaceutically acceptable (safe and non-toxic for administration to a human) and is useful for the preparation of a liquid formulation. Illustrative carriers include sterile water for injection (SWFI), bacteriostatic water for injection (BWFI), a pH buffered solution (*e.g.*, phosphate-buffered saline), sterile saline solution, Ringer's solution or dextrose solution.

[0302] The protein of the present disclosure could exist in a lyophilized formulation including the proteins and a lyoprotectant. The lyoprotectant may be sugar, *e.g.*, disaccharides. In certain embodiments, the lyoprotectant may be sucrose or maltose. The lyophilized formulation may also include one or more of a buffering agent, a surfactant, a bulking agent, and/or a preservative.

[0303] The amount of sucrose or maltose useful for stabilization of the lyophilized drug product may be in a weight ratio of at least 1:2 protein to sucrose or maltose. In certain embodiments, the protein to sucrose or maltose weight ratio may be of from 1:2 to 1:5.

[0304] In certain embodiments, the pH of the formulation, prior to lyophilization, may be set by addition of a pharmaceutically acceptable acid and/or base. In certain embodiments the pharmaceutically acceptable acid may be hydrochloric acid. In certain embodiments, the pharmaceutically acceptable base may be sodium hydroxide.

[0305] Before lyophilization, the pH of the solution containing the protein of the present disclosure may be adjusted between 6 to 8. In certain embodiments, the pH range for the lyophilized drug product may be from 7 to 8.

[0306] In certain embodiments, a salt or buffer components may be added in an amount of 10 mM - 200 mM. The salts and/or buffers are pharmaceutically acceptable and are derived from various known acids (inorganic and organic) with "base forming" metals or amines. In certain embodiments, the buffer may be phosphate buffer. In certain embodiments, the buffer may be glycinate, carbonate, citrate buffers, in which case, sodium, potassium or ammonium ions can serve as counterion.

[0307] In certain embodiments, a "bulking agent" may be added. A "bulking agent" is a compound which adds mass to a lyophilized mixture and contributes to the physical structure of the lyophilized cake (*e.g.*, facilitates the production of an essentially uniform lyophilized cake which maintains an open pore structure). Illustrative bulking agents include mannitol, glycine, polyethylene glycol and sorbitol. The lyophilized formulations of the present invention may contain such bulking agents.

[0308] A preservative may be optionally added to the formulations herein to reduce bacterial action. The addition of a preservative may, for example, facilitate the production of a multi-use (multiple-dose) formulation.

[0309] In certain embodiments, the lyophilized drug product may be constituted with an aqueous carrier. The aqueous carrier of interest herein is one which is pharmaceutically

acceptable (*e.g.*, safe and non-toxic for administration to a human) and is useful for the preparation of a liquid formulation, after lyophilization. Illustrative diluents include sterile water for injection (SWFI), bacteriostatic water for injection (BWFI), a pH buffered solution (*e.g.*, phosphate-buffered saline), sterile saline solution, Ringer's solution or dextrose solution.

[0310] In certain embodiments, the lyophilized drug product of the current disclosure is reconstituted with either Sterile Water for Injection, USP (SWFI) or 0.9% Sodium Chloride Injection, USP. During reconstitution, the lyophilized powder dissolves into a solution.

[0311] In certain embodiments, the lyophilized protein product of the instant disclosure is constituted to about 4.5 mL water for injection and diluted with 0.9% saline solution (sodium chloride solution).

[0312] Actual dosage levels of the active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active ingredient which is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient.

[0313] The specific dose can be a uniform dose for each patient, for example, 50-5000 mg of protein. Alternatively, a patient's dose can be tailored to the approximate body weight or surface area of the patient. Other factors in determining the appropriate dosage can include the disease or condition to be treated or prevented, the severity of the disease, the route of administration, and the age, sex and medical condition of the patient. Further refinement of the calculations necessary to determine the appropriate dosage for treatment is routinely made by those skilled in the art, especially in light of the dosage information and assays disclosed herein. The dosage can also be determined through the use of known assays for determining dosages used in conjunction with appropriate dose-response data. An individual patient's dosage can be adjusted as the progress of the disease is monitored. Blood levels of the targetable construct or complex in a patient can be measured to see if the dosage needs to be adjusted to reach or maintain an effective concentration. Pharmacogenomics may be used to determine which targetable constructs and/or complexes, and dosages thereof, are most likely to be effective for a given individual (Schmitz *et al.*, *Clinica Chimica Acta* 308: 43-53, 2001; Steimer *et al.*, *Clinica Chimica Acta* 308: 33-41, 2001).

[0314] In general, dosages based on body weight are from about 0.01 μg to about 100 mg per kg of body weight, such as about 0.01 μg to about 100 mg/kg of body weight, about 0.01

μg to about 50 mg/kg of body weight, about 0.01 μg to about 10 mg/kg of body weight, about 0.01 μg to about 1 mg/kg of body weight, about 0.01 μg to about 100 μg/kg of body weight, about 0.01 μg to about 50 μg/kg of body weight, about 0.01 μg to about 10 μg/kg of body weight, about 0.01 μg to about 1 μg/kg of body weight, about 0.01 μg to about 0.1 μg/kg of body weight, about 0.1 μg to about 100 mg/kg of body weight, about 0.1 μg to about 50 mg/kg of body weight, about 0.1 μg to about 10 mg/kg of body weight, about 0.1 μg to about 1 mg/kg of body weight, about 0.1 μg to about 100 μg/kg of body weight, about 0.1 μg to about 10 μg/kg of body weight, about 0.1 μg to about 1 μg/kg of body weight, about 1 μg to about 100 mg/kg of body weight, about 1 μg to about 50 mg/kg of body weight, about 1 μg to about 10 mg/kg of body weight, about 1 μg to about 1 mg/kg of body weight, about 1 μg to about 100 μg/kg of body weight, about 1 μg to about 50 μg/kg of body weight, about 1 μg to about 10 μg/kg of body weight, about 10 μg to about 100 mg/kg of body weight, about 10 μg to about 50 mg/kg of body weight, about 10 μg to about 10 mg/kg of body weight, about 10 μg to about 1 mg/kg of body weight, about 10 μg to about 100 μg/kg of body weight, about 10 μg to about 50 μg/kg of body weight, about 50 μg to about 100 mg/kg of body weight, about 50μg to about 50 mg/kg of body weight, about 50 μg to about 10 mg/kg of body weight, about 50 μg to about 1 mg/kg of body weight, about 50 μg to about 100 μg/kg of body weight, about 100 μg to about 100 mg/kg of body weight, about 100 μg to about 50 mg/kg of body weight, about 100 μg to about 10 mg/kg of body weight, about 100 μg to about 1 mg/kg of body weight, about 1 mg to about 100 mg/kg of body weight, about 1 mg to about 50 mg/kg of body weight, about 1 mg to about 10 mg/kg of body weight, about 10 mg to about 100 mg/kg of body weight, about 10 mg to about 50 mg/kg of body weight, about 50 mg to about 100 mg/kg of body weight.

[0315] Doses may be given once or more times daily, weekly, monthly or yearly, or even once every 2 to 20 years. Persons of ordinary skill in the art can easily estimate repetition rates for dosing based on measured residence times and concentrations of the targetable construct or complex in bodily fluids or tissues. Administration of the present invention could be intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, intrapleural, intrathecal, intracavitary, by perfusion through a catheter or by direct intralesional injection. This may be administered once or more times daily, once or more times weekly, once or more times monthly, and once or more times annually.

[0316] The description above describes multiple aspects and embodiments of the invention. The patent application specifically contemplates all combinations and permutations of the aspects and embodiments.

EXAMPLES

[0317] The invention now being generally described, will be more readily understood by reference to the following examples, which are included merely for purposes of illustration of certain aspects and embodiments of the present invention, and which are not intended to limit the invention.

Example 1 – NKG2D binding domains bind to NKG2D

NKG2D-binding domains bind to purified recombinant NKG2D

[0318] The nucleic acid sequences of human, mouse, or cynomolgus NKG2D ectodomains were fused with nucleic acid sequences encoding human IgG1 Fc domains and introduced into mammalian cells to be expressed. After purification, NKG2D-Fc fusion proteins were adsorbed to wells of microplates. After blocking the wells with bovine serum albumin to prevent non-specific binding, NKG2D-binding domains were titrated and added to the wells pre-adsorbed with NKG2D-Fc fusion proteins. Primary antibody binding was detected using a secondary antibody which was conjugated to horseradish peroxidase and specifically recognizes a human kappa light chain to avoid Fc cross-reactivity. 3,3',5,5'-Tetramethylbenzidine (TMB), a substrate for horseradish peroxidase, was added to the wells to visualize the binding signal, whose absorbance was measured at 450 nM and corrected at 540 nM. An NKG2D-binding domain clone, an isotype control or a positive control (comprising heavy chain and light chain variable domains selected from SEQ ID NOs:101-104, or anti-mouse NKG2D clones MI-6 and CX-5 available at eBioscience) was added to each well.

[0319] The isotype control showed minimal binding to recombinant NKG2D-Fc proteins, while the positive control bound strongest to the recombinant antigens. NKG2D-binding domains produced by all clones demonstrated binding across human, mouse, and cynomolgus recombinant NKG2D-Fc proteins, although with varying affinities from clone to clone. Generally, each anti-NKG2D clone bound to human (FIG. 3) and cynomolgus (FIG. 4) recombinant NKG2D-Fc with similar affinity, but with lower affinity to mouse (FIG. 5) recombinant NKG2D-Fc.

NKG2D-binding domains bind to cells expressing NKG2D

[0320] EL4 mouse lymphoma cell lines were engineered to express human or mouse NKG2D-CD3 zeta signaling domain chimeric antigen receptors. An NKG2D-binding clone, an isotype control, or a positive control was used at a 100 nM concentration to stain extracellular NKG2D expressed on the EL4 cells. The antibody binding was detected using fluorophore-conjugated anti-human IgG secondary antibodies. Cells were analyzed by flow cytometry, and fold-over-background (FOB) was calculated using the mean fluorescence intensity (MFI) of NKG2D-expressing cells compared to parental EL4 cells.

[0321] NKG2D-binding domains produced by all clones bound to EL4 cells expressing human and mouse NKG2D. Positive control antibodies (comprising heavy chain and light chain variable domains selected from SEQ ID NOs:101-104, or anti-mouse NKG2D clones MI-6 and CX-5 available at eBioscience) gave the best FOB binding signal. The NKG2D-binding affinity for each clone was similar between cells expressing human NKG2D (FIG. 6) and mouse (FIG. 7) NKG2D.

Example 2 – NKG2D-binding domains block natural ligand binding to NKG2D

Competition With ULBP-6

[0322] Recombinant human NKG2D-Fc proteins were adsorbed to wells of a microplate, and the wells were blocked with bovine serum albumin to reduce non-specific binding. A saturating concentration of ULBP-6-His-biotin was added to the wells, followed by addition of the NKG2D-binding domain clones. After a 2-hour incubation, wells were washed and ULBP-6-His-biotin that remained bound to the NKG2D-Fc coated wells was detected by streptavidin-conjugated to horseradish peroxidase and TMB substrate. Absorbance was measured at 450 nM and corrected at 540 nM. After subtracting background, specific binding of NKG2D-binding domains to the NKG2D-Fc proteins was calculated from the percentage of ULBP-6-His-biotin that was blocked from binding to the NKG2D-Fc proteins in wells. The positive control antibody (comprising heavy chain and light chain variable domains selected from SEQ ID NOs:101-104) and various NKG2D-binding domains blocked ULBP-6 binding to NKG2D, while isotype control showed little competition with ULBP-6 (FIG. 8).

ULBP-6 sequence is represented by SEQ ID NO:108

MAAAAIPALLLCLPLLFLLFGWSRARRDDPHSLCYDITVIPKFRPGPRWCAVQ
GQVDEKTFLHYDCGNKTVTPVSPLGKKLNVTMAWKAQNPVLREVVDILTEQ

LLDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSIDGQTFLLFDSEKRM
WTTVHPGARKMKEKWENDKDVAMSFHYISMGDCIGWLEDFLMGMDSTLEP
SAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI (SEQ ID NO:108)

Competition With MICA

[0323] Recombinant human MICA-Fc proteins were adsorbed to wells of a microplate, and the wells were blocked with bovine serum albumin to reduce non-specific binding. NKG2D-Fc-biotin was added to wells followed by NKG2D-binding domains. After incubation and washing, NKG2D-Fc-biotin that remained bound to MICA-Fc coated wells was detected using streptavidin-HRP and TMB substrate. Absorbance was measured at 450 nM and corrected at 540 nM. After subtracting background, specific binding of NKG2D-binding domains to the NKG2D-Fc proteins was calculated from the percentage of NKG2D-Fc-biotin that was blocked from binding to the MICA-Fc coated wells. The positive control antibody (comprising heavy chain and light chain variable domains selected from SEQ ID NOs:101-104) and various NKG2D-binding domains blocked MICA binding to NKG2D, while isotype control showed little competition with MICA (FIG. 9).

Competition With Rae-1 delta

[0324] Recombinant mouse Rae-1delta-Fc (purchased from R&D Systems) was adsorbed to wells of a microplate, and the wells were blocked with bovine serum albumin to reduce non-specific binding. Mouse NKG2D-Fc-biotin was added to the wells followed by NKG2D-binding domains. After incubation and washing, NKG2D-Fc-biotin that remained bound to Rae-1delta-Fc coated wells was detected using streptavidin-HRP and TMB substrate. Absorbance was measured at 450 nM and corrected at 540 nM. After subtracting background, specific binding of NKG2D-binding domains to the NKG2D-Fc proteins was calculated from the percentage of NKG2D-Fc-biotin that was blocked from binding to the Rae-1delta-Fc coated wells. The positive control (comprising heavy chain and light chain variable domains selected from SEQ ID NOs:101-104, or anti-mouse NKG2D clones MI-6 and CX-5 available at eBioscience) and various NKG2D-binding domain clones blocked Rae-1delta binding to mouse NKG2D, while the isotype control antibody showed little competition with Rae-1delta (FIG. 10).

Example 3 – NKG2D-binding domain clones activate NKG2D

[0325] Nucleic acid sequences of human and mouse NKG2D were fused to nucleic acid sequences encoding a CD3 zeta signaling domain to obtain chimeric antigen receptor (CAR) constructs. The NKG2D-CAR constructs were then cloned into a retrovirus vector using Gibson assembly and transfected into expi293 cells for retrovirus production. EL4 cells were infected with viruses containing NKG2D-CAR together with 8 μg/mL polybrene. 24 hours after infection, the expression levels of NKG2D-CAR in the EL4 cells were analyzed by flow cytometry, and clones which express high levels of the NKG2D-CAR on the cell surface were selected.

[0326] To determine whether NKG2D-binding domains activate NKG2D, they were adsorbed to wells of a microplate, and NKG2D-CAR EL4 cells were cultured on the antibody fragment-coated wells for 4 hours in the presence of brefeldin-A and monensin. Intracellular TNF-α production, an indicator for NKG2D activation, was assayed by flow cytometry. The percentage of TNF-α positive cells was normalized to the cells treated with the positive control. All NKG2D-binding domains activated both human NKG2D (FIG. 11) and mouse NKG2D (FIG. 12).

Example 4 – NKG2D-binding domains activate NK cells

Primary human NK cells

[0327] Peripheral blood mononuclear cells (PBMCs) were isolated from human peripheral blood buffy coats using density gradient centrifugation. NK cells ($CD3^-CD56^+$) were isolated using negative selection with magnetic beads from PBMCs, and the purity of the isolated NK cells was typically >95%. Isolated NK cells were then cultured in media containing 100 ng/mL IL-2 for 24-48 hours before they were transferred to the wells of a microplate to which the NKG2D-binding domains were adsorbed, and cultured in the media containing fluorophore-conjugated anti-CD107a antibody, brefeldin-A, and monensin. Following culture, NK cells were assayed by flow cytometry using fluorophore-conjugated antibodies against CD3, CD56 and IFN-γ. CD107a and IFN-γ staining were analyzed in $CD3^-CD56^+$ cells to assess NK cell activation. The increase in CD107a/IFN-γ double-positive cells is indicative of better NK cell activation through engagement of two activating receptors rather than one receptor. NKG2D-binding domains and the positive control (*e.g.*, heavy chain variable domain represent by SEQ ID NO:101 or SEQ ID NO:103, and light chain variable domain represented by SEQ ID NO:102 or SEQ ID NO:104) showed a higher percentage of

NK cells becoming CD107a$^+$ and IFN-γ^+ than the isotype control (FIG. 13 & FIG. 14 represent data from two independent experiments, each using a different donor's PBMC for NK cell preparation).

Primary mouse NK cells

[0328] Spleens were obtained from C57Bl/6 mice and crushed through a 70 µm cell strainer to obtain single cell suspension. Cells were pelleted and resuspended in ACK lysis buffer (purchased from Thermo Fisher Scientific #A1049201; 155 mM ammonium chloride, 10 mM potassium bicarbonate, 0.01 mM EDTA) to remove red blood cells. The remaining cells were cultured with 100 ng/mL hIL-2 for 72 hours before being harvested and prepared for NK cell isolation. NK cells (CD3$^-$NK1.1$^+$) were then isolated from spleen cells using a negative depletion technique with magnetic beads with typically >90% purity. Purified NK cells were cultured in media containing 100 ng/mL mIL-15 for 48 hours before they were transferred to the wells of a microplate to which the NKG2D-binding domains were adsorbed, and cultured in the media containing fluorophore-conjugated anti-CD107a antibody, brefeldin-A, and monensin. Following culture in NKG2D-binding domain-coated wells, NK cells were assayed by flow cytometry using fluorophore-conjugated antibodies against CD3, NK1.1 and IFN-γ. CD107a and IFN-γ staining were analyzed in CD3$^-$NK1.1$^+$ cells to assess NK cell activation. The increase in CD107a/IFN-γ double-positive cells is indicative of better NK cell activation through engagement of two activating receptors rather than one receptor. NKG2D-binding domains and the positive control (selected from anti-mouse NKG2D clones MI-6 and CX-5 available at eBioscience) showed a higher percentage of NK cells becoming CD107a$^+$ and IFN-γ^+ than the isotype control (FIG. 15 & FIG. 16 represent data from two independent experiments, each using a different mouse for NK cell preparation).

Example 5 – NKG2D-binding domains enable cytotoxicity of target tumor cells

[0329] Human and mouse primary NK cell activation assays demonstrated increased cytotoxicity markers on NK cells after incubation with NKG2D-binding domains. To address whether this translates into increased tumor cell lysis, a cell-based assay was utilized where each NKG2D-binding domain was developed into a monospecific antibody. The Fc region was used as one targeting arm, while the Fab fragment regions (NKG2D-binding domain) acted as another targeting arm to activate NK cells. THP-1 cells, which are of human origin and express high levels of Fc receptors, were used as a tumor target and a Perkin Elmer

DELFIA Cytotoxicity Kit was used. THP-1 cells were labeled with BATDA reagent, and resuspended at 10^5/mL in culture media. Labeled THP-1 cells were then combined with NKG2D antibodies and isolated mouse NK cells in wells of a microtiter plate at 37 °C for 3 hours. After incubation, 20 µL of the culture supernatant was removed, mixed with 200 µL of Europium solution and incubated with shaking for 15 minutes in the dark. Fluorescence was measured over time by a PheraStar plate reader equipped with a time-resolved fluorescence module (Excitation 337 nM, Emission 620 nM) and specific lysis was calculated according to the kit instructions.

[0330] The positive control, ULBP-6 - a natural ligand for NKG2D – conjugated to Fc, showed increased specific lysis of THP-1 target cells by mouse NK cells. NKG2D antibodies also increased specific lysis of THP-1 target cells, while isotype control antibody showed reduced specific lysis. The dotted line indicates specific lysis of THP-1 cells by mouse NK cells without antibody added (FIG. 17).

Example 6 – NKG2D antibodies show high thermostability

[0331] Melting temperatures of NKG2D-binding domains were assayed using differential scanning fluorimetry. The extrapolated apparent melting temperatures are high relative to typical IgG1 antibodies (FIG. 18).

Example 7 – Synergistic activation of human NK cells by cross-linking NKG2D and CD16

Primary human NK cell activation assay

[0332] Peripheral blood mononuclear cells (PBMCs) were isolated from peripheral human blood buffy coats using density gradient centrifugation. NK cells were purified from PBMCs using negative magnetic beads (StemCell # 17955). NK cells were >90% $CD3^-$ $CD56^+$ as determined by flow cytometry. Cells were then expanded 48 hours in media containing 100 ng/mL hIL-2 (Peprotech #200-02) before use in activation assays. Antibodies were coated onto a 96-well flat-bottom plate at a concentration of 2 µg/mL (anti-CD16, Biolegend # 302013) and 5 µg/mL (anti-NKG2D, R&D #MAB139) in 100 µL sterile PBS overnight at 4 °C followed by washing the wells thoroughly to remove excess antibody. For the assessment of degranulation IL-2-activated NK cells were resuspended at 5×10^5 cells/mL in culture media supplemented with 100 ng/mL human IL-2 (hIL2) and 1 µg/mL APC-conjugated anti-CD107a mAb (Biolegend # 328619). 1×10^5 cells/well were then added onto

antibody coated plates. The protein transport inhibitors Brefeldin A (BFA, Biolegend # 420601) and Monensin (Biolegend # 420701) were added at a final dilution of 1:1000 and 1:270, respectively. Plated cells were incubated for 4 hours at 37 °C in 5% CO_2. For intracellular staining of IFN-γ, NK cells were labeled with anti-CD3 (Biolegend #300452) and anti-CD56 mAb (Biolegend # 318328), and subsequently fixed, permeabilized and labeled with anti-IFN-γ mAb (Biolegend # 506507). NK cells were analyzed for expression of CD107a and IFN-γ by flow cytometry after gating on live $CD56^+CD3^-$cells.

[0333] To investigate the relative potency of receptor combination, crosslinking of NKG2D or CD16, and co-crosslinking of both receptors by plate-bound stimulation was performed. As shown in Figure 19 (FIGs. 19A-19C), combined stimulation of CD16 and NKG2D resulted in highly elevated levels of CD107a (degranulation) (FIG. 19A) and/or IFN-γ production (FIG. 19B). Dotted lines represent an additive effect of individual stimulations of each receptor.

[0334] CD107a levels and intracellular IFN-γ production of IL-2-activated NK cells were analyzed after 4 hours of plate-bound stimulation with anti-CD16, anti-NKG2D or a combination of both monoclonal antibodies. Graphs indicate the mean (n = 2) ± Sd. FIG. 19A demonstrates levels of CD107a; FIG. 19B demonstrates levels of IFN-γ; FIG. 19C demonstrates levels of CD107a and IFN-γ. Data shown in FIGs. 19A-19C are representative of five independent experiments using five different healthy donors.

Example 8 – Trispecific binding protein (TriNKET)-mediated enhanced cytotoxicity of target cells

Expression of CXCR4 on human cancer cell lines

[0335] Human cancer cell lines were screened for surface expression of CXCR4 using flow cytometry. A commercially available antibody against human CXCR4 (clone 12G5) was used for cell staining. Cell lines were harvested from culture, and cells were washed in FACS buffer before staining. Cells were incubated with anti-CXCR4, or corresponding isotype control antibody for 20 minutes on ice. Cells were then washed and resuspended in FACS buffer for analysis. CXCR4 staining was compared to isotype control antibody.

[0336] FIG. 35 shows expression of CXCR4 on the surface of Raji human B cell lymphoma cell line. Raji cells demonstrated about a log shift in binding median fluorescent intensity (MFI) when stained with an antibody specific for CXCR4 compared to an isotype control antibody.

Cytotoxicity assay

[0337] PBMCs were isolated from human peripheral blood buffy coats using density gradient centrifugation. Isolated PBMCs were washed and prepared for NK cell isolation. NK cells were isolated using a negative selection technique with magnetic beads. Purity of isolated NK cells achieved was typically greater than 90% $CD3^-$ $CD56^+$. Isolated NK cells were incubated overnight without cytokine, and used the following day in cytotoxicity assays.

[0338] KHYG-1 cells transduced to express CD16-F158V were used to investigate the contribution of dual NKG2D and CD16 stimulation. KHYG-1-CD16V cells were maintained in 10%HI-FBS-RPMI-1640 with 10 ng/mL IL-2. The day before use as effector cells in killing assays, KHYG-1-CD16V cells were harvested from culture, and cells were washed out of the IL-2 containing media. After washing KHYG-1 cells were resuspended in 10%HI-FBS-RPMI-1640, and were rested overnight without cytokine.

KHYG-1-CD16V cytotoxicity assay

FIG. 36 shows CXCR4-targeted TriNKETs enhance KHYG-1 killing of Raji target cells in a dose-dependent manor. KHYG-1 cells showed weak activity against Raji cells at a 10:1 effector-to-target ratio, with about 6% lysis of target cells. A monoclonal antibody against CXCR4, Hz515H7, was able to enhance KHYG-1 activity. Three TriNKETs using the Hz515H7 CXCR4 binding domain were designed using three different NKG2D binding domains. TriNKETs tested were A49-TriNKET-CXCR4-Hz515H7 (an NKG2D-binding domain from clone ADI-27749 and a CXCR4-binding domain derived from Hz515H7), A44-TriNKET-CXCR4-Hz515H7 (an NKG2D-binding domain from clone ADI-27744 and a CXCR4-binding domain derived from Hz515H7), and C26-TriNKET-CXCR4-Hz515H7 (an NKG2D-binding domain from clone ADI-28226 and a CXCR4-binding domain derived from Hz515H7). All three TriNKETs showed enhanced potency and maximum lysis of Raji target cells compared to the monoclonal antibody.

DELFIA cytotoxicity assay

[0339] Human cancer cell lines expressing a target of interest were harvested from culture, washed with HBS, and resuspended in growth media at 10^6 cells/mL for labeling with BATDA reagent (Perkin Elmer, AD0116). Manufacturer instructions were followed for labeling of the target cells. After labeling, cells were washed 3 times with HBS and resuspended at $0.5x10^5$ cells/mL in culture media. To prepare the background wells, an aliquot of the labeled cells was put aside, and the cells were spun out of the media. 100 µL of

the media was carefully added to wells in triplicate to avoid disturbing the pelleted cells. 100 µL of BATDA-labeled cells were added to each well of the 96-well plate. Wells were saved for spontaneous release from target cells and prepared for lysis of target cells by addition of 1% Triton-X. Monoclonal antibodies or TriNKETs against the tumor target of interest were diluted in culture media, and 50 µL of diluted mAb or TriNKET was added to each well. Rested NK cells were harvested from culture, washed, and resuspended at $1.0x10^5$-$2.0x10^6$ cell/mL in culture media, depending on the desired effector to target cell ratio. 50 µL of NK cells were added to each well of the plate to provide a total of 200 µL culture volume. The plate was incubated at 37 °C with 5% CO_2 for 2-4 hours before developing the assay.

[0340] After culturing for 2-3 hours, the plate was removed from the incubator and the cells were pelleted by centrifugation at 200xg for 5 minutes. 20 µL of culture supernatant was transferred to a clean microplate provided from the manufacturer, and 200 µL of room temperature Europium solution was added to each well. The plate was protected from light and incubated on a plate shaker at 250 rpm for 15 minutes. The plate was read using a SpectraMax® i3X instrument (Molecular Devices), and percent specific lysis was calculated (% Specific lysis = (Experimental release – Spontaneous release) / (Maximum release – Spontaneous release)) x 100).

Primary human NK cytotoxicity assay

[0341] FIG. 37 shows CXCR4-targeted TriNKETs enhance primary NK cell killing of the CXCR4 positive tumor cell line Raji. Human NK cells showed weak activity against Raji cells at a 5:1 effector-to-target ratio, with 8% lysis of target cells. A monoclonal antibody against CXCR4, Hz515H7, was able to enhance NK cell activity to about 15% lysis. Three TriNKETs using the Hz515H7 CXCR4 binding domain were designed using three different NKG2D binding domains. All three TriNKETs showed enhanced NK cell mediated lysis compared to the monoclonal antibody.

INCORPORATION BY REFERENCE

[0342] The entire disclosure of each of the patent documents and scientific articles referred to herein is incorporated by reference for all purposes.

EQUIVALENTS

[0343] The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting the invention described herein. Scope of the invention is thus indicated by the appended claims rather than by the foregoing description, and all changes that come within the meaning and range of equivalency of the claims are intended to be embraced therein.

Claims:

1. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds an antigen selected from the group consisting of: CXCR4, CD25, VLA4, CD44, CD13, CD15, CD47, CD81, CD23, CD40, CD70, CD79a, CD79b, CD80, CRLF2, SLAMF7, CD138, CD38, T-cell receptor beta-1 chain C region (TRBC1), T-cell receptor beta-2 chain C region (TRBC2), leukocyte immunoglobulin-like receptor family member selected from LILRB2, LILRB1, LILRB3, LILRB4, LILRB5, LILRA1, LILRA2, LILRA3, LILRA4, LILRA5, and LILRA6, and a protein expressed from regulatory T cells selected from a group consisting of CCR8, CD7, CTLA4, CX3CR1, ENTPD1, HAVCR2, IL-1R2, PDCD1LG2, TIGIT, TNFRSF4, TNFRSF8, TNFRSF9, GEM, NT5E, and TNFRSF18; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

2. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds CXCR4; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

3. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds CD25; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

4. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds a tumor associated antigen selected from VLA4, CD44, CD13, CD15, CD47, and CD81; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

5. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds a tumor associated antigen selected from CD23, CD40, CD70, CD79a, CD79b, CD80, and CRLF2; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

6. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds a multiple myeloma associated antigen selected from SLAMF7, CD138 and CD38; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

7. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds a T-cell associated tumor antigen selected from T-cell receptor beta-1 chain C region (TRBC1) and T-cell receptor beta-2 chain C region (TRBC2); and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

8. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds a leukocyte immunoglobulin-like receptor family member selected from LILRB2, LILRB1, LILRB3, LILRB4, LILRB5, LILRA1, LILRA2, LILRA3, LILRA4, LILRA5, and LILRA6; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

9. A protein comprising:

(a) a first antigen-binding site that binds NKG2D;

(b) a second antigen-binding site that binds a protein expressed from regulatory T cells selected from a group consisting of CCR8, CD7, CTLA4, CX3CR1, ENTPD1, HAVCR2, IL-1R2, PDCD1LG2, TIGIT, TNFRSF4, TNFRSF8, TNFRSF9, GEM, NT5E, and TNFRSF18; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

10. The protein of any one of claims 1-9, wherein the first antigen-binding site binds to NKG2D in humans, non-human primates, and rodents.

11. The protein of claim any one of claims 1-10, wherein the first antigen-binding site comprises a heavy chain variable domain and a light chain variable domain.

12. A protein according to claim 11, wherein the heavy chain variable domain and the light chain variable domain are present on the same polypeptide.

13. A protein according to claims 11 or 12, wherein the second antigen-binding site comprises a heavy chain variable domain and a light chain variable domain.

14. A protein according to claim 13, wherein the heavy chain variable domain and the light chain variable domain of the second antigen-binding site are present on the same polypeptide.

15. A protein according to claim 13 or 14, wherein the light chain variable domain of the first antigen-binding site has an amino acid sequence identical to the amino acid sequence of the light chain variable domain of the second antigen-binding site.

16. A protein according to any one of the preceding claims, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to an amino acid sequence selected from: SEQ ID NO:1, SEQ ID NO:41, SEQ ID NO:49, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:69, SEQ ID NO:77, SEQ ID NO:85, and SEQ ID NO:93.

17. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:41 and a light chain variable domain at least 90% identical to SEQ ID NO:42.

18. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:49 and a light chain variable domain at least 90% identical to SEQ ID NO:50.

19. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:57 and a light chain variable domain at least 90% identical to SEQ ID NO:58.

20. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:59 and a light chain variable domain at least 90% identical to SEQ ID NO:60.

21. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:61 and a light chain variable domain at least 90% identical to SEQ ID NO:62.

22. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:69 and a light chain variable domain at least 90% identical to SEQ ID NO:70.

23. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:77 and a light chain variable domain at least 90% identical to SEQ ID NO:78.

24. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:85 and a light chain variable domain at least 90% identical to SEQ ID NO:86.

25. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:93 and a light chain variable domain at least 90% identical to SEQ ID NO:94.

26. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:101 and a light chain variable domain at least 90% identical to SEQ ID NO:102.

27. A protein according to any one of claims 1-15, wherein the first antigen-binding site comprises a heavy chain variable domain at least 90% identical to SEQ ID NO:103 and a light chain variable domain at least 90% identical to SEQ ID NO:104.

28. The protein of any one of claims 1-10, wherein the first antigen-binding site is a single-domain antibody.

29. The protein of claim 28, wherein the single-domain antibody is a V_HH fragment or a V_{NAR} fragment.

30. A protein of any one of claims 1-10 or 28-29, wherein the second antigen-binding site comprises a heavy chain variable domain and a light chain variable domain.

31. A protein of claim 30, wherein the heavy chain variable domain and the light chain variable domain of the second antigen-binding site are present on the same polypeptide.

32. A protein of any of claims 1, 2, or 16-31, wherein the second antigen-binding site binds CXCR4, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:109 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:110.

33. A protein of claim 32, wherein the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence including:

a heavy chain CDR1 sequence identical to the amino acid sequence of SEQ ID NO:111;

a heavy chain CDR2 sequence identical to the amino acid sequence of SEQ ID NO:112; and

a heavy chain CDR3 sequence identical to the amino acid sequence of SEQ ID NO:113.

34. A protein of claim 33, wherein the light chain variable domain of the second antigen-binding site comprises an amino acid sequence including:

a light chain CDR1 sequence identical to the amino acid sequence of SEQ ID NO:114;

a light chain CDR2 sequence identical to the amino acid sequence of SEQ ID NO:115;

and a light chain CDR3 sequence identical to the amino acid sequence of SEQ ID NO:116.

35. A protein of any one of claims 1, 2, or 16-31, wherein the second antigen-binding site binds CXCR4, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:117 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:118.

36. A protein of claim 35, wherein the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence including:

a heavy chain CDR1 sequence identical to the amino acid sequence of SEQ ID NO:119;

a heavy chain CDR2 sequence identical to the amino acid sequence of SEQ ID NO:120; and

a heavy chain CDR3 sequence identical to the amino acid sequence of SEQ ID NO:121.

37. A protein according to claim 36, wherein the light chain variable domain of the second antigen-binding site comprises an amino acid sequence including:

a light chain CDR1 sequence identical to the amino acid sequence of SEQ ID NO:122;

a light chain CDR2 sequence identical to the amino acid sequence of SEQ ID NO:123; and

a light chain CDR3 sequence identical to the amino acid sequence of SEQ ID NO:124.

38. A protein of any one of claims 1, 2, or 16-31, wherein the second antigen-binding site binds CXCR4, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:522 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:526.

39. A protein of claim 38, wherein the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence including:

a heavy chain CDR1 sequence identical to the amino acid sequence of SEQ ID NO:523;

a heavy chain CDR2 sequence identical to the amino acid sequence of SEQ ID NO:524; and

a heavy chain CDR3 sequence identical to the amino acid sequence of SEQ ID NO:525.

40. A protein of claim 39, wherein the light chain variable domain of the second antigen-binding site comprises an amino acid sequence including:

a light chain CDR1 sequence identical to the amino acid sequence of SEQ ID NO:527;

a light chain CDR2 sequence identical to the amino acid sequence of SEQ ID NO:528; and

a light chain CDR3 sequence identical to the amino acid sequence of SEQ ID NO:529.

41. A protein of any one of claims 1, 3, or 16-31, wherein the second antigen-binding site binds CD25, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:134 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:135.

42. A protein of any one of claims 1, 3, or 16-31, wherein the second antigen-binding site binds CD25, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:142 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:143.

43. A protein of any one of claims 1, 3, or 16-31, wherein the second antigen-binding site binds CD25, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:150 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:151.

44. A protein of any one of claims 1, 4, or 16-31, wherein the second antigen-binding site binds VLA4/VCAM-1, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:166 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:167.

45. A protein of any one of claims 1, 4, or 16-31, wherein the second antigen-binding site binds CD44, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:174 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:175.

46. A protein of any one of claims 1, 4, or 16-31, wherein the second antigen-binding site binds CD47, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:182 and the light chain variable

domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:183.

47. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD23, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:197 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:198.

48. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD40, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:205 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:206.

49. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD40, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:213 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:214.

50. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD40, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:221 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:222.

51. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD40, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:229 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:230.

52. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD70, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:237 and the light chain variable

domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:238.

53. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD79b, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:245 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:246.

54. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CD80, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:253 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:254.

55. A protein of any one of claims 1, 5, or 16-31, wherein the second antigen-binding site binds CRLF2, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:261 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:262.

56. A protein of any one of claims 1, 6, or 16-31, wherein the second antigen-binding site binds SLAMF7, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:272 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:273.

57. A protein of any one of claims 1, 6, or 16-31, wherein the second antigen-binding site binds SLAMF7, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:280 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:281.

58. A protein of any one of claims 1, 6, or 16-31, wherein the second antigen-binding site binds CD138, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:288 and the light chain variable

domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:289.

59. A protein of any one of claims 1, 6, or 16-31, wherein the second antigen-binding site binds CD38, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:296 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:297.

60. A protein of any one of claims 1, 6, or 16-31, wherein the second antigen-binding site binds CD38, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:304 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:305.

61. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds CD7, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:325 or SEQ ID NO:329.

62. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds CTLA4, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:333 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:334.

63. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds CTLA4, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:341 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:342.

64. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds CX3CR1, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:349 or SEQ ID NO:353.

65. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds ENTPD1, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:358 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:359.

66. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds ENTPD1, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:366 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:367.

67. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds HAVCR2, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:374 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:375.

68. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds HAVCR2, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:382 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:383.

69. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds PDCDILG2, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:390 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:391.

70. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds PDCDILG2, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:398 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:399.

71. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TIGIT, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:406 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:407.

72. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TIGIT, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:414 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:415.

73. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF4, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:422 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:423.

74. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF4, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:430 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:431.

75. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF8, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:438 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:439.

76. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF8, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:446 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:447.

77. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF9, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:454 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:455.

78. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF9, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:462 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:463.

79. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds NST5, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:470 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:471.

80. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds NST5, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:478 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:479.

81. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF18, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:486 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:487.

82. A protein of any one of claims 1, 9, or 16-31, wherein the second antigen-binding site binds TNFRSF18, the heavy chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:494 and the light chain variable domain of the second antigen-binding site comprises an amino acid sequence at least 90% identical to SEQ ID NO:495.

83. A protein of any one of claims 1-12 or 16-29, wherein the second antigen-binding site is a single-domain antibody.

84. The protein of claim 83, wherein the second antigen-binding site is a V_HH fragment or a V_{NAR} fragment.

85. A protein according to any one of claims 1-84, wherein the antibody Fc domain comprises a hinge and a CH2 domain.

86. A protein according to any one of claims 1-84, wherein the antibody Fc domain comprises hinge and CH2 domains of a human IgG1 antibody.

87. A protein of claim 85 or 86, wherein the Fc domain comprises an amino acid sequence at least 90% identical to amino acids 234-332 of a human IgG1 antibody.

88. A protein of claim 87, wherein the Fc domain comprises amino acid sequence at least 90% identical to the Fc domain of human IgG1 and differs at one or more positions selected from the group consisting of Q347, Y349, L351, S354, E356, E357, K360, Q362, S364, T366, L368, K370, N390, K392, T394, D399, S400, D401, F405, Y407, K409, T411, K439.

89. A formulation comprising a protein according to any one of the preceding claims and a pharmaceutically acceptable carrier.

90. A cell comprising one or more nucleic acids expressing a protein according to any one of claims 1-88.

91. A method of directly and/or indirectly enhancing tumor cell death, the method comprising exposing a tumor and natural killer cells to a protein according to any one of claims 1-88.

92. A method of treating cancer, wherein the method comprises administering a protein according to any one of claims 1-88 or a formulation according to claim 89 to a patient.

93. The method of claim 92, wherein when the second binding site binds CXCR4, the cancer is selected from the group consisting of acute myeloid leukemia, multiple myeloma, diffuse large B cell lymphoma, thymoma, adenoid cystic carcinoma, gastrointestinal cancer, renal cancer, breast cancer, glioblastoma, lung cancer, ovarian cancer, brain cancer, prostate cancer, pancreatic cancer, and melanoma.

94. The method of claim 92, wherein when the second binding site binds CD25, the cancer is selected from the group consisting of acute myeloid leukemia, chronic lymphocytic leukemia, glioblastoma, bladder cancer, colon cancer, germ cell tumors, lung cancer, osteosarcoma, melanoma, ovarian cancer, multiple myeloma, head and neck cancer, renal cell cancer, and breast cancer.

95. The method of claim 92, wherein, when the second binding site binds VLA4, CD44, CD13, CD15, CD47, or CD81, the cancer is selected from the group consisting of acute myeloid leukemia, multiple myeloma, chronic lymphocytic leukemia, B cell lymphoma, T cell lymphoma, Hodgkin lymphoma, breast cancer, glioblastoma, head and neck cancer, ovarian cancer, prostate cancer, melanoma, lung cancer, pancreatic cancer, liver cancer, gastric cancer, thyroid cancer, and brain cancer.

96. The method of claim 92, wherein when the second binding site binds CD23, CD40, CD70, CD79a, CD79b, CD80, or CRLF2, the cancer is selected from the group consisting of a B cell malignancies, Non-Hodgkin lymphoma, chronic lymphocytic leukemia, acute lymphoblastic leukemia, multiple myeloma, diffuse large B cell lymphoma, follicular lymphoma, T cell lymphoma, renal cancer, glioblastoma, head and neck cancer, nasopharyngeal carcinoma, bladder cancer, cervical cancer, kidney cancer, and ovarian cancer.

97. The method of claim 92, wherein when the second binding site binds LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, LILRA1, LILRA2, LILRA3, LILRA4, LILRA5, or LILRA6, the cancer is selected from the group consisting of AML, B cell leukemia, B cell lymphoma, multiple myeloma, T cell leukemia, T cell lymphoma, lung cancer, gastric cancer, breast cancer, and pancreas cancer.

FIG. 1

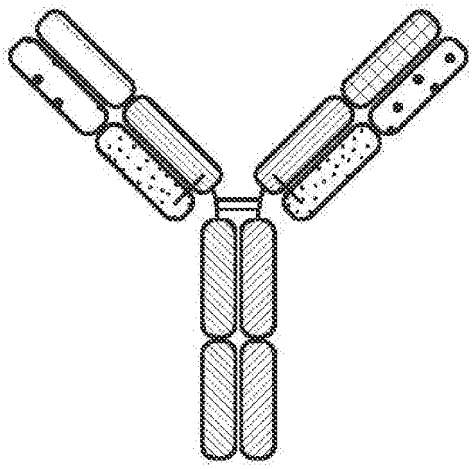


FIG. 2

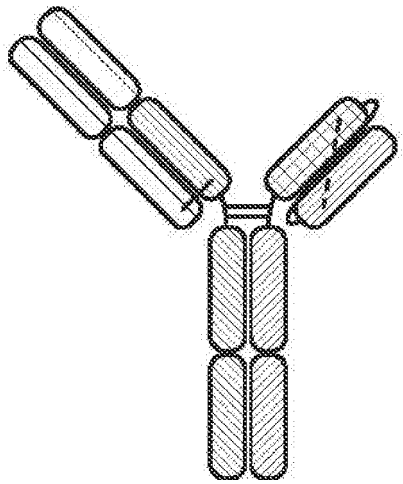


FIG. 3

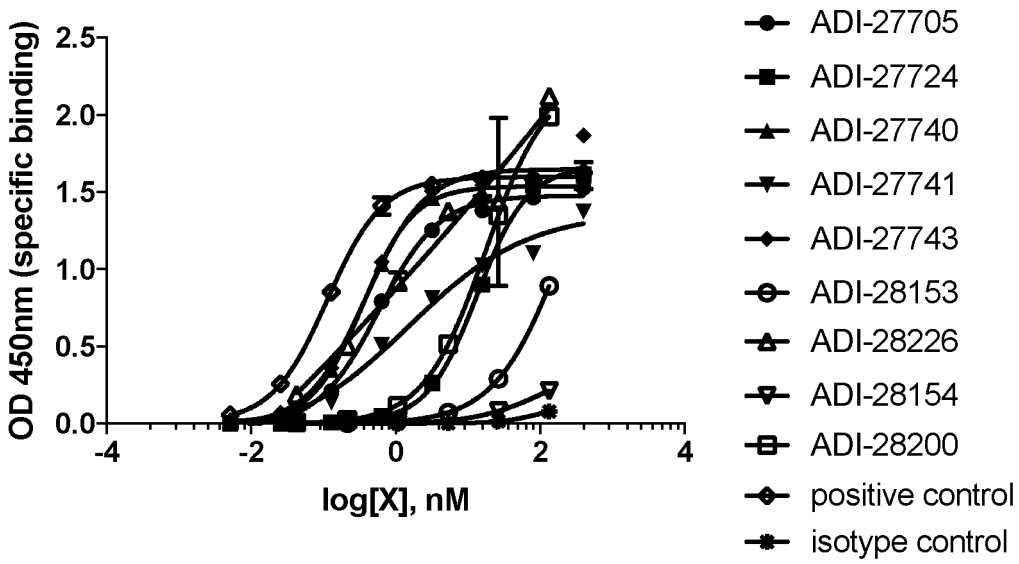

OD 450nm (specific binding)
2.5
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[X], nM
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
positive control
isotype control

FIG. 4

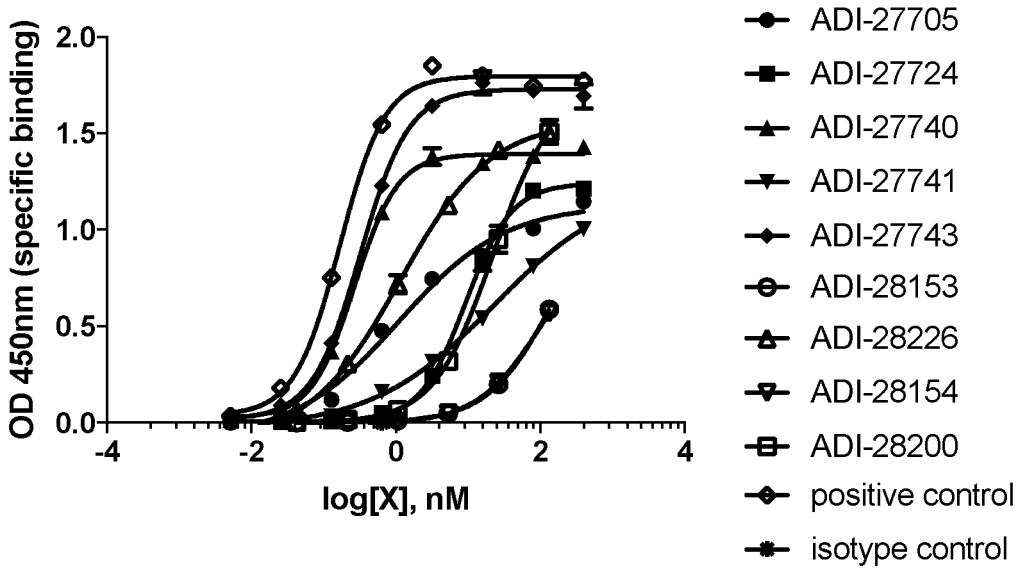

OD 450nm (specific binding)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[X], nM
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
positive control
isotype control

FIG. 5

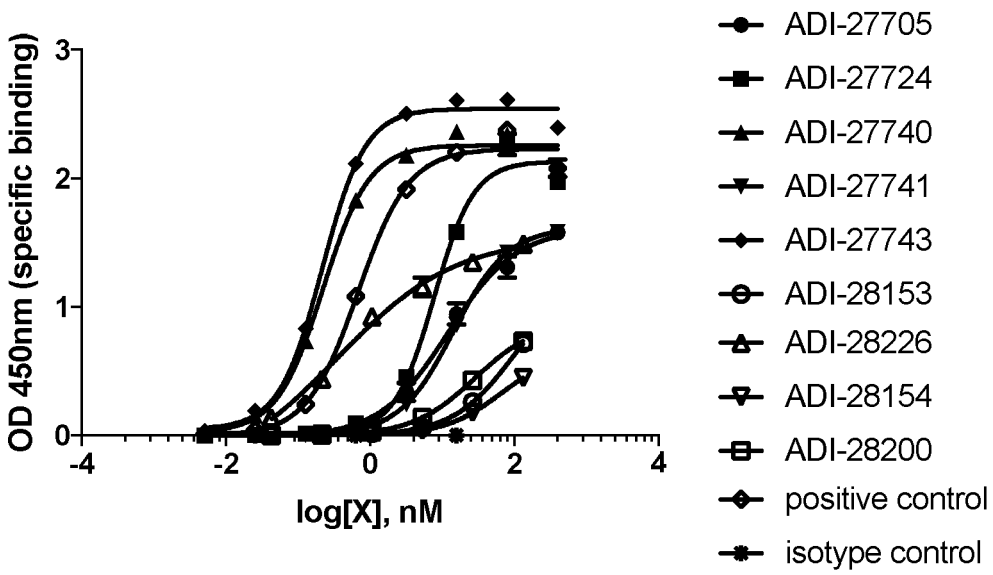

OD 450nm (specific binding)
3
2
1
0
-4
-2
0
2
4
log[X], nM
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
positive control
isotype control

FIG. 6

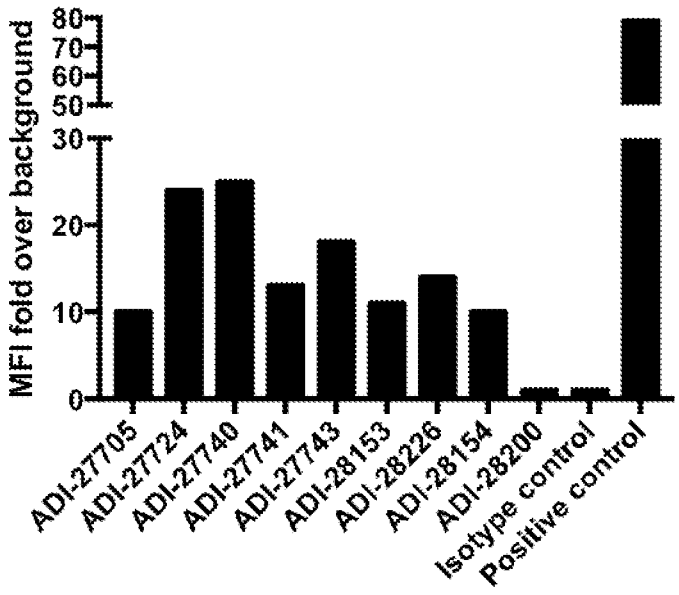

MFI fold over background
80
70
60
50
30
20
10
0
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 7

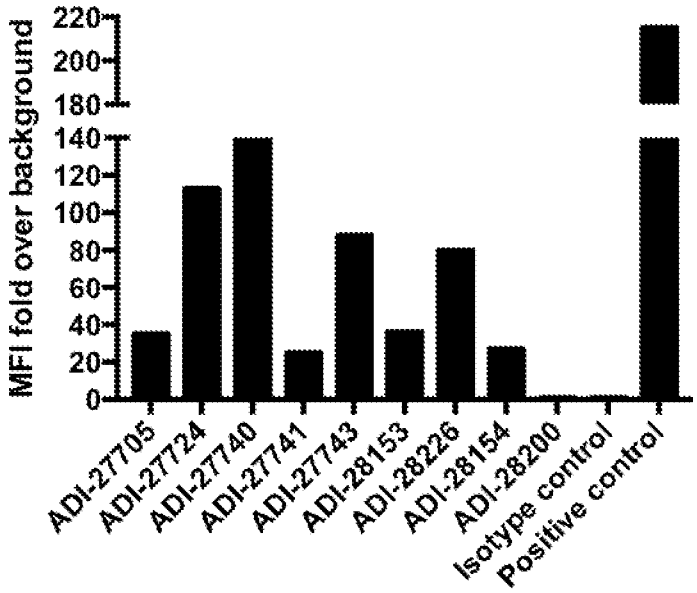

MFI fold over background
220
200
180
140
120
100
80
60
40
20
0
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 8

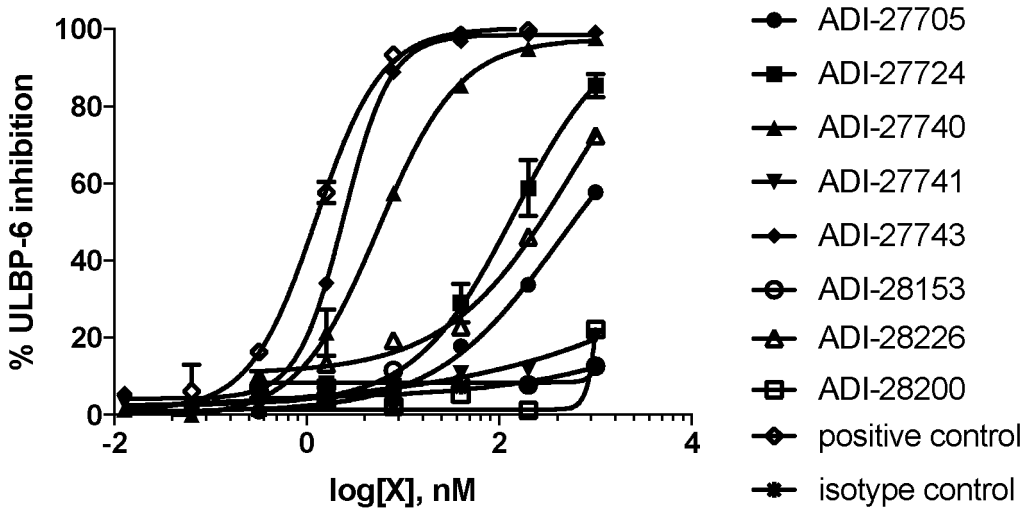

% ULBP-6 inhibition
100
80
60
40
20
0
-2
0
2
4
log[X], nM
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28200
positive control
isotype control

FIG. 9

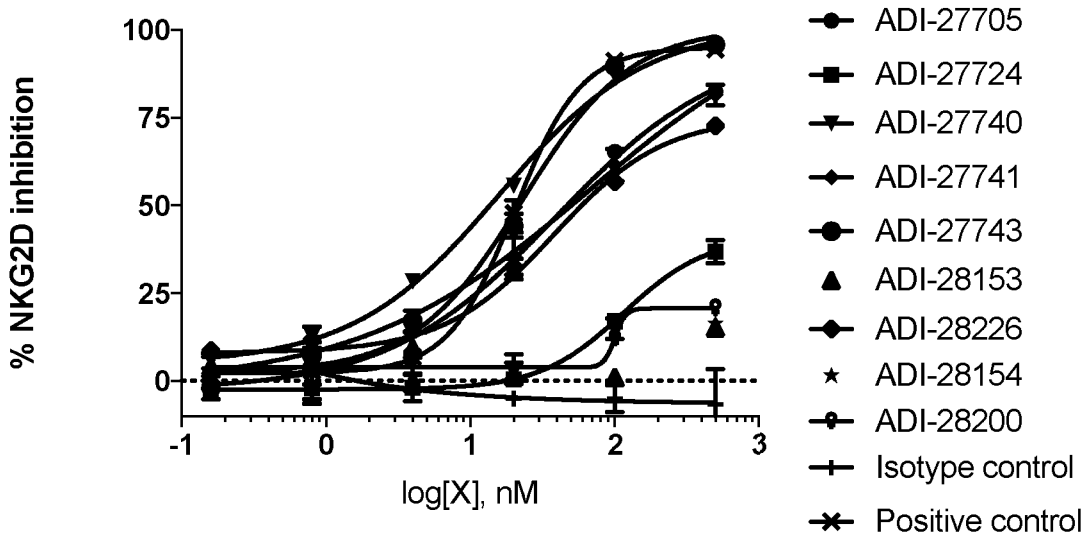

% NKG2D inhibition
100
75
50
25
0
-1
0
1
2
3
log[X], nM
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 10

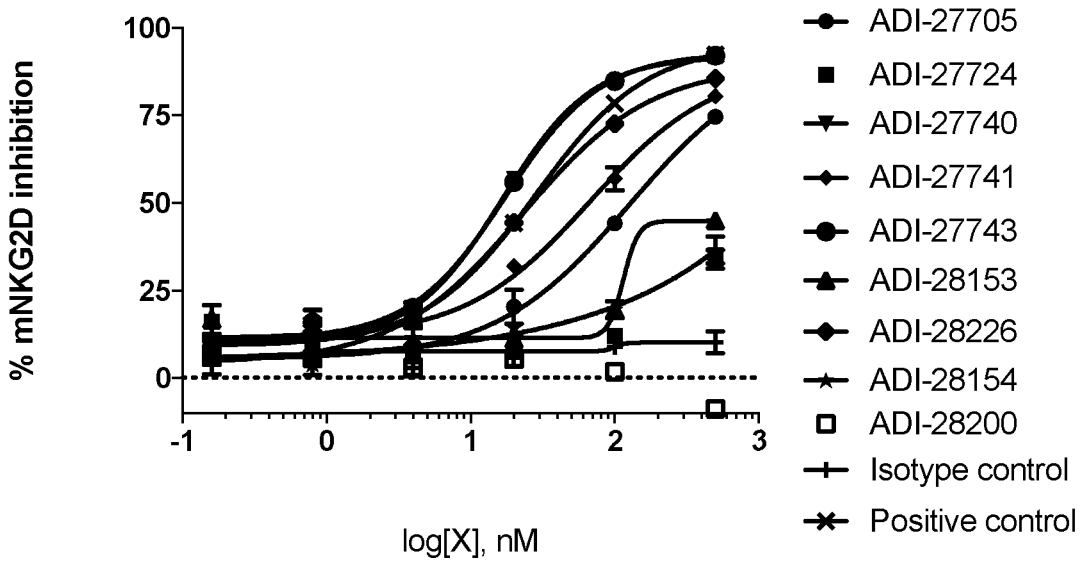

% mNKG2D inhibition
100
75
50
25
0
-1
0
1
2
3
log[X], nM
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 11

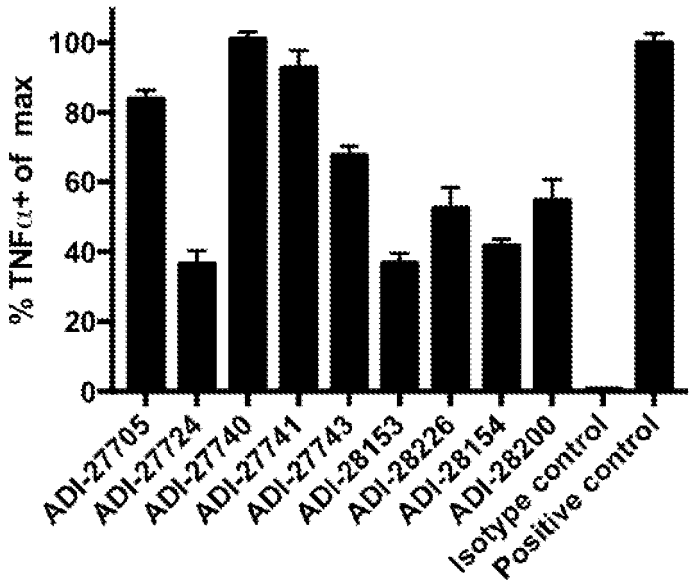

% TNFα+ of max
100
80
60
40
20
0
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 12

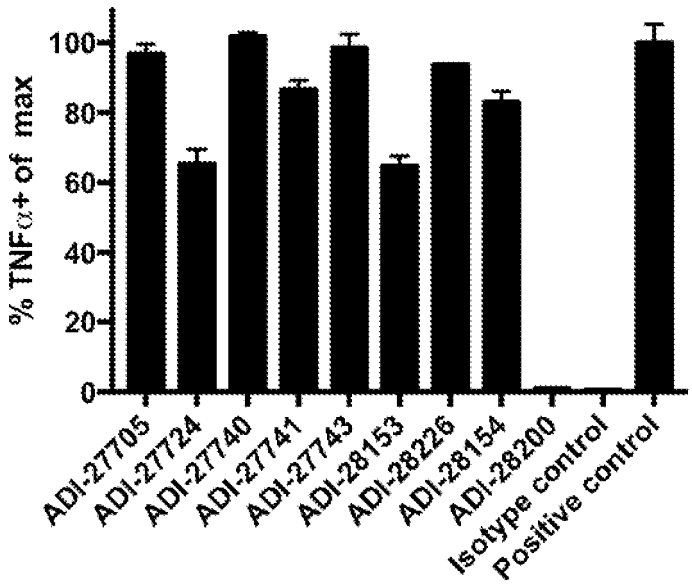

% TNFα+ of max
100
80
60
40
20
0
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 13

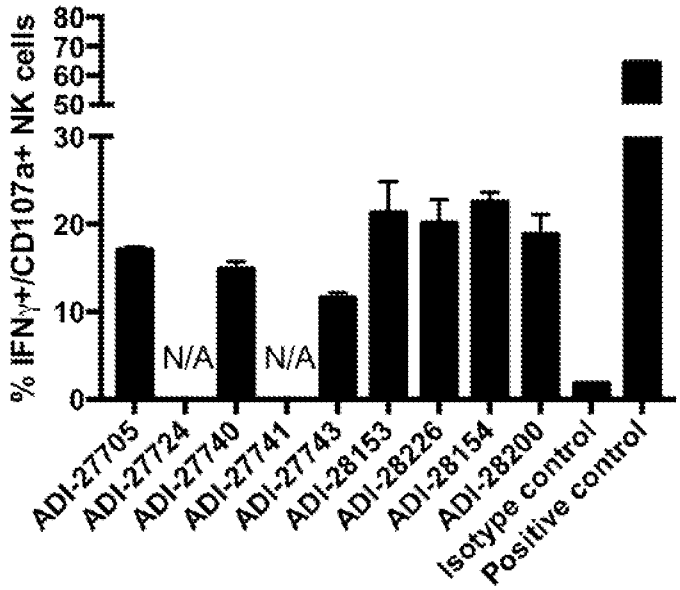

% IFNγ+/CD107a+ NK cells
80
70
60
50
30
20
10
0
N/A
N/A
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 14

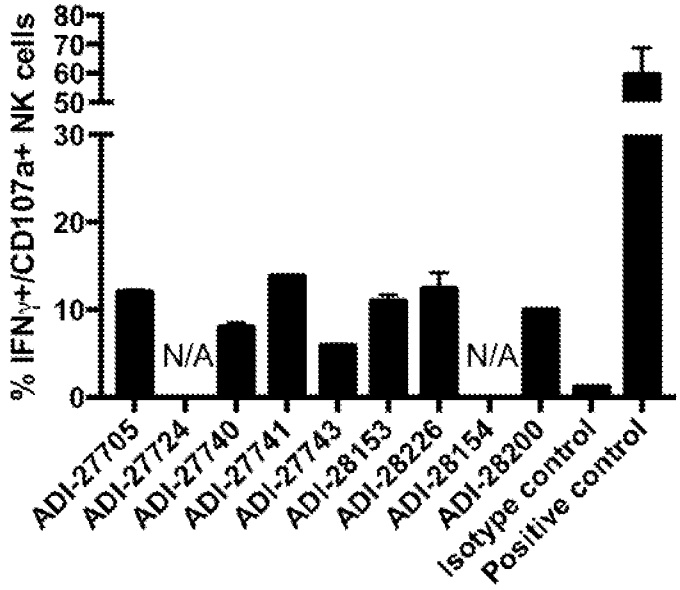

% IFNγ+/CD107a+ NK cells
80
70
60
50
30
20
10
0
N/A
N/A
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
ADI-28200
Isotype control
Positive control

FIG. 15

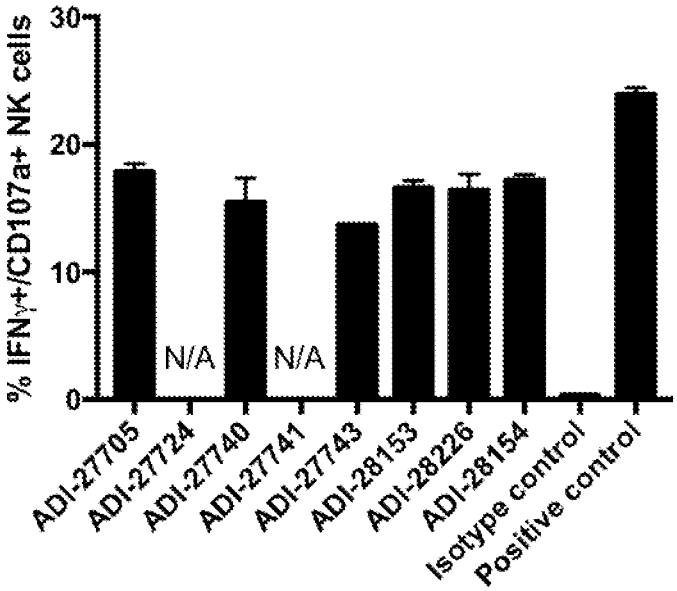

% IFNγ+/CD107a+ NK cells
30
20
10
0
N/A
N/A
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
Isotype control
Positive control

FIG. 16

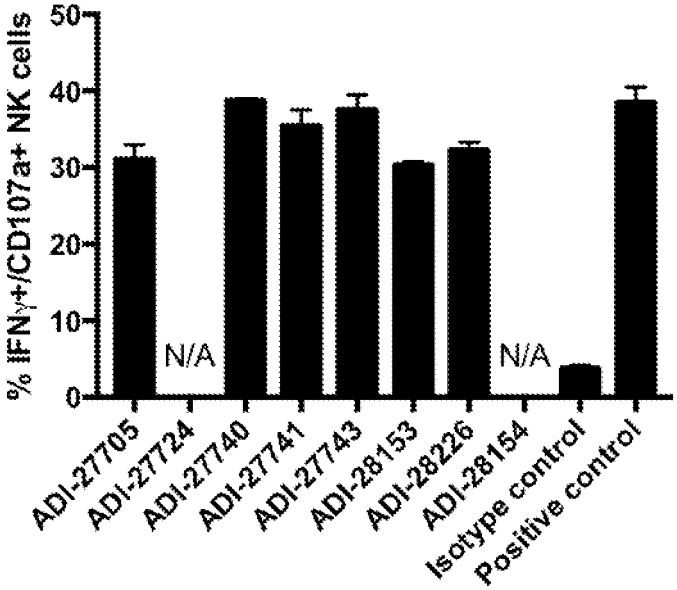

% IFNγ+/CD107a+ NK cells
50
40
30
20
10
0
N/A
N/A
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
Isotype control
Positive control

FIG. 17

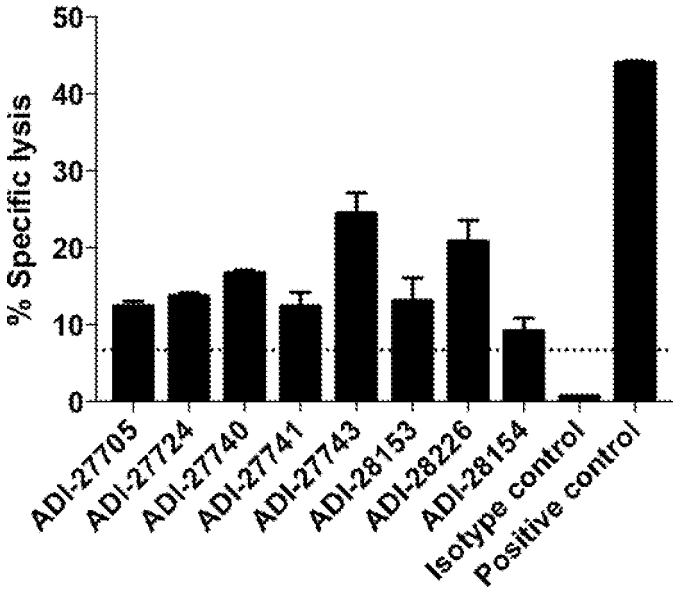

% Specific lysis
50
40
30
20
10
0
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154
Isotype control
Positive control

FIG. 18

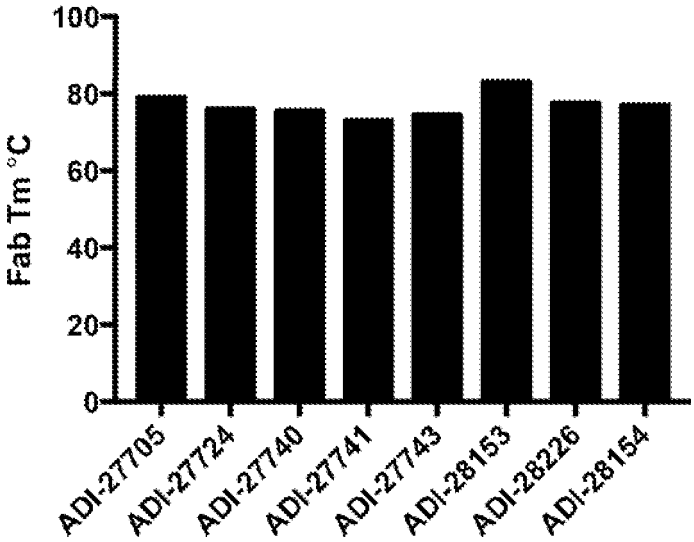

Fab Tm °C
100
80
60
40
20
0
ADI-27705
ADI-27724
ADI-27740
ADI-27741
ADI-27743
ADI-28153
ADI-28226
ADI-28154

FIG. 19A

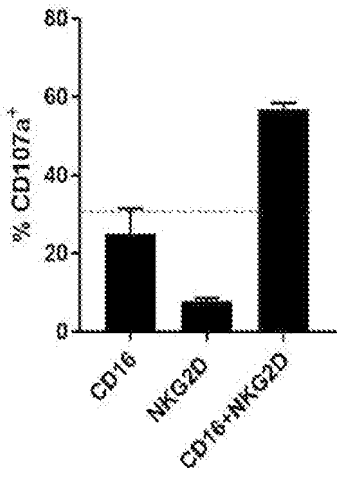


FIG. 19B

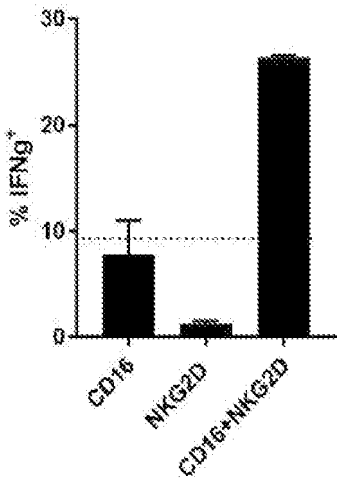


FIG. 19C

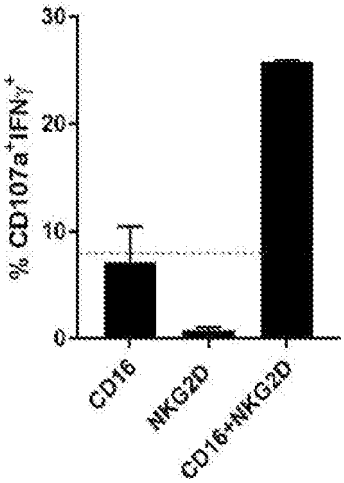


FIG. 20

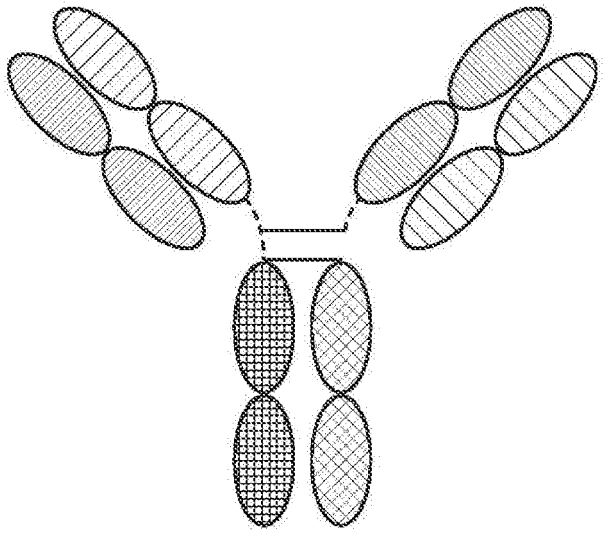


FIG. 21

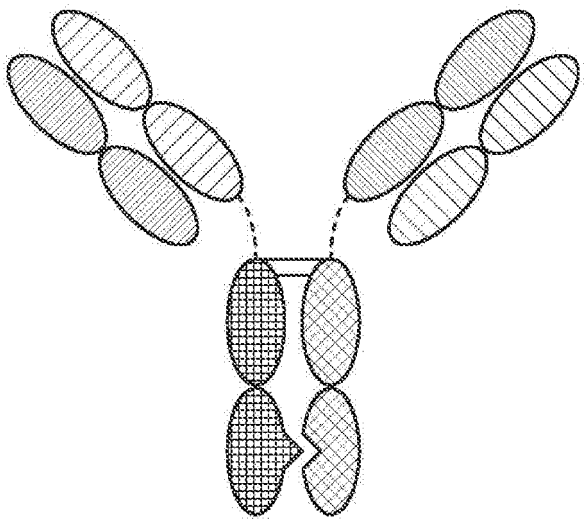


FIG. 22

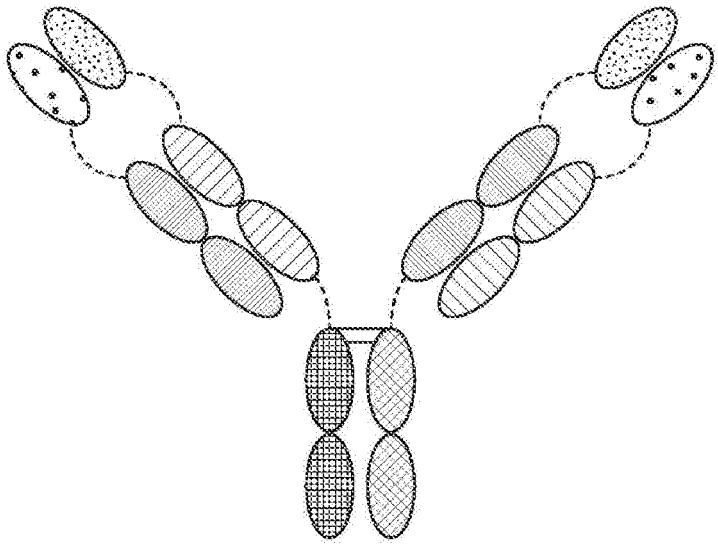


FIG. 23

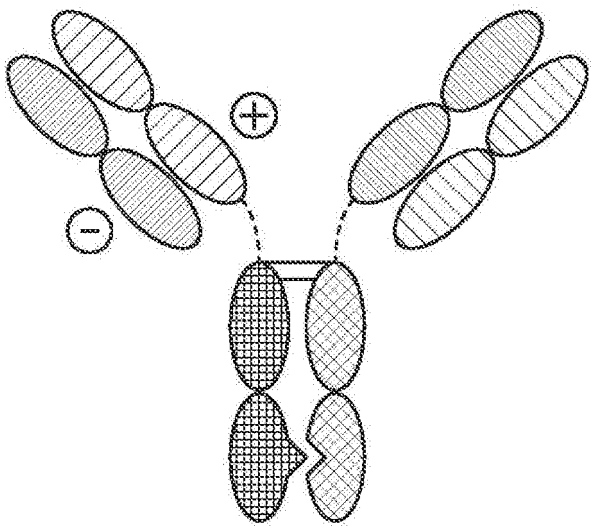


FIG. 24

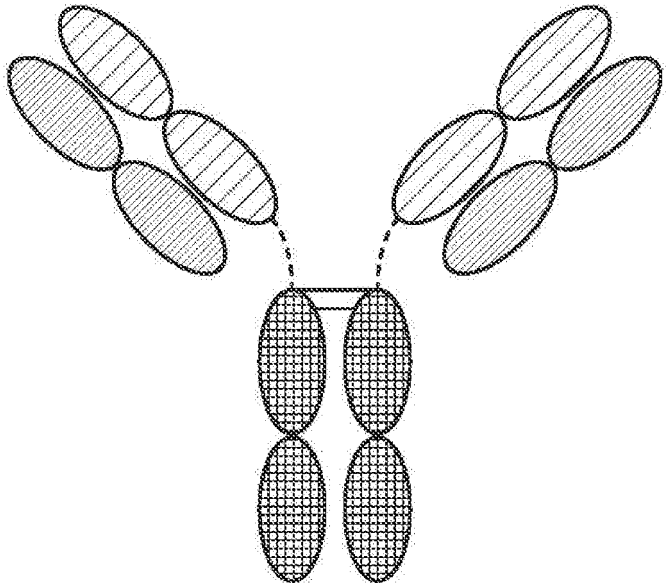


FIG. 25

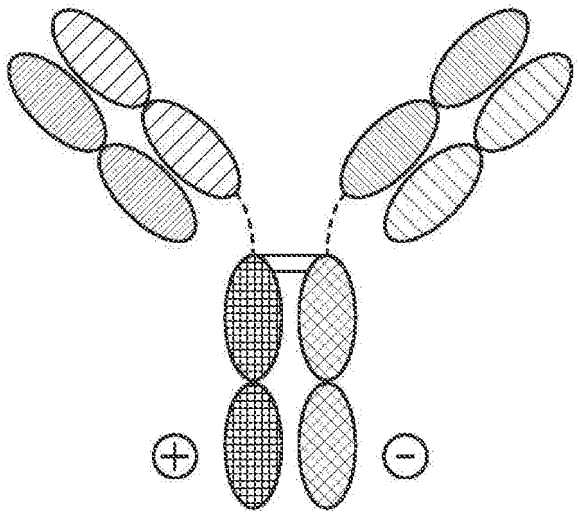


FIG. 26

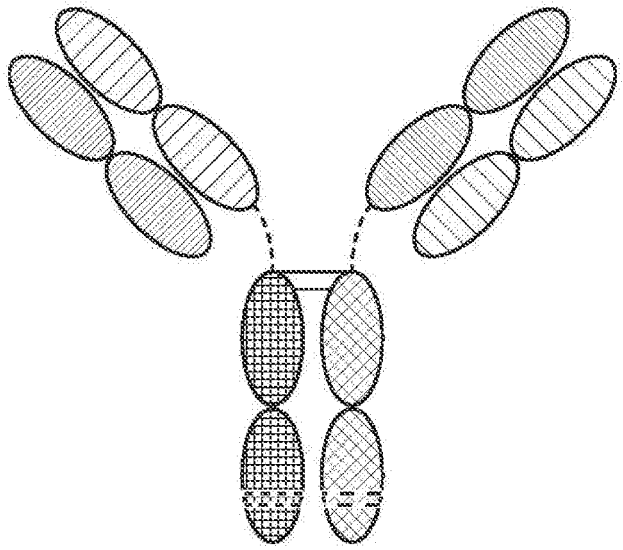


FIG. 27

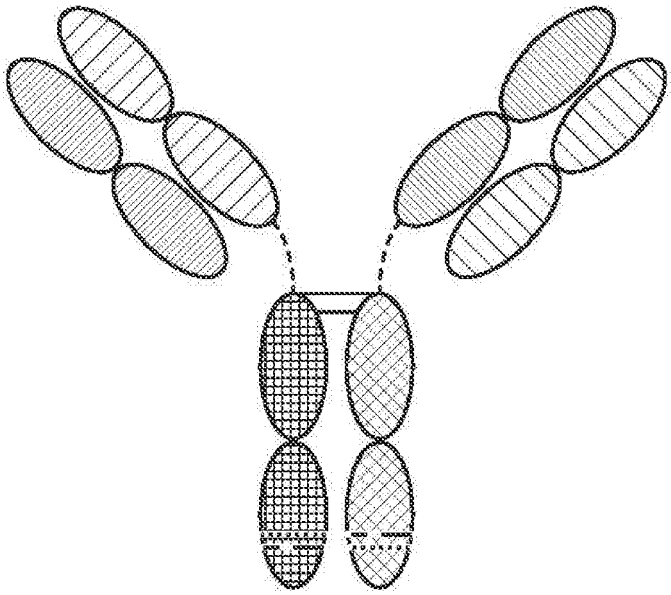


FIG. 28

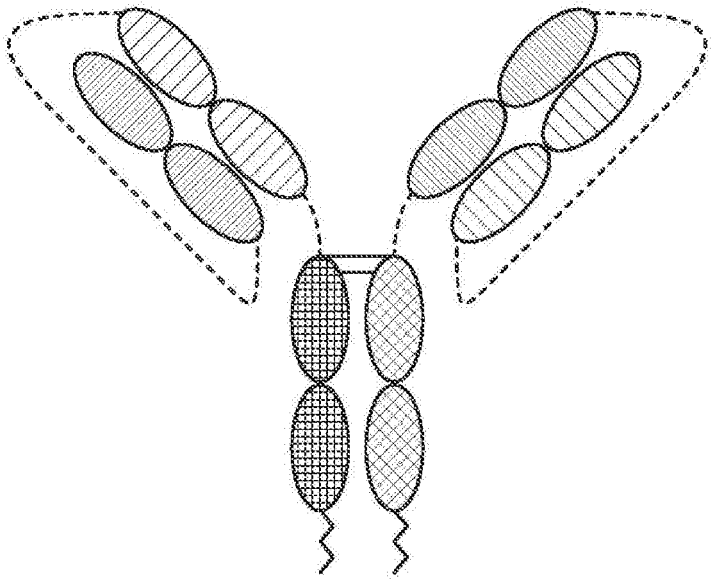


FIG. 29

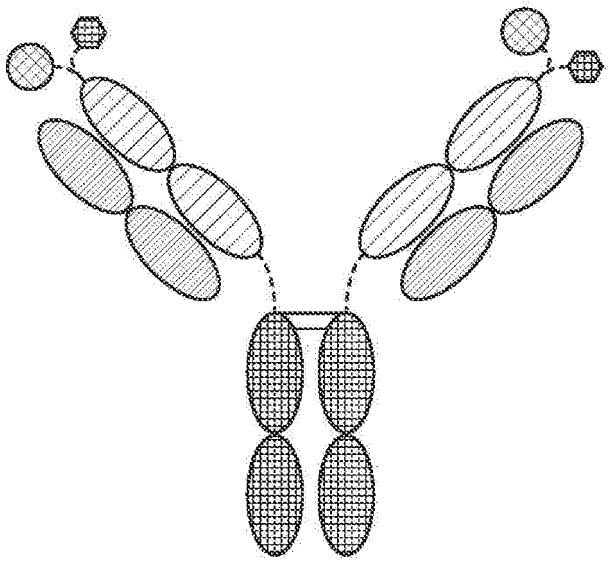


FIG. 30A

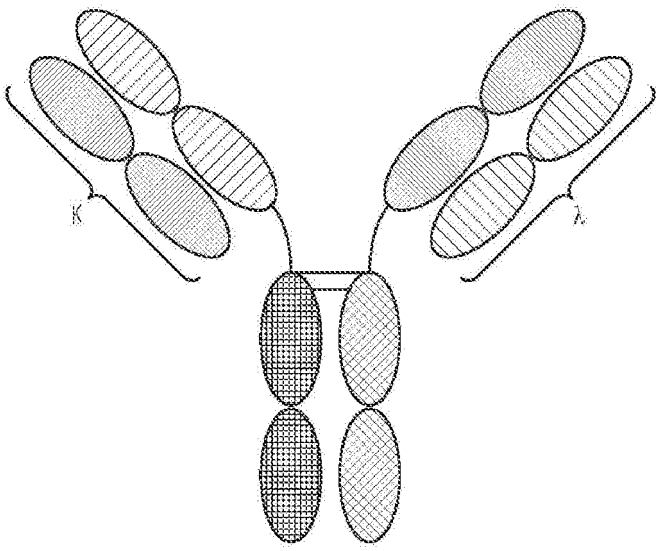


FIG. 30B

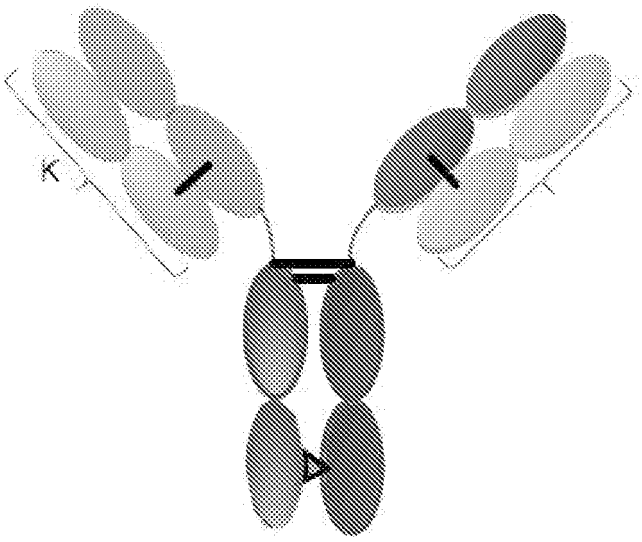


FIG. 31

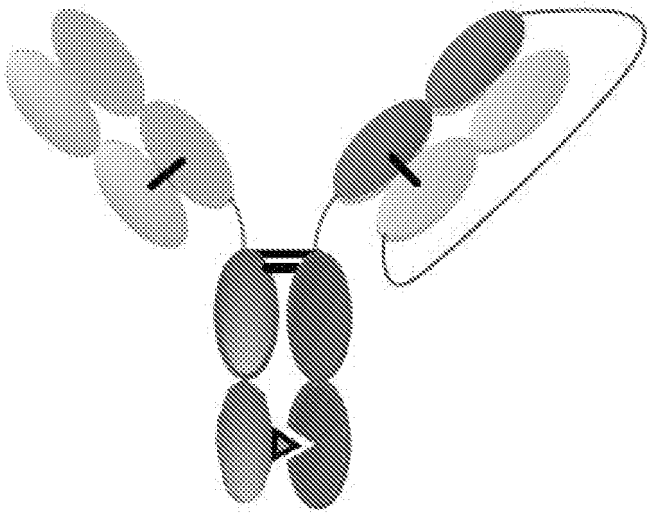


FIG. 32

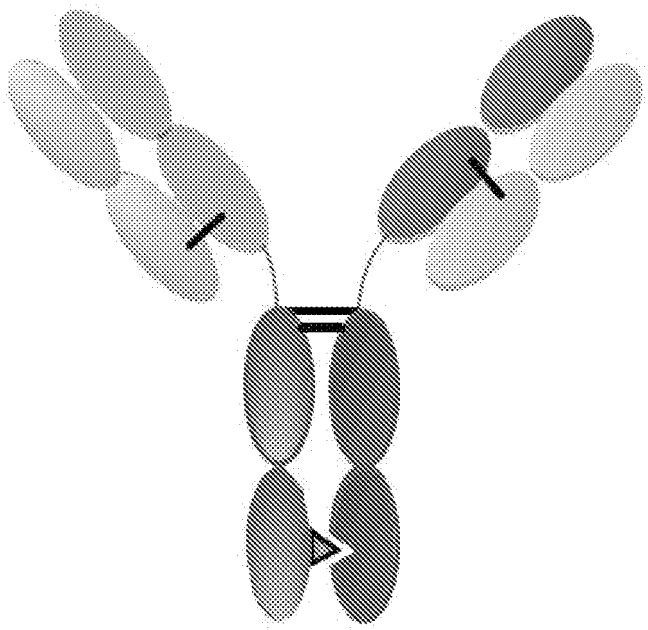


FIG. 33

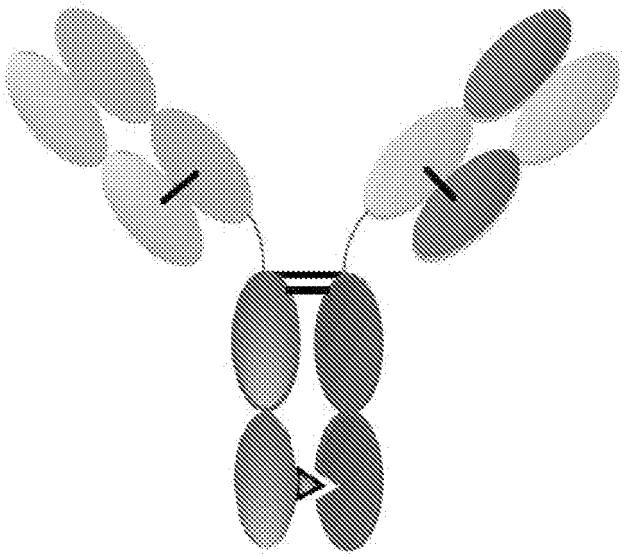


FIG. 34

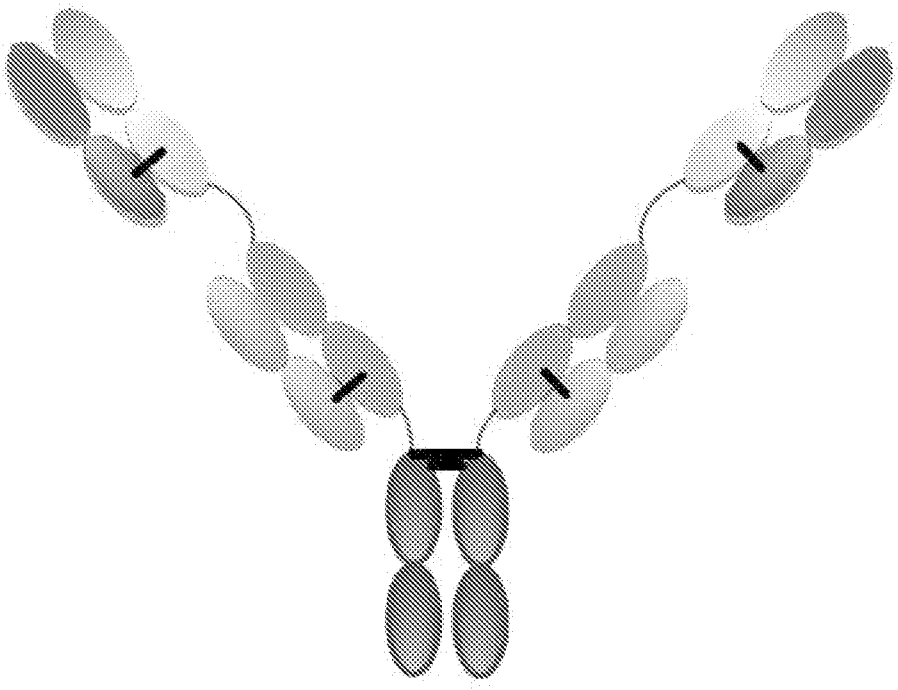


FIG. 35

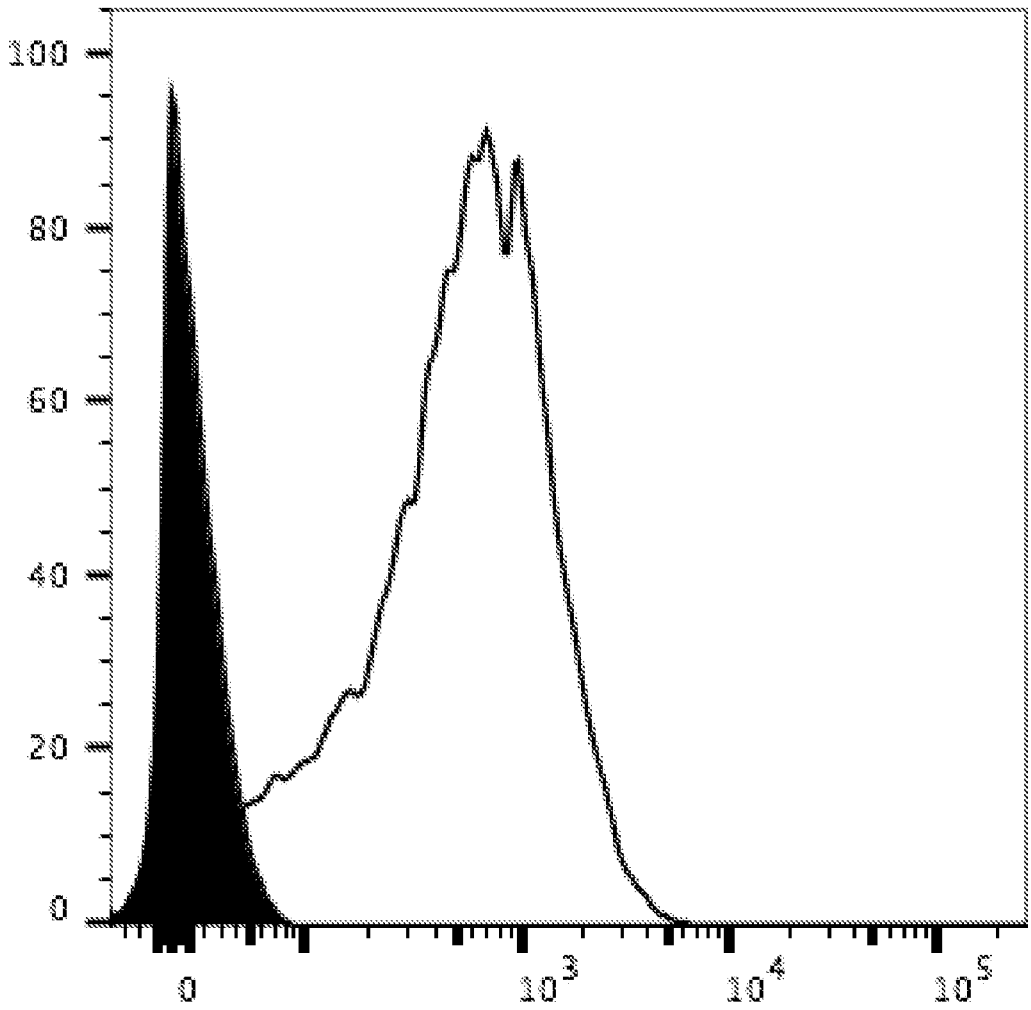
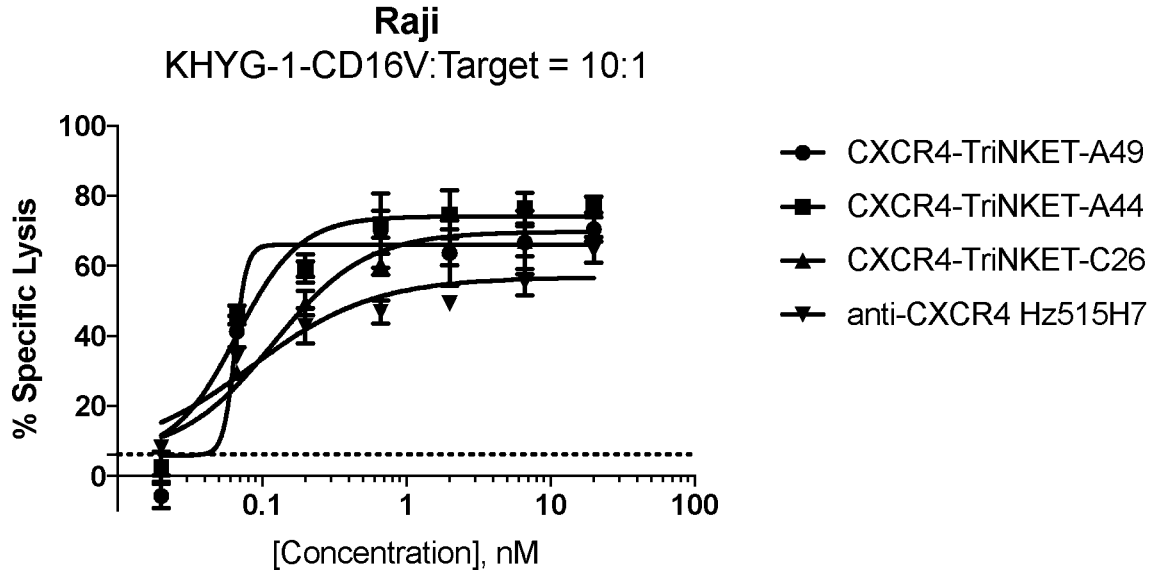


FIG. 36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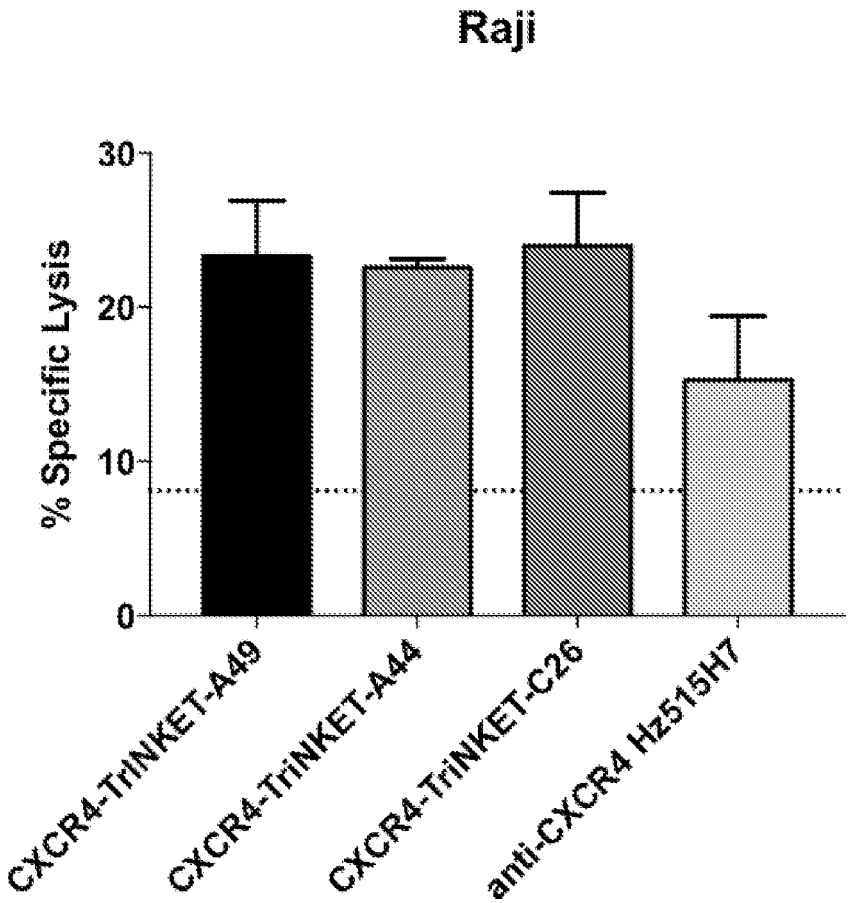
100
80
60
40
20
0
0.1
1
10
100
[Concentration], nM
CXCR4-TriNKET-A49
CXCR4-TriNKET-A44
CXCR4-TriNKET-C26
anti-CXCR4 Hz515H7

FIG. 37


Raji
% Specific Lysis
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20
10
0
CXCR4-TriNKET-A49
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CXCR4-TriNKET-C26
anti-CXCR4 Hz515H7

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Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
            20                  25                  30


Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


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      polypeptide

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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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
```

50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Ile
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

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Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
        115

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<223> Description of Artificial Sequence: Synthetic
      polypeptide

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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20   25   30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35   40   45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50   55   60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85   90   95

Ile Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

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      polypeptide

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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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

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polypeptide

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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr His Ser Phe Tyr Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

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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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


<210> 8
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<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

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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 Ala Ser Gln Ser Ile Gly 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Asn Ser Tyr Tyr Thr
                85                  90                  95


Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 9
<211> 117
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

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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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 10
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<212> PRT
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polypeptide

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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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 11
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<213> Artificial Sequence

<220>
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polypeptide

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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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

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Glu Leu 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 Thr Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp 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 Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Asp Ile Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 13

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polypeptide

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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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

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polypeptide

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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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Gly Ser Phe Pro Ile
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

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<220>
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1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


<210> 16
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      polypeptide

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1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser 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 Lys 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


Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Lys Glu Val Pro Trp
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 17
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 18
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

polypeptide

<400> 18
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Phe Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 19
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 19
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

```
Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


<210> 20
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 20
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 Ala Ser Gln Ser Ile Gly 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Ile Tyr Pro Thr
```

85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 21
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 21
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 22
<211> 106
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 22
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Ser Tyr Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 23
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 23
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 Gly Ser Phe Ser Gly Tyr
20 25 30

```
Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


<210> 24
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 24
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
```

65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Gly Ser Phe Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 25
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 25
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 26
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 26
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Gln Ser Phe Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 27
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 27
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 28
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 28
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Ser Phe Ser Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 29
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 29
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
        115

<210> 30
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 30
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Glu Ser Tyr Ser Thr
                85   90   95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 31
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 31
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 32
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 32
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Ser Phe Ile Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 33
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 33
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 34
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 34
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Gln Ser Tyr Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 35
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 35
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 36
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 36
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 Ala Ser Gln Ser Ile Gly 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr His Ser Phe Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 37
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 37
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 38
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 38
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 Ala Ser Gln Ser Ile Gly 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Glu Leu Tyr Ser Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 39

<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 39
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 40
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 40
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Thr Phe Ile Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 41
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 41
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 Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

```
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu 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 Gly Asp Ser Ser Ile Arg His Ala Tyr Tyr Tyr Tyr Gly Met
            100                 105                 110


Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> 42
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 42
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
            20                  25                  30


Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
                85                  90                  95


Tyr Tyr Ser Thr Pro Ile Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
```

100 105 110

Lys

<210> 43
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 43
Gly Thr Phe Ser Ser Tyr Ala Ile Ser
1 5

<210> 44
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 44
Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 45
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 45
Ala Arg Gly Asp Ser Ser Ile Arg His Ala Tyr Tyr Tyr Tyr Gly Met
1 5 10 15

Asp Val

<210> 46
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 46
Lys Ser Ser Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 47
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 47
Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 48
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 48
Gln Gln Tyr Tyr Ser Thr Pro Ile Thr
1 5

<210> 49

<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 49
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 Gly Ser Asp Arg Phe His Pro Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 50
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 50
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly

1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Phe Asp Thr Trp Pro Pro
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 51
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 51
Gly Ser Ile Ser Ser Ser Ser Tyr Tyr Trp Gly
1 5 10

<210> 52
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 52
Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser

1 5 10 15

<210> 53
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 53
Ala Arg Gly Ser Asp Arg Phe His Pro Tyr Phe Asp Tyr
1 5 10

<210> 54
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 54
Arg Ala Ser Gln Ser Val Ser Arg Tyr Leu Ala
1 5 10

<210> 55
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 55
Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 56
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 56
Gln Gln Phe Asp Thr Trp Pro Pro Thr
1 5

<210> 57
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 57
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp His 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 Ala Arg Gly Pro Trp Ser Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 58
<211> 106
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 58
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 Ala Ser Gln Ser 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 Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Glu Gln Tyr Asp Ser Tyr Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 59
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 59
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 Gly Thr Phe Ser Ser Tyr
20 25 30

```
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Ile Thr Ala Asp Glu 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 Arg Gly Arg Lys Ala Ser Gly Ser Phe Tyr Tyr Tyr Tyr Gly
            100                 105                 110


Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> 60
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 60
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Glu Ser Ser Gln Ser Leu Leu Asn Ser
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Pro Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
```

65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 61
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 61
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

Tyr Met 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 Thr Ser 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 Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Pro Asn Tyr Gly Asp Thr Thr His Asp Tyr Tyr Tyr
100 105 110

Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115   120   125

<210> 62
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 62
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asp Asp Trp Pro Phe
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 63
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 63
Tyr Thr Phe Thr Ser Tyr Tyr Met His
1 5

<210> 64
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 64
Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 65
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 65
Ala Arg Gly Ala Pro Asn Tyr Gly Asp Thr Thr His Asp Tyr Tyr Tyr
1 5 10 15

Met Asp Val

<210> 66
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 66
Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala

1 5 10

<210> 67
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 67
Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 68
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 68
Gln Gln Tyr Asp Asp Trp Pro Phe Thr
1 5

<210> 69
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 69
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 Gly 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 Arg Asp Thr Gly Glu Tyr Tyr Asp Thr Asp Asp His Gly Met Asp
            100                 105                 110


Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 70
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 70
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45


Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65                  70                  75                  80


Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asp Asp Tyr Trp Pro Pro
```

85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 71
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 71
Tyr Thr Phe Thr Gly Tyr Tyr Met His
1 5

<210> 72
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 72
Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 73
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 73
Ala Arg Asp Thr Gly Glu Tyr Tyr Asp Thr Asp Asp His Gly Met Asp
1 5 10 15

Val

<210> 74
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 74
Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 75
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 75
Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 76
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 76
Gln Gln Asp Asp Tyr Trp Pro Pro Thr
1 5

<210> 77
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 77
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 Asp Gly Gly Tyr Tyr Asp Ser Gly Ala Gly Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 78
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 78
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 Asp 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 Gly Val Ser Tyr Pro Arg
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 79
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 79
Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5

<210> 80
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 80
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 81
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 81
Ala Lys Asp Gly Gly Tyr Tyr Asp Ser Gly Ala Gly Asp Tyr
1 5 10

<210> 82
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 82
Arg Ala Ser Gln Gly Ile Asp Ser Trp Leu Ala
1 5 10

<210> 83
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 83
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 84
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 84
Gln Gln Gly Val Ser Tyr Pro Arg Thr
1 5

<210> 85
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 85
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 Gly Ala Pro Met Gly Ala Ala Ala Gly Trp Phe Asp Pro Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 86
<211> 107
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 86
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 Gly Val Ser Phe Pro Arg
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 87
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 87
Phe Thr Phe Ser Ser Tyr Ser Met Asn
1 5

<210> 88
<211> 17
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 88
Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 89
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 89
Ala Arg Gly Ala Pro Met Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10 15

<210> 90
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 90
Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
1 5 10

<210> 91
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 91
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 92
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 92
Gln Gln Gly Val Ser Phe Pro Arg Thr
1 5

<210> 93
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 93
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

Tyr Met 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 Thr Ser 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 Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Glu Gly Ala Gly Phe Ala Tyr Gly Met Asp Tyr Tyr Tyr Met
            100                 105                 110


Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> 94
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 94
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45


Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80


Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Asp Asn Trp Pro Phe
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 95
<211> 9
<212> PRT
<213> Artificial Sequence
```

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 95
Tyr Thr Phe Thr Ser Tyr Tyr Met His
1 5

<210> 96
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 96
Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 97
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 97
Ala Arg Glu Gly Ala Gly Phe Ala Tyr Gly Met Asp Tyr Tyr Tyr Met
1 5 10 15

Asp Val

<210> 98
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 98
Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 99
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 99
Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 100
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 100
Gln Gln Ser Asp Asn Trp Pro Phe Thr
1 5

<210> 101
<211> 121
<212> PRT
<213> Homo sapiens

<400> 101
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 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 Phe Ile Arg 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 Lys Asp Arg Gly Leu Gly Asp Gly Thr Tyr Phe Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 102
<211> 110
<212> PRT
<213> Homo sapiens

<400> 102
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1               5                   10                  15


Ser Ile Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn
            20                  25                  30


Ala Val Asn Trp Tyr Gln Gln Leu Pro Gly Lys Ala Pro Lys Leu Leu
        35                  40                  45


Ile Tyr Tyr Asp Asp Leu Leu Pro Ser Gly Val Ser Asp Arg Phe Ser
    50                  55                  60


Gly Ser Lys Ser Gly Thr Ser Ala Phe Leu Ala Ile Ser Gly Leu Gln
65                  70                  75                  80


Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
                85                  90                  95


Asn Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
```

100 105 110

<210> 103
<211> 115
<212> PRT
<213> Homo sapiens

<400> 103
Gln Val His Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Asp Asp 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 His Ile Ser Tyr Ser Gly Ser Ala 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

Asn Trp Asp Asp Ala Phe Asn Ile Trp Gly Gln Gly Thr Met Val Thr
100 105 110

Val Ser Ser
115

<210> 104
<211> 108
<212> PRT
<213> Homo sapiens

<400> 104
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser

20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 105
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 105
Gly Ser Phe Ser Gly Tyr Tyr Trp Ser
1 5

<210> 106
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 106
Glu Ile Asp His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 107

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 107
Ala Arg Ala Arg Gly Pro Trp Ser Phe Asp Pro
1 5 10

<210> 108
<211> 246
<212> PRT
<213> Homo sapiens

<400> 108
Met Ala Ala Ala Ala Ile Pro Ala Leu Leu Leu Cys Leu Pro Leu Leu
1 5 10 15

Phe Leu Leu Phe Gly Trp Ser Arg Ala Arg Arg Asp Asp Pro His Ser
20 25 30

Leu Cys Tyr Asp Ile Thr Val Ile Pro Lys Phe Arg Pro Gly Pro Arg
35 40 45

Trp Cys Ala Val Gln Gly Gln Val Asp Glu Lys Thr Phe Leu His Tyr
50 55 60

Asp Cys Gly Asn Lys Thr Val Thr Pro Val Ser Pro Leu Gly Lys Lys
65 70 75 80

Leu Asn Val Thr Met Ala Trp Lys Ala Gln Asn Pro Val Leu Arg Glu
85 90 95

Val Val Asp Ile Leu Thr Glu Gln Leu Leu Asp Ile Gln Leu Glu Asn
100 105 110

Tyr Thr Pro Lys Glu Pro Leu Thr Leu Gln Ala Arg Met Ser Cys Glu
115 120 125

Gln Lys Ala Glu Gly His Ser Ser Gly Ser Trp Gln Phe Ser Ile Asp

130 135 140

Gly Gln Thr Phe Leu Leu Phe Asp Ser Glu Lys Arg Met Trp Thr Thr
145 150 155 160

Val His Pro Gly Ala Arg Lys Met Lys Glu Lys Trp Glu Asn Asp Lys
165 170 175

Asp Val Ala Met Ser Phe His Tyr Ile Ser Met Gly Asp Cys Ile Gly
180 185 190

Trp Leu Glu Asp Phe Leu Met Gly Met Asp Ser Thr Leu Glu Pro Ser
195 200 205

Ala Gly Ala Pro Leu Ala Met Ser Ser Gly Thr Thr Gln Leu Arg Ala
210 215 220

Thr Ala Thr Thr Leu Ile Leu Cys Cys Leu Leu Ile Ile Leu Pro Cys
225 230 235 240

Phe Ile Leu Pro Gly Ile
245

<210> 109
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 109
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 Ala 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 Arg Ser Arg 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 Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Asp Tyr Gly Gly Gln Pro Pro Tyr Tyr Tyr Tyr Tyr Gly Met
            100   105   110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala
        115   120   125

<210> 110
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 110
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 Gly Ile Ser Ser Trp
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser 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 Val Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Arg

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 111
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 111
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 112
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 112
Ser Ser Arg Ser Arg Thr
1 5

<210> 113
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 113
Asp Tyr Gly Gly Gln Pro Pro Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 114
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 114
Gln Gly Ile Ser Ser Trp Leu Ala
1 5

<210> 115
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 115
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 116
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 116
Gln Gln Tyr Asn Ser Tyr Pro Arg Thr
1 5

<210> 117
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 117
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 Thr Pro Gly Ile Ala Ala Arg Arg Tyr Tyr Tyr Tyr Gly
            100                 105                 110


Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> 118
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 118
Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15


Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Lys Phe Phe Ala
            20                  25                  30


Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45


Gly Lys Asn Ser Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
```

50 55 60

Asn Ser Arg Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Gly Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Arg Asp Asn His
85 90 95

Gln Val Phe Gly Ala Gly Thr Lys Val Thr Val Leu Ser
100 105

<210> 119
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 119
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 120
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 120
Ser Ala Tyr Asn Gly Asn
1 5

<210> 121
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 121
Asp Thr Pro Gly Ile Ala Ala Arg Arg Tyr Tyr Tyr Tyr Gly Met Asp
1   5   10   15

Val

<210> 122
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 122
Ser Leu Arg Lys Phe Phe Ala Ser
1   5

<210> 123
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 123
Gly Lys Asn Ser Arg Pro Ser
1   5

<210> 124
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 124
Asn Ser Arg Asp Ser Arg Asp Asn His Gln Val
1   5   10

<210> 125

<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 125
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 Ser Thr Asp Tyr
20 25 30

Tyr Phe Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Phe Ile Arg Thr Lys Ser Lys Gly Tyr Thr Thr Glu Tyr Ser Gly
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
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 Ala Arg Glu Pro Ile Thr Thr Asp Pro Arg Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 126
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 126
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly

1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Phe Asn Ser
20 25 30

Arg Thr Arg Lys Lys Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Lys Arg Lys Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Lys Gln
85 90 95

Ser Arg Phe Leu Arg Ala Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 127
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 127
Gly Phe Thr Ser Thr Asp Tyr Tyr Phe Ser
1 5 10

<210> 128
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 128
Phe Ile Arg Thr Lys Ser Lys Gly Tyr Thr Thr Glu Tyr Ser Gly Ser

1 5 10 15

Val Lys Gly

<210> 129
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 129
Glu Pro Ile Thr Thr Asp Pro Arg Asp Tyr
1 5 10

<210> 130
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 130
Lys Ser Ser Gln Ser Leu Phe Asn Ser Arg Thr Arg Lys Lys Tyr Leu
1 5 10 15

<210> 131
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 131
Trp Ala Ser Lys Arg Lys Ser
1 5

<210> 132
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 132
Lys Gln Ser Arg Phe Leu Arg Ala
1 5

<210> 133
<211> 352
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 133
Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
1 5 10 15

Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
20 25 30

Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
35 40 45

Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
50 55 60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65 70 75 80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
85 90 95

Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
100 105 110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
115 120 125

```
Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser
    130                 135                 140

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145                 150                 155                 160

Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
                165                 170                 175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
            180                 185                 190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
        195                 200                 205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
    210                 215                 220

Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
225                 230                 235                 240

Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr
                245                 250                 255

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
            260                 265                 270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
        275                 280                 285

Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe
    290                 295                 300

Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala Leu Thr Ser Val
305                 310                 315                 320

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
                325                 330                 335
```

```
His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
            340                 345                 350


<210> 134
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 134
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


Arg Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Tyr Ile Asn Pro Ser Thr Gly Tyr Thr Glu Tyr Asn Gln Lys Phe
    50                  55                  60


Lys Asp 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 Gly Gly Gly Val Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser Ala
        115


<210> 135
<211> 107
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 135
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 Ser Ala Ser Ser Ser Ile Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Thr Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys His Gln Arg Ser Thr Tyr Pro Leu Thr
85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg
100 105

<210> 136
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 136
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 137
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 137
Asn Pro Ser Thr Gly Tyr
1 5

<210> 138
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 138
Gly Gly Gly Val Phe Asp Tyr
1 5

<210> 139
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 139
Ser Ser Ile Ser Tyr Met His
1 5

<210> 140
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 140
Thr Thr Ser Asn Leu Ala Ser
1 5

<210> 141

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 141
His Gln Arg Ser Thr Tyr Pro Leu Thr
1 5

<210> 142
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 142
Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val
1 5 10 15

Lys Met Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Arg Tyr Trp Met
20 25 30

His Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala
35 40 45

Ile Tyr Pro Gly Asn Ser Asp Thr Ser Tyr Asn Gln Lys Phe Glu Gly
50 55 60

Lys Ala Lys Leu Thr Ala Val Thr Ser Ala Ser Thr Ala Tyr Met Glu
65 70 75 80

Leu Ser Ser Leu Thr His Glu Asp Ser Ala Val Tyr Tyr Cys Ser Arg
85 90 95

Asp Tyr Gly Tyr Tyr Phe Asp Phe Trp Gly Gln Gly Thr Thr Leu Thr
100 105 110

Val Ser Ser Ala

115

<210> 143
<211> 105
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 143
Gln Ile Val Ser Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Arg Ser Tyr Met
20 25 30

Gln Trp Tyr Gln Gln Lys Pro Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys His Gln Arg Ser Ser Tyr Thr Phe Gly
85 90 95

Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105

<210> 144
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 144
Gly Tyr Ser Phe Thr Arg Tyr

1 5

<210> 145
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 145
Tyr Pro Gly Asn Ser Asp
1 5

<210> 146
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 146
Asp Tyr Gly Tyr Tyr Phe Asp Phe
1 5

<210> 147
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 147
Ser Ser Arg Ser Tyr Met Gln
1 5

<210> 148
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 148
Asp Thr Ser Lys Leu Ala Ser
1 5

<210> 149
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 149
His Gln Arg Ser Ser Tyr Thr
1 5

<210> 150
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 150
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 Gly Thr Phe Ser Arg Tyr
20 25 30

Ile Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Gln 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 Lys Asp Trp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Ala
115

<210> 151
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 151
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 152
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 152
Gly Gly Thr Phe Ser Arg Tyr Ile Ile Asn
1 5 10

<210> 153
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 153
Arg Ile Ile Pro Ile Leu Gly Val Glu Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 154
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 154
Lys Asp Trp Phe Asp Tyr
1 5

<210> 155
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 155
Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 156
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 156
Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 157
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 157
Gln Gln Tyr Gly Ser Ser Pro Leu Thr
1 5

<210> 158
<211> 272
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 158
Met Asp Ser Tyr Leu Leu Met Trp Gly Leu Leu Thr Phe Ile Met Val
1 5 10 15

Pro Gly Cys Gln Ala Glu Leu Cys Asp Asp Asp Pro Pro Glu Ile Pro
20 25 30

His Ala Thr Phe Lys Ala Met Ala Tyr Lys Glu Gly Thr Met Leu Asn

```
        35                  40                  45

Cys Glu Cys Lys Arg Gly Phe Arg Arg Ile Lys Ser Gly Ser Leu Tyr
    50                  55                  60

Met Leu Cys Thr Gly Asn Ser Ser His Ser Ser Trp Asp Asn Gln Cys
65                  70                  75                  80

Gln Cys Thr Ser Ser Ala Thr Arg Asn Thr Thr Lys Gln Val Thr Pro
                85                  90                  95

Gln Pro Glu Glu Gln Lys Glu Arg Lys Thr Thr Glu Met Gln Ser Pro
            100                 105                 110

Met Gln Pro Val Asp Gln Ala Ser Leu Pro Gly His Cys Arg Glu Pro
        115                 120                 125

Pro Pro Trp Glu Asn Glu Ala Thr Glu Arg Ile Tyr His Phe Val Val
    130                 135                 140

Gly Gln Met Val Tyr Tyr Gln Cys Val Gln Gly Tyr Arg Ala Leu His
145                 150                 155                 160

Arg Gly Pro Ala Glu Ser Val Cys Lys Met Thr His Gly Lys Thr Arg
                165                 170                 175

Trp Thr Gln Pro Gln Leu Ile Cys Thr Gly Glu Met Glu Thr Ser Gln
            180                 185                 190

Phe Pro Gly Glu Glu Lys Pro Gln Ala Ser Pro Glu Gly Arg Pro Glu
        195                 200                 205

Ser Glu Thr Ser Cys Leu Val Thr Thr Thr Asp Phe Gln Ile Gln Thr
    210                 215                 220

Glu Met Ala Ala Thr Met Glu Thr Ser Ile Phe Thr Thr Glu Tyr Gln
225                 230                 235                 240

Val Ala Val Ala Gly Cys Val Phe Leu Leu Ile Ser Val Leu Leu Leu
```

245 250 255

Ser Gly Leu Thr Trp Gln Arg Arg Gln Arg Lys Ser Arg Arg Thr Ile
260 265 270

<210> 159
<211> 1032
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 159
Met Ala Trp Glu Ala Arg Arg Glu Pro Gly Pro Arg Arg Ala Ala Val
1 5 10 15

Arg Glu Thr Val Met Leu Leu Leu Cys Leu Gly Val Pro Thr Gly Arg
20 25 30

Pro Tyr Asn Val Asp Thr Glu Ser Ala Leu Leu Tyr Gln Gly Pro His
35 40 45

Asn Thr Leu Phe Gly Tyr Ser Val Val Leu His Ser His Gly Ala Asn
50 55 60

Arg Trp Leu Leu Val Gly Ala Pro Thr Ala Asn Trp Leu Ala Asn Ala
65 70 75 80

Ser Val Ile Asn Pro Gly Ala Ile Tyr Arg Cys Arg Ile Gly Lys Asn
85 90 95

Pro Gly Gln Thr Cys Glu Gln Leu Gln Leu Gly Ser Pro Asn Gly Glu
100 105 110

Pro Cys Gly Lys Thr Cys Leu Glu Glu Arg Asp Asn Gln Trp Leu Gly
115 120 125

Val Thr Leu Ser Arg Gln Pro Gly Glu Asn Gly Ser Ile Val Thr Cys
130 135 140

```
Gly His Arg Trp Lys Asn Ile Phe Tyr Ile Lys Asn Glu Asn Lys Leu
145                 150                 155                 160

Pro Thr Gly Gly Cys Tyr Gly Val Pro Pro Asp Leu Arg Thr Glu Leu
                165                 170                 175

Ser Lys Arg Ile Ala Pro Cys Tyr Gln Asp Tyr Val Lys Lys Phe Gly
            180                 185                 190

Glu Asn Phe Ala Ser Cys Gln Ala Gly Ile Ser Ser Phe Tyr Thr Lys
        195                 200                 205

Asp Leu Ile Val Met Gly Ala Pro Gly Ser Ser Tyr Trp Thr Gly Ser
    210                 215                 220

Leu Phe Val Tyr Asn Ile Thr Thr Asn Lys Tyr Lys Ala Phe Leu Asp
225                 230                 235                 240

Lys Gln Asn Gln Val Lys Phe Gly Ser Tyr Leu Gly Tyr Ser Val Gly
                245                 250                 255

Ala Gly His Phe Arg Ser Gln His Thr Thr Glu Val Val Gly Gly Ala
            260                 265                 270

Pro Gln His Glu Gln Ile Gly Lys Ala Tyr Ile Phe Ser Ile Asp Glu
        275                 280                 285

Lys Glu Leu Asn Ile Leu His Glu Met Lys Gly Lys Lys Leu Gly Ser
    290                 295                 300

Tyr Phe Gly Ala Ser Val Cys Ala Val Asp Leu Asn Ala Asp Gly Phe
305                 310                 315                 320

Ser Asp Leu Leu Val Gly Ala Pro Met Gln Ser Thr Ile Arg Glu Glu
                325                 330                 335

Gly Arg Val Phe Val Tyr Ile Asn Ser Gly Ser Gly Ala Val Met Asn
            340                 345                 350
```

```
Ala Met Glu Thr Asn Leu Val Gly Ser Asp Lys Tyr Ala Ala Arg Phe
        355                 360                 365

Gly Glu Ser Ile Val Asn Leu Gly Asp Ile Asp Asn Asp Gly Phe Glu
    370                 375                 380

Asp Val Ala Ile Gly Ala Pro Gln Glu Asp Asp Leu Gln Gly Ala Ile
385                 390                 395                 400

Tyr Ile Tyr Asn Gly Arg Ala Asp Gly Ile Ser Ser Thr Phe Ser Gln
                405                 410                 415

Arg Ile Glu Gly Leu Gln Ile Ser Lys Ser Leu Ser Met Phe Gly Gln
            420                 425                 430

Ser Ile Ser Gly Gln Ile Asp Ala Asp Asn Asn Gly Tyr Val Asp Val
        435                 440                 445

Ala Val Gly Ala Phe Arg Ser Asp Ser Ala Val Leu Leu Arg Thr Arg
    450                 455                 460

Pro Val Val Ile Val Asp Ala Ser Leu Ser His Pro Glu Ser Val Asn
465                 470                 475                 480

Arg Thr Lys Phe Asp Cys Val Glu Asn Gly Trp Pro Ser Val Cys Ile
                485                 490                 495

Asp Leu Thr Leu Cys Phe Ser Tyr Lys Gly Lys Glu Val Pro Gly Tyr
            500                 505                 510

Ile Val Leu Phe Tyr Asn Met Ser Leu Asp Val Asn Arg Lys Ala Glu
        515                 520                 525

Ser Pro Pro Arg Phe Tyr Phe Ser Ser Asn Gly Thr Ser Asp Val Ile
    530                 535                 540

Thr Gly Ser Ile Gln Val Ser Ser Arg Glu Ala Asn Cys Arg Thr His
545                 550                 555                 560
```

```
Gln Ala Phe Met Arg Lys Asp Val Arg Asp Ile Leu Thr Pro Ile Gln
               565                 570                 575

Ile Glu Ala Ala Tyr His Leu Gly Pro His Val Ile Ser Lys Arg Ser
            580                 585                 590

Thr Glu Glu Phe Pro Pro Leu Gln Pro Ile Leu Gln Gln Lys Lys Glu
        595                 600                 605

Lys Asp Ile Met Lys Lys Thr Ile Asn Phe Ala Arg Phe Cys Ala His
    610                 615                 620

Glu Asn Cys Ser Ala Asp Leu Gln Val Ser Ala Lys Ile Gly Phe Leu
625                 630                 635                 640

Lys Pro His Glu Asn Lys Thr Tyr Leu Ala Val Gly Ser Met Lys Thr
               645                 650                 655

Leu Met Leu Asn Val Ser Leu Phe Asn Ala Gly Asp Asp Ala Tyr Glu
            660                 665                 670

Thr Thr Leu His Val Lys Leu Pro Val Gly Leu Tyr Phe Ile Lys Ile
        675                 680                 685

Leu Glu Leu Glu Glu Lys Gln Ile Asn Cys Glu Val Thr Asp Asn Ser
    690                 695                 700

Gly Val Val Gln Leu Asp Cys Ser Ile Gly Tyr Ile Tyr Val Asp His
705                 710                 715                 720

Leu Ser Arg Ile Asp Ile Ser Phe Leu Leu Asp Val Ser Ser Leu Ser
               725                 730                 735

Arg Ala Glu Glu Asp Leu Ser Ile Thr Val His Ala Thr Cys Glu Asn
            740                 745                 750

Glu Glu Glu Met Asp Asn Leu Lys His Ser Arg Val Thr Val Ala Ile
        755                 760                 765
```

```
Pro Leu Lys Tyr Glu Val Lys Leu Thr Val His Gly Phe Val Asn Pro
    770                 775                 780

Thr Ser Phe Val Tyr Gly Ser Asn Asp Glu Asn Glu Pro Glu Thr Cys
785                 790                 795                 800

Met Val Glu Lys Met Asn Leu Thr Phe His Val Ile Asn Thr Gly Asn
                805                 810                 815

Ser Met Ala Pro Asn Val Ser Val Glu Ile Met Val Pro Asn Ser Phe
            820                 825                 830

Ser Pro Gln Thr Asp Lys Leu Phe Asn Ile Leu Asp Val Gln Thr Thr
        835                 840                 845

Thr Gly Glu Cys His Phe Glu Asn Tyr Gln Arg Val Cys Ala Leu Glu
    850                 855                 860

Gln Gln Lys Ser Ala Met Gln Thr Leu Lys Gly Ile Val Arg Phe Leu
865                 870                 875                 880

Ser Lys Thr Asp Lys Arg Leu Leu Tyr Cys Ile Lys Ala Asp Pro His
                885                 890                 895

Cys Leu Asn Phe Leu Cys Asn Phe Gly Lys Met Glu Ser Gly Lys Glu
            900                 905                 910

Ala Ser Val His Ile Gln Leu Glu Gly Arg Pro Ser Ile Leu Glu Met
        915                 920                 925

Asp Glu Thr Ser Ala Leu Lys Phe Glu Ile Arg Ala Thr Gly Phe Pro
    930                 935                 940

Glu Pro Asn Pro Arg Val Ile Glu Leu Asn Lys Asp Glu Asn Val Ala
945                 950                 955                 960

His Val Leu Leu Glu Gly Leu His His Gln Arg Pro Lys Arg Tyr Phe
                965                 970                 975
```

```
Thr Ile Val Ile Ile Ser Ser Ser Leu Leu Leu Gly Leu Ile Val Leu
            980                 985                 990


Leu Leu Ile Ser Tyr Val Met Trp  Lys Ala Gly Phe Phe  Lys Arg Gln
        995                 1000                1005


Tyr Lys  Ser Ile Leu Gln Glu  Glu Asn Arg Arg Asp  Ser Trp Ser
    1010                1015                1020


Tyr Ile  Asn Ser Lys Ser Asn  Asp Asp
    1025                1030


<210> 160
<211> 798
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 160
Met Asn Leu Gln Pro Ile Phe Trp Ile Gly Leu Ile Ser Ser Val Cys
1               5                   10                  15


Cys Val Phe Ala Gln Thr Asp Glu Asn Arg Cys Leu Lys Ala Asn Ala
            20                  25                  30


Lys Ser Cys Gly Glu Cys Ile Gln Ala Gly Pro Asn Cys Gly Trp Cys
        35                  40                  45


Thr Asn Ser Thr Phe Leu Gln Glu Gly Met Pro Thr Ser Ala Arg Cys
    50                  55                  60


Asp Asp Leu Glu Ala Leu Lys Lys Lys Gly Cys Pro Pro Asp Asp Ile
65                  70                  75                  80


Glu Asn Pro Arg Gly Ser Lys Asp Ile Lys Lys Asn Lys Asn Val Thr
                85                  90                  95


Asn Arg Ser Lys Gly Thr Ala Glu Lys Leu Lys Pro Glu Asp Ile Thr
```

```
            100                 105                 110

Gln Ile Gln Pro Gln Gln Leu Val Leu Arg Leu Arg Ser Gly Glu Pro
        115                 120                 125

Gln Thr Phe Thr Leu Lys Phe Lys Arg Ala Glu Asp Tyr Pro Ile Asp
    130                 135                 140

Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Glu
145                 150                 155                 160

Asn Val Lys Ser Leu Gly Thr Asp Leu Met Asn Glu Met Arg Arg Ile
                165                 170                 175

Thr Ser Asp Phe Arg Ile Gly Phe Gly Ser Phe Val Glu Lys Thr Val
            180                 185                 190

Met Pro Tyr Ile Ser Thr Thr Pro Ala Lys Leu Arg Asn Pro Cys Thr
        195                 200                 205

Ser Glu Gln Asn Cys Thr Ser Pro Phe Ser Tyr Lys Asn Val Leu Ser
    210                 215                 220

Leu Thr Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys Gln Arg
225                 230                 235                 240

Ile Ser Gly Asn Leu Asp Ser Pro Glu Gly Gly Phe Asp Ala Ile Met
                245                 250                 255

Gln Val Ala Val Cys Gly Ser Leu Ile Gly Trp Arg Asn Val Thr Arg
            260                 265                 270

Leu Leu Val Phe Ser Thr Asp Ala Gly Phe His Phe Ala Gly Asp Gly
        275                 280                 285

Lys Leu Gly Gly Ile Val Leu Pro Asn Asp Gly Gln Cys His Leu Glu
    290                 295                 300

Asn Asn Met Tyr Thr Met Ser His Tyr Tyr Asp Tyr Pro Ser Ile Ala
```

```
305                 310                 315                 320

His Leu Val Gln Lys Leu Ser Glu Asn Asn Ile Gln Thr Ile Phe Ala
                325                 330                 335

Val Thr Glu Glu Phe Gln Pro Val Tyr Lys Glu Leu Lys Asn Leu Ile
            340                 345                 350

Pro Lys Ser Ala Val Gly Thr Leu Ser Ala Asn Ser Ser Asn Val Ile
        355                 360                 365

Gln Leu Ile Ile Asp Ala Tyr Asn Ser Leu Ser Ser Glu Val Ile Leu
    370                 375                 380

Glu Asn Gly Lys Leu Ser Glu Gly Val Thr Ile Ser Tyr Lys Ser Tyr
385                 390                 395                 400

Cys Lys Asn Gly Val Asn Gly Thr Gly Glu Asn Gly Arg Lys Cys Ser
                405                 410                 415

Asn Ile Ser Ile Gly Asp Glu Val Gln Phe Glu Ile Ser Ile Thr Ser
            420                 425                 430

Asn Lys Cys Pro Lys Lys Asp Ser Asp Ser Phe Lys Ile Arg Pro Leu
        435                 440                 445

Gly Phe Thr Glu Glu Val Glu Val Ile Leu Gln Tyr Ile Cys Glu Cys
    450                 455                 460

Glu Cys Gln Ser Glu Gly Ile Pro Glu Ser Pro Lys Cys His Glu Gly
465                 470                 475                 480

Asn Gly Thr Phe Glu Cys Gly Ala Cys Arg Cys Asn Glu Gly Arg Val
                485                 490                 495

Gly Arg His Cys Glu Cys Ser Thr Asp Glu Val Asn Ser Glu Asp Met
            500                 505                 510

Asp Ala Tyr Cys Arg Lys Glu Asn Ser Ser Glu Ile Cys Ser Asn Asn
```

```
        515                 520                 525

Gly Glu Cys Val Cys Gly Gln Cys Val Cys Arg Lys Arg Asp Asn Thr
    530                 535                 540

Asn Glu Ile Tyr Ser Gly Lys Phe Cys Glu Cys Asp Asn Phe Asn Cys
545                 550                 555                 560

Asp Arg Ser Asn Gly Leu Ile Cys Gly Gly Asn Gly Val Cys Lys Cys
                565                 570                 575

Arg Val Cys Glu Cys Asn Pro Asn Tyr Thr Gly Ser Ala Cys Asp Cys
            580                 585                 590

Ser Leu Asp Thr Ser Thr Cys Glu Ala Ser Asn Gly Gln Ile Cys Asn
        595                 600                 605

Gly Arg Gly Ile Cys Glu Cys Gly Val Cys Lys Cys Thr Asp Pro Lys
    610                 615                 620

Phe Gln Gly Gln Thr Cys Glu Met Cys Gln Thr Cys Leu Gly Val Cys
625                 630                 635                 640

Ala Glu His Lys Glu Cys Val Gln Cys Arg Ala Phe Asn Lys Gly Glu
                645                 650                 655

Lys Lys Asp Thr Cys Thr Gln Glu Cys Ser Tyr Phe Asn Ile Thr Lys
            660                 665                 670

Val Glu Ser Arg Asp Lys Leu Pro Gln Pro Val Gln Pro Asp Pro Val
        675                 680                 685

Ser His Cys Lys Glu Lys Asp Val Asp Asp Cys Trp Phe Tyr Phe Thr
    690                 695                 700

Tyr Ser Val Asn Gly Asn Asn Glu Val Met Val His Val Val Glu Asn
705                 710                 715                 720

Pro Glu Cys Pro Thr Gly Pro Asp Ile Ile Pro Ile Val Ala Gly Val
```

725 730 735

Val Ala Gly Ile Val Leu Ile Gly Leu Ala Leu Leu Leu Ile Trp Lys
740 745 750

Leu Leu Met Ile Ile His Asp Arg Arg Glu Phe Ala Lys Phe Glu Lys
755 760 765

Glu Lys Met Asn Ala Lys Trp Asp Thr Gly Glu Asn Pro Ile Tyr Lys
770 775 780

Ser Ala Val Thr Thr Val Val Asn Pro Lys Tyr Glu Gly Lys
785 790 795

<210> 161
<211> 742
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 161
Met Asp Lys Phe Trp Trp His Ala Ala Trp Gly Leu Cys Leu Val Pro
1 5 10 15

Leu Ser Leu Ala Gln Ile Asp Leu Asn Ile Thr Cys Arg Phe Ala Gly
20 25 30

Val Phe His Val Glu Lys Asn Gly Arg Tyr Ser Ile Ser Arg Thr Glu
35 40 45

Ala Ala Asp Leu Cys Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala
50 55 60

Gln Met Glu Lys Ala Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly
65 70 75 80

Phe Ile Glu Gly His Val Val Ile Pro Arg Ile His Pro Asn Ser Ile
85 90 95

```
Cys Ala Ala Asn Asn Thr Gly Val Tyr Ile Leu Thr Ser Asn Thr Ser
            100                 105                 110

Gln Tyr Asp Thr Tyr Cys Phe Asn Ala Ser Ala Pro Pro Glu Glu Asp
        115                 120                 125

Cys Thr Ser Val Thr Asp Leu Pro Asn Ala Phe Asp Gly Pro Ile Thr
    130                 135                 140

Ile Thr Ile Val Asn Arg Asp Gly Thr Arg Tyr Val Gln Lys Gly Glu
145                 150                 155                 160

Tyr Arg Thr Asn Pro Glu Asp Ile Tyr Pro Ser Asn Pro Thr Asp Asp
                165                 170                 175

Asp Val Ser Ser Gly Ser Ser Ser Glu Arg Ser Ser Thr Ser Gly Gly
            180                 185                 190

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

Ser Pro Trp Ile Thr Asp Ser Thr Asp Arg Ile Pro Ala Thr Thr Leu
    210                 215                 220

Met Ser Thr Ser Ala Thr Ala Thr Glu Thr Ala Thr Lys Arg Gln Glu
225                 230                 235                 240

Thr Trp Asp Trp Phe Ser Trp Leu Phe Leu Pro Ser Glu Ser Lys Asn
                245                 250                 255

His Leu His Thr Thr Thr Gln Met Ala Gly Thr Ser Ser Asn Thr Ile
            260                 265                 270

Ser Ala Gly Trp Glu Pro Asn Glu Glu Asn Glu Asp Glu Arg Asp Arg
        275                 280                 285

His Leu Ser Phe Ser Gly Ser Gly Ile Asp Asp Asp Glu Asp Phe Ile
    290                 295                 300
```

```
Ser Ser Thr Ile Ser Thr Thr Pro Arg Ala Phe Asp His Thr Lys Gln
305                 310                 315                 320

Asn Gln Asp Trp Thr Gln Trp Asn Pro Ser His Ser Asn Pro Glu Val
                325                 330                 335

Leu Leu Gln Thr Thr Thr Arg Met Thr Asp Val Asp Arg Asn Gly Thr
            340                 345                 350

Thr Ala Tyr Glu Gly Asn Trp Asn Pro Glu Ala His Pro Pro Leu Ile
        355                 360                 365

His His Glu His His Glu Glu Glu Glu Thr Pro His Ser Thr Ser Thr
    370                 375                 380

Ile Gln Ala Thr Pro Ser Ser Thr Thr Glu Glu Thr Ala Thr Gln Lys
385                 390                 395                 400

Glu Gln Trp Phe Gly Asn Arg Trp His Glu Gly Tyr Arg Gln Thr Pro
                405                 410                 415

Lys Glu Asp Ser His Ser Thr Thr Gly Thr Ala Ala Ala Ser Ala His
            420                 425                 430

Thr Ser His Pro Met Gln Gly Arg Thr Thr Pro Ser Pro Glu Asp Ser
        435                 440                 445

Ser Trp Thr Asp Phe Phe Asn Pro Ile Ser His Pro Met Gly Arg Gly
    450                 455                 460

His Gln Ala Gly Arg Arg Met Asp Met Asp Ser Ser His Ser Ile Thr
465                 470                 475                 480

Leu Gln Pro Thr Ala Asn Pro Asn Thr Gly Leu Val Glu Asp Leu Asp
                485                 490                 495

Arg Thr Gly Pro Leu Ser Met Thr Thr Gln Gln Ser Asn Ser Gln Ser
            500                 505                 510
```

```
Phe Ser Thr Ser His Glu Gly Leu Glu Glu Asp Lys Asp His Pro Thr
        515                 520                 525

Thr Ser Thr Leu Thr Ser Ser Asn Arg Asn Asp Val Thr Gly Gly Arg
    530                 535                 540

Arg Asp Pro Asn His Ser Glu Gly Ser Thr Thr Leu Leu Glu Gly Tyr
545                 550                 555                 560

Thr Ser His Tyr Pro His Thr Lys Glu Ser Arg Thr Phe Ile Pro Val
                565                 570                 575

Thr Ser Ala Lys Thr Gly Ser Phe Gly Val Thr Ala Val Thr Val Gly
            580                 585                 590

Asp Ser Asn Ser Asn Val Asn Arg Ser Leu Ser Gly Asp Gln Asp Thr
        595                 600                 605

Phe His Pro Ser Gly Gly Ser His Thr Thr His Gly Ser Glu Ser Asp
    610                 615                 620

Gly His Ser His Gly Ser Gln Glu Gly Gly Ala Asn Thr Thr Ser Gly
625                 630                 635                 640

Pro Ile Arg Thr Pro Gln Ile Pro Glu Trp Leu Ile Ile Leu Ala Ser
                645                 650                 655

Leu Leu Ala Leu Ala Leu Ile Leu Ala Val Cys Ile Ala Val Asn Ser
            660                 665                 670

Arg Arg Arg Cys Gly Gln Lys Lys Lys Leu Val Ile Asn Ser Gly Asn
        675                 680                 685

Gly Ala Val Glu Asp Arg Lys Pro Ser Gly Leu Asn Gly Glu Ala Ser
    690                 695                 700

Lys Ser Gln Glu Met Val His Leu Val Asn Lys Glu Ser Ser Glu Thr
705                 710                 715                 720
```

```
Pro Asp Gln Phe Met Thr Ala Asp Glu Thr Arg Asn Leu Gln Asn Val
                725                 730                 735


Asp Met Lys Ile Gly Val
            740


<210> 162
<211> 967
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 162
Met Ala Lys Gly Phe Tyr Ile Ser Lys Ser Leu Gly Ile Leu Gly Ile
1               5                   10                  15


Leu Leu Gly Val Ala Ala Val Cys Thr Ile Ile Ala Leu Ser Val Val
            20                  25                  30


Tyr Ser Gln Glu Lys Asn Lys Asn Ala Asn Ser Ser Pro Val Ala Ser
        35                  40                  45


Thr Thr Pro Ser Ala Ser Ala Thr Thr Asn Pro Ala Ser Ala Thr Thr
    50                  55                  60


Leu Asp Gln Ser Lys Ala Trp Asn Arg Tyr Arg Leu Pro Asn Thr Leu
65                  70                  75                  80


Lys Pro Asp Ser Tyr Arg Val Thr Leu Arg Pro Tyr Leu Thr Pro Asn
                85                  90                  95


Asp Arg Gly Leu Tyr Val Phe Lys Gly Ser Ser Thr Val Arg Phe Thr
            100                 105                 110


Cys Lys Glu Ala Thr Asp Val Ile Ile Ile His Ser Lys Lys Leu Asn
        115                 120                 125


Tyr Thr Leu Ser Gln Gly His Arg Val Val Leu Arg Gly Val Gly Gly
```

```
    130                 135                 140

Ser Gln Pro Pro Asp Ile Asp Lys Thr Glu Leu Val Glu Pro Thr Glu
145                 150                 155                 160

Tyr Leu Val Val His Leu Lys Gly Ser Leu Val Lys Asp Ser Gln Tyr
                165                 170                 175

Glu Met Asp Ser Glu Phe Glu Gly Glu Leu Ala Asp Asp Leu Ala Gly
            180                 185                 190

Phe Tyr Arg Ser Glu Tyr Met Glu Gly Asn Val Arg Lys Val Val Ala
        195                 200                 205

Thr Thr Gln Met Gln Ala Ala Asp Ala Arg Lys Ser Phe Pro Cys Phe
    210                 215                 220

Asp Glu Pro Ala Met Lys Ala Glu Phe Asn Ile Thr Leu Ile His Pro
225                 230                 235                 240

Lys Asp Leu Thr Ala Leu Ser Asn Met Leu Pro Lys Gly Pro Ser Thr
                245                 250                 255

Pro Leu Pro Glu Asp Pro Asn Trp Asn Val Thr Glu Phe His Thr Thr
            260                 265                 270

Pro Lys Met Ser Thr Tyr Leu Leu Ala Phe Ile Val Ser Glu Phe Asp
        275                 280                 285

Tyr Val Glu Lys Gln Ala Ser Asn Gly Val Leu Ile Arg Ile Trp Ala
    290                 295                 300

Arg Pro Ser Ala Ile Ala Ala Gly His Gly Asp Tyr Ala Leu Asn Val
305                 310                 315                 320

Thr Gly Pro Ile Leu Asn Phe Phe Ala Gly His Tyr Asp Thr Pro Tyr
                325                 330                 335

Pro Leu Pro Lys Ser Asp Gln Ile Gly Leu Pro Asp Phe Asn Ala Gly
```

```
            340                 345                 350

Ala Met Glu Asn Trp Gly Leu Val Thr Tyr Arg Glu Asn Ser Leu Leu
        355                 360                 365

Phe Asp Pro Leu Ser Ser Ser Ser Ser Asn Lys Glu Arg Val Val Thr
    370                 375                 380

Val Ile Ala His Glu Leu Ala His Gln Trp Phe Gly Asn Leu Val Thr
385                 390                 395                 400

Ile Glu Trp Trp Asn Asp Leu Trp Leu Asn Glu Gly Phe Ala Ser Tyr
                405                 410                 415

Val Glu Tyr Leu Gly Ala Asp Tyr Ala Glu Pro Thr Trp Asn Leu Lys
            420                 425                 430

Asp Leu Met Val Leu Asn Asp Val Tyr Arg Val Met Ala Val Asp Ala
        435                 440                 445

Leu Ala Ser Ser His Pro Leu Ser Thr Pro Ala Ser Glu Ile Asn Thr
    450                 455                 460

Pro Ala Gln Ile Ser Glu Leu Phe Asp Ala Ile Ser Tyr Ser Lys Gly
465                 470                 475                 480

Ala Ser Val Leu Arg Met Leu Ser Ser Phe Leu Ser Glu Asp Val Phe
                485                 490                 495

Lys Gln Gly Leu Ala Ser Tyr Leu His Thr Phe Ala Tyr Gln Asn Thr
            500                 505                 510

Ile Tyr Leu Asn Leu Trp Asp His Leu Gln Glu Ala Val Asn Asn Arg
        515                 520                 525

Ser Ile Gln Leu Pro Thr Thr Val Arg Asp Ile Met Asn Arg Trp Thr
    530                 535                 540

Leu Gln Met Gly Phe Pro Val Ile Thr Val Asp Thr Ser Thr Gly Thr
```

```
545                 550                 555                 560

Leu Ser Gln Glu His Phe Leu Leu Asp Pro Asp Ser Asn Val Thr Arg
                565                 570                 575

Pro Ser Glu Phe Asn Tyr Val Trp Ile Val Pro Ile Thr Ser Ile Arg
            580                 585                 590

Asp Gly Arg Gln Gln Gln Asp Tyr Trp Leu Ile Asp Val Arg Ala Gln
        595                 600                 605

Asn Asp Leu Phe Ser Thr Ser Gly Asn Glu Trp Val Leu Leu Asn Leu
    610                 615                 620

Asn Val Thr Gly Tyr Tyr Arg Val Asn Tyr Asp Glu Glu Asn Trp Arg
625                 630                 635                 640

Lys Ile Gln Thr Gln Leu Gln Arg Asp His Ser Ala Ile Pro Val Ile
                645                 650                 655

Asn Arg Ala Gln Ile Ile Asn Asp Ala Phe Asn Leu Ala Ser Ala His
            660                 665                 670

Lys Val Pro Val Thr Leu Ala Leu Asn Asn Thr Leu Phe Leu Ile Glu
        675                 680                 685

Glu Arg Gln Tyr Met Pro Trp Glu Ala Ala Leu Ser Ser Leu Ser Tyr
    690                 695                 700

Phe Lys Leu Met Phe Asp Arg Ser Glu Val Tyr Gly Pro Met Lys Asn
705                 710                 715                 720

Tyr Leu Lys Lys Gln Val Thr Pro Leu Phe Ile His Phe Arg Asn Asn
                725                 730                 735

Thr Asn Asn Trp Arg Glu Ile Pro Glu Asn Leu Met Asp Gln Tyr Ser
            740                 745                 750

Glu Val Asn Ala Ile Ser Thr Ala Cys Ser Asn Gly Val Pro Glu Cys
```

```
        755                 760                 765

Glu Glu Met Val Ser Gly Leu Phe Lys Gln Trp Met Glu Asn Pro Asn
    770                 775                 780

Asn Asn Pro Ile His Pro Asn Leu Arg Ser Thr Val Tyr Cys Asn Ala
785                 790                 795                 800

Ile Ala Gln Gly Gly Glu Glu Glu Trp Asp Phe Ala Trp Glu Gln Phe
                805                 810                 815

Arg Asn Ala Thr Leu Val Asn Glu Ala Asp Lys Leu Arg Ala Ala Leu
            820                 825                 830

Ala Cys Ser Lys Glu Leu Trp Ile Leu Asn Arg Tyr Leu Ser Tyr Thr
        835                 840                 845

Leu Asn Pro Asp Leu Ile Arg Lys Gln Asp Ala Thr Ser Thr Ile Ile
    850                 855                 860

Ser Ile Thr Asn Asn Val Ile Gly Gln Gly Leu Val Trp Asp Phe Val
865                 870                 875                 880

Gln Ser Asn Trp Lys Lys Leu Phe Asn Asp Tyr Gly Gly Gly Ser Phe
                885                 890                 895

Ser Phe Ser Asn Leu Ile Gln Ala Val Thr Arg Arg Phe Ser Thr Glu
            900                 905                 910

Tyr Glu Leu Gln Gln Leu Glu Gln Phe Lys Lys Asp Asn Glu Glu Thr
        915                 920                 925

Gly Phe Gly Ser Gly Thr Arg Ala Leu Glu Gln Ala Leu Glu Lys Thr
    930                 935                 940

Lys Ala Asn Ile Lys Trp Val Lys Glu Asn Lys Glu Val Val Leu Gln
945                 950                 955                 960

Trp Phe Thr Glu Asn Ser Lys
```

965

<210> 163
<211> 323
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 163

Met Trp Pro Leu Val Ala Ala Leu Leu Leu Gly Ser Ala Cys Cys Gly
1 5 10 15

Ser Ala Gln Leu Leu Phe Asn Lys Thr Lys Ser Val Glu Phe Thr Phe
20 25 30

Cys Asn Asp Thr Val Val Ile Pro Cys Phe Val Thr Asn Met Glu Ala
35 40 45

Gln Asn Thr Thr Glu Val Tyr Val Lys Trp Lys Phe Lys Gly Arg Asp
50 55 60

Ile Tyr Thr Phe Asp Gly Ala Leu Asn Lys Ser Thr Val Pro Thr Asp
65 70 75 80

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

Ser Leu Lys Met Asp Lys Ser Asp Ala Val Ser His Thr Gly Asn Tyr
100 105 110

Thr Cys Glu Val Thr Glu Leu Thr Arg Glu Gly Glu Thr Ile Ile Glu
115 120 125

Leu Lys Tyr Arg Val Val Ser Trp Phe Ser Pro Asn Glu Asn Ile Leu
130 135 140

Ile Val Ile Phe Pro Ile Phe Ala Ile Leu Leu Phe Trp Gly Gln Phe
145 150 155 160

```
Gly Ile Lys Thr Leu Lys Tyr Arg Ser Gly Gly Met Asp Glu Lys Thr
                165                 170                 175

Ile Ala Leu Leu Val Ala Gly Leu Val Ile Thr Val Ile Val Ile Val
            180                 185                 190

Gly Ala Ile Leu Phe Val Pro Gly Glu Tyr Ser Leu Lys Asn Ala Thr
        195                 200                 205

Gly Leu Gly Leu Ile Val Thr Ser Thr Gly Ile Leu Ile Leu Leu His
    210                 215                 220

Tyr Tyr Val Phe Ser Thr Ala Ile Gly Leu Thr Ser Phe Val Ile Ala
225                 230                 235                 240

Ile Leu Val Ile Gln Val Ile Ala Tyr Ile Leu Ala Val Val Gly Leu
                245                 250                 255

Ser Leu Cys Ile Ala Ala Cys Ile Pro Met His Gly Pro Leu Leu Ile
            260                 265                 270

Ser Gly Leu Ser Ile Leu Ala Leu Ala Gln Leu Leu Gly Leu Val Tyr
        275                 280                 285

Met Lys Phe Val Ala Ser Asn Gln Lys Thr Ile Gln Pro Pro Arg Lys
    290                 295                 300

Ala Val Glu Glu Pro Leu Asn Ala Phe Lys Glu Ser Lys Gly Met Met
305                 310                 315                 320

Asn Asp Glu
```

<210> 164
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

polypeptide

<400> 164

```
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                  10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
```

195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Leu
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly
325

<210> 165
<211> 236
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 165
Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val
1 5 10 15

Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala
20 25 30

```
Leu Trp Leu Arg His Asp Pro Gln Thr Thr Asn Leu Leu Tyr Leu Glu
        35                  40                  45

Leu Gly Asp Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile
    50                  55                  60

Leu Ile Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys
65                  70                  75                  80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
                85                  90                  95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
            100                 105                 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
        115                 120                 125

Gln Ala Leu Gln Gln Ala Val Val Asp Asp Asp Ala Asn Asn Ala Lys
    130                 135                 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asp Cys Cys Gly Ser Ser
145                 150                 155                 160

Thr Leu Thr Ala Leu Thr Thr Ser Val Leu Lys Asn Asn Leu Cys Pro
                165                 170                 175

Ser Gly Ser Asn Ile Ile Ser Asn Leu Phe Lys Glu Asp Cys His Gln
            180                 185                 190

Lys Ile Asp Asp Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala
        195                 200                 205

Ala Ile Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met
    210                 215                 220

Val Leu Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr
225                 230                 235
```

<210> 166
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 166
Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser
1 5 10 15

Val Lys Leu Phe Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr
20 25 30

Met His Trp Val Lys Gln Arg Pro Gln Gln Gly Leu Glu Trp Ile Gly
35 40 45

Arg Ile Asp Pro Ala Ser Gly Asp Thr Lys Tyr Asp Pro Lys Phe Gln
50 55 60

Val Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Trp Leu
65 70 75 80

Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Asp Gly Met Trp Val Ser Thr Gly Tyr Ala Leu Asp Phe Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 167
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 167
Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Thr Asn Asp
            20   25   30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
        35   40   45

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

Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala
65   70   75   80

Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Tyr
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
            100   105

<210> 168
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 168
Gly Phe Asn Ile Lys Asp Thr
1   5

<210> 169
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 169
Asp Pro Ala Ser Gly Asp
1 5

<210> 170
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 170
Gly Met Trp Val Ser Thr Gly Tyr Ala Leu Asp Phe
1 5 10

<210> 171
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 171
Gln Ser Val Thr Asn Asp Val Ala
1 5

<210> 172
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 172
Tyr Ala Ser Asn Arg Tyr Thr
1 5

<210> 173
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 173
Gln Gln Asp Tyr Ser Ser Pro Tyr Thr
1 5

<210> 174
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 174
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

Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Leu Asp Ser Ile
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 Gln Gly Leu Asp Tyr Trp Gly Arg Gly Thr Leu Val Thr Val
100 105 110

Ser Ser Ala
115

<210> 175

<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 175
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Ser Ala Ser Ser Ser Ile Asn Tyr Ile
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
35 40 45

Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Leu Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 176
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 176
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 177

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 177
Ser Ser Gly Gly Ser Tyr
1 5

<210> 178
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 178
Gln Gly Leu Asp Tyr
1 5

<210> 179
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 179
Ser Ser Ile Asn Tyr Ile Tyr
1 5

<210> 180
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 180
Leu Thr Ser Asn Leu Ala Ser

1 5

<210> 181
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 181
Leu Gln Trp Ser Ser Asn Pro Leu Thr
1 5

<210> 182
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 182
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 Asn Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Thr Ile Tyr Pro Gly Asn Asp Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Ala 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 Arg Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu

100 105 110

Val Thr Val Ser Ser
115

<210> 183
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 183
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val Tyr Ser
20 25 30

Asn Gly Asn Thr Tyr Leu Gly Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln 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 Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 184
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 184
Gly Tyr Thr Phe Thr Asn Tyr Asn Met His
1 5 10

<210> 185
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 185
Thr Ile Tyr Pro Gly Asn Asp Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 186
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 186
Gly Gly Tyr Arg Ala Met Asp Tyr
1 5

<210> 187
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 187
Arg Ser Ser Gln Ser Ile Val Tyr Ser Asn Gly Asn Thr Tyr Leu Gly
1 5 10 15

<210> 188
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 188
Lys Val Ser Asn Arg Phe Ser
1 5

<210> 189
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 189
Phe Gln Gly Ser His Val Pro Tyr Thr
1 5

<210> 190
<211> 321
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 190
Met Glu Glu Gly Gln Tyr Ser Glu Ile Glu Glu Leu Pro Arg Arg Arg
1 5 10 15

Cys Cys Arg Arg Gly Thr Gln Ile Val Leu Leu Gly Leu Val Thr Ala
20 25 30

Ala Leu Trp Ala Gly Leu Leu Thr Leu Leu Leu Leu Trp His Trp Asp
35 40 45

Thr Thr Gln Ser Leu Lys Gln Leu Glu Glu Arg Ala Ala Arg Asn Val

```
    50                  55                  60

Ser Gln Val Ser Lys Asn Leu Glu Ser His His Gly Asp Gln Met Ala
65                  70                  75                  80

Gln Lys Ser Gln Ser Thr Gln Ile Ser Gln Glu Leu Glu Glu Leu Arg
                85                  90                  95

Ala Glu Gln Gln Arg Leu Lys Ser Gln Asp Leu Glu Leu Ser Trp Asn
            100                 105                 110

Leu Asn Gly Leu Gln Ala Asp Leu Ser Ser Phe Lys Ser Gln Glu Leu
        115                 120                 125

Asn Glu Arg Asn Glu Ala Ser Asp Leu Leu Glu Arg Leu Arg Glu Glu
    130                 135                 140

Val Thr Lys Leu Arg Met Glu Leu Gln Val Ser Ser Gly Phe Val Cys
145                 150                 155                 160

Asn Thr Cys Pro Glu Lys Trp Ile Asn Phe Gln Arg Lys Cys Tyr Tyr
                165                 170                 175

Phe Gly Lys Gly Thr Lys Gln Trp Val His Ala Arg Tyr Ala Cys Asp
            180                 185                 190

Asp Met Glu Gly Gln Leu Val Ser Ile His Ser Pro Glu Glu Gln Asp
        195                 200                 205

Phe Leu Thr Lys His Ala Ser His Thr Gly Ser Trp Ile Gly Leu Arg
    210                 215                 220

Asn Leu Asp Leu Lys Gly Glu Phe Ile Trp Val Asp Gly Ser His Val
225                 230                 235                 240

Asp Tyr Ser Asn Trp Ala Pro Gly Glu Pro Thr Ser Arg Ser Gln Gly
                245                 250                 255

Glu Asp Cys Val Met Met Arg Gly Ser Gly Arg Trp Asn Asp Ala Phe
```

260 265 270

Cys Asp Arg Lys Leu Gly Ala Trp Val Cys Asp Arg Leu Ala Thr Cys
275 280 285

Thr Pro Pro Ala Ser Glu Gly Ser Ala Glu Ser Met Gly Pro Asp Ser
290 295 300

Arg Pro Asp Pro Asp Gly Arg Leu Pro Thr Pro Ser Ala Pro Leu His
305 310 315 320

Ser

<210> 191
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 191
Met Val Arg Leu Pro Leu Gln Cys Val Leu Trp Gly Cys Leu Leu Thr
1 5 10 15

Ala Val His Pro Glu Pro Pro Thr Ala Cys Arg Glu Lys Gln Tyr Leu
20 25 30

Ile Asn Ser Gln Cys Cys Ser Leu Cys Gln Pro Gly Gln Lys Leu Val
35 40 45

Ser Asp Cys Thr Glu Phe Thr Glu Thr Glu Cys Leu Pro Cys Gly Glu
50 55 60

Ser Glu Phe Leu Asp Thr Trp Asn Arg Glu Thr His Cys His Gln His
65 70 75 80

Lys Tyr Cys Asp Pro Asn Leu Gly Leu Arg Val Gln Gln Lys Gly Thr
85 90 95

```
Ser Glu Thr Asp Thr Ile Cys Thr Cys Glu Glu Gly Trp His Cys Thr
            100                 105                 110

Ser Glu Ala Cys Glu Ser Cys Val Leu His Arg Ser Cys Ser Pro Gly
        115                 120                 125

Phe Gly Val Lys Gln Ile Ala Thr Gly Val Ser Asp Thr Ile Cys Glu
    130                 135                 140

Pro Cys Pro Val Gly Phe Phe Ser Asn Val Ser Ser Ala Phe Glu Lys
145                 150                 155                 160

Cys His Pro Trp Thr Ser Cys Glu Thr Lys Asp Leu Val Val Gln Gln
                165                 170                 175

Ala Gly Thr Asn Lys Thr Asp Val Val Cys Gly Pro Gln Asp Arg Leu
            180                 185                 190

Arg Ala Leu Val Val Ile Pro Ile Ile Phe Gly Ile Leu Phe Ala Ile
        195                 200                 205

Leu Leu Val Leu Val Phe Ile Lys Lys Val Ala Lys Lys Pro Thr Asn
    210                 215                 220

Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn Phe Pro Asp
225                 230                 235                 240

Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu His
                245                 250                 255

Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser
            260                 265                 270

Val Gln Glu Arg Gln
        275


<210> 192
<211> 193
<212> PRT
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<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 192
Met Pro Glu Glu Gly Ser Gly Cys Ser Val Arg Arg Arg Pro Tyr Gly
1 5 10 15

Cys Val Leu Arg Ala Ala Leu Val Pro Leu Val Ala Gly Leu Val Ile
20 25 30

Cys Leu Val Val Cys Ile Gln Arg Phe Ala Gln Ala Gln Gln Gln Leu
35 40 45

Pro Leu Glu Ser Leu Gly Trp Asp Val Ala Glu Leu Gln Leu Asn His
50 55 60

Thr Gly Pro Gln Gln Asp Pro Arg Leu Tyr Trp Gln Gly Gly Pro Ala
65 70 75 80

Leu Gly Arg Ser Phe Leu His Gly Pro Glu Leu Asp Lys Gly Gln Leu
85 90 95

Arg Ile His Arg Asp Gly Ile Tyr Met Val His Ile Gln Val Thr Leu
100 105 110

Ala Ile Cys Ser Ser Thr Thr Ala Ser Arg His His Pro Thr Thr Leu
115 120 125

Ala Val Gly Ile Cys Ser Pro Ala Ser Arg Ser Ile Ser Leu Leu Arg
130 135 140

Leu Ser Phe His Gln Gly Cys Thr Ile Ala Ser Gln Arg Leu Thr Pro
145 150 155 160

Leu Ala Arg Gly Asp Thr Leu Cys Thr Asn Leu Thr Gly Thr Leu Leu
165 170 175

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

180 185 190

Pro

<210> 193
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 193
Met Pro Gly Gly Pro Gly Val Leu Gln Ala Leu Pro Ala Thr Ile Phe
1 5 10 15

Leu Leu Phe Leu Leu Ser Ala Val Tyr Leu Gly Pro Gly Cys Gln Ala
20 25 30

Leu Trp Met His Lys Val Pro Ala Ser Leu Met Val Ser Leu Gly Glu
35 40 45

Asp Ala His Phe Gln Cys Pro His Asn Ser Ser Asn Asn Ala Asn Val
50 55 60

Thr Trp Trp Arg Val Leu His Gly Asn Tyr Thr Trp Pro Pro Glu Phe
65 70 75 80

Leu Gly Pro Gly Glu Asp Pro Asn Gly Thr Leu Ile Ile Gln Asn Val
85 90 95

Asn Lys Ser His Gly Gly Ile Tyr Val Cys Arg Val Gln Glu Gly Asn
100 105 110

Glu Ser Tyr Gln Gln Ser Cys Gly Thr Tyr Leu Arg Val Arg Gln Pro
115 120 125

Pro Pro Arg Pro Phe Leu Asp Met Gly Glu Gly Thr Lys Asn Arg Ile
130 135 140

```
Ile Thr Ala Glu Gly Ile Ile Leu Leu Phe Cys Ala Val Val Pro Gly
145                 150                 155                 160


Thr Leu Leu Leu Phe Arg Lys Arg Trp Gln Asn Glu Lys Leu Gly Leu
                165                 170                 175


Asp Ala Gly Asp Glu Tyr Glu Asp Glu Asn Leu Tyr Glu Gly Leu Asn
            180                 185                 190


Leu Asp Asp Cys Ser Met Tyr Glu Asp Ile Ser Arg Gly Leu Gln Gly
        195                 200                 205


Thr Tyr Gln Asp Val Gly Ser Leu Asn Ile Gly Asp Val Gln Leu Glu
    210                 215                 220


Lys Pro
225


<210> 194
<211> 229
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 194
Met Ala Arg Leu Ala Leu Ser Pro Val Pro Ser His Trp Met Val Ala
1               5                   10                  15


Leu Leu Leu Leu Leu Ser Ala Glu Pro Val Pro Ala Ala Arg Ser Glu
            20                  25                  30


Asp Arg Tyr Arg Asn Pro Lys Gly Ser Ala Cys Ser Arg Ile Trp Gln
        35                  40                  45


Ser Pro Arg Phe Ile Ala Arg Lys Arg Gly Phe Thr Val Lys Met His
    50                  55                  60


Cys Tyr Met Asn Ser Ala Ser Gly Asn Val Ser Trp Leu Trp Lys Gln
```

65 70 75 80

Glu Met Asp Glu Asn Pro Gln Gln Leu Lys Leu Glu Lys Gly Arg Met
85 90 95

Glu Glu Ser Gln Asn Glu Ser Leu Ala Thr Leu Thr Ile Gln Gly Ile
100 105 110

Arg Phe Glu Asp Asn Gly Ile Tyr Phe Cys Gln Gln Lys Cys Asn Asn
115 120 125

Thr Ser Glu Val Tyr Gln Gly Cys Gly Thr Glu Leu Arg Val Met Gly
130 135 140

Phe Ser Thr Leu Ala Gln Leu Lys Gln Arg Asn Thr Leu Lys Asp Gly
145 150 155 160

Ile Ile Met Ile Gln Thr Leu Leu Ile Ile Leu Phe Ile Ile Val Pro
165 170 175

Ile Phe Leu Leu Leu Asp Lys Asp Asp Ser Lys Ala Gly Met Glu Glu
180 185 190

Asp His Thr Tyr Glu Gly Leu Asp Ile Asp Gln Thr Ala Thr Tyr Glu
195 200 205

Asp Ile Val Thr Leu Arg Thr Gly Glu Val Lys Trp Ser Val Gly Glu
210 215 220

His Pro Gly Gln Glu
225

<210> 195
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 195

```
Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser Lys Cys Pro Tyr
1               5                  10                  15

Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys
            20                  25                  30

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
        35                  40                  45

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
    50                  55                  60

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65                  70                  75                  80

Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
                85                  90                  95

Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
            100                 105                 110

Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
        115                 120                 125

Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr
    130                 135                 140

Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
145                 150                 155                 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
                165                 170                 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
            180                 185                 190

Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
        195                 200                 205
```

```
Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
    210                 215                 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
225                 230                 235                 240

Asp Asn Leu Leu Pro Ser Trp Ala Ile Thr Leu Ile Ser Val Asn Gly
                245                 250                 255

Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala Pro Arg Cys Arg
            260                 265                 270

Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val Arg Pro Val
        275                 280                 285


<210> 196
<211> 371
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 196
Met Gly Arg Leu Val Leu Leu Trp Gly Ala Ala Val Phe Leu Leu Gly
1               5                   10                  15

Gly Trp Met Ala Leu Gly Gln Gly Gly Ala Ala Glu Gly Val Gln Ile
            20                  25                  30

Gln Ile Ile Tyr Phe Asn Leu Glu Thr Val Gln Val Thr Trp Asn Ala
        35                  40                  45

Ser Lys Tyr Ser Arg Thr Asn Leu Thr Phe His Tyr Arg Phe Asn Gly
    50                  55                  60

Asp Glu Ala Tyr Asp Gln Cys Thr Asn Tyr Leu Leu Gln Glu Gly His
65                  70                  75                  80

Thr Ser Gly Cys Leu Leu Asp Ala Glu Gln Arg Asp Asp Ile Leu Tyr
```

85 90 95

Phe Ser Ile Arg Asn Gly Thr His Pro Val Phe Thr Ala Ser Arg Trp
100 105 110

Met Val Tyr Tyr Leu Lys Pro Ser Ser Pro Lys His Val Arg Phe Ser
115 120 125

Trp His Gln Asp Ala Val Thr Val Thr Cys Ser Asp Leu Ser Tyr Gly
130 135 140

Asp Leu Leu Tyr Glu Val Gln Tyr Arg Ser Pro Phe Asp Thr Glu Trp
145 150 155 160

Gln Ser Lys Gln Glu Asn Thr Cys Asn Val Thr Ile Glu Gly Leu Asp
165 170 175

Ala Glu Lys Cys Tyr Ser Phe Trp Val Arg Val Lys Ala Met Glu Asp
180 185 190

Val Tyr Gly Pro Asp Thr Tyr Pro Ser Asp Trp Ser Glu Val Thr Cys
195 200 205

Trp Gln Arg Gly Glu Ile Arg Asp Ala Cys Ala Glu Thr Pro Thr Pro
210 215 220

Pro Lys Pro Lys Leu Ser Lys Phe Ile Leu Ile Ser Ser Leu Ala Ile
225 230 235 240

Leu Leu Met Val Ser Leu Leu Leu Leu Ser Leu Trp Lys Leu Trp Arg
245 250 255

Val Lys Lys Phe Leu Ile Pro Ser Val Pro Asp Pro Lys Ser Ile Phe
260 265 270

Pro Gly Leu Phe Glu Ile His Gln Gly Asn Phe Gln Glu Trp Ile Thr
275 280 285

Asp Thr Gln Asn Val Ala His Leu His Lys Met Ala Gly Ala Glu Gln

290 295 300

Glu Ser Gly Pro Glu Glu Pro Leu Val Val Gln Leu Ala Lys Thr Glu
305 310 315 320

Ala Glu Ser Pro Arg Met Leu Asp Pro Gln Thr Glu Glu Lys Glu Ala
325 330 335

Ser Gly Gly Ser Leu Gln Leu Pro His Gln Pro Leu Gln Gly Gly Asp
340 345 350

Val Val Thr Ile Gly Gly Phe Thr Phe Val Met Asn Asp Arg Ser Tyr
355 360 365

Val Ala Leu
370

<210> 197
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 197
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe Thr Phe Asn
20 25 30

Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu
35 40 45

Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Asn Asn Thr
65 70 75 80

```
Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95


Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly Gln Gly Val
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210> 198
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 198
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 Asp Ile Arg Tyr Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Val Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Val Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Val Tyr Ser Thr Pro Arg
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 199
```

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 199
Gly Phe Arg Phe Thr Phe Asn Asn Tyr
1 5

<210> 200
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 200
Ser Ser Ser Gly Asp Pro
1 5

<210> 201
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 201
Leu Thr Thr Gly Ser Asp Ser
1 5

<210> 202
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 202
Gln Asp Ile Arg Tyr Tyr Leu Asn

1 5

<210> 203
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 203
Val Ala Ser Ser Leu Gln Ser
1 5

<210> 204
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 204
Leu Gln Val Tyr Ser Thr Pro Arg Thr
1 5

<210> 205
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 205
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 Phe Thr Gly Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ala Arg Val Ile Pro Asn Ala Gly Gly Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Gly Arg Phe Thr Leu Ser Val Asp Asn Ser Lys Asn Thr Ala 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 Gly Ile Tyr Trp Trp Gly Gln Gly Thr Leu Val Thr Val
            100                 105                 110

Ser Ser Ala
        115


<210> 206
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 206
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 Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

Asn Gly Asn Thr Phe Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        35                  40                  45

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

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65                  70                  75                  80

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Ser Gln Thr
```

85 90 95

Thr His Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg

<210> 207
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 207
Gly Tyr Ser Phe Thr Gly Tyr
1 5

<210> 208
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 208
Ile Pro Asn Ala Gly Gly
1 5

<210> 209
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 209
Glu Gly Ile Tyr Trp
1 5

<210> 210
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 210
Gln Ser Leu Val His Ser Asn Gly Asn Thr Phe Leu His
1 5 10

<210> 211
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 211
Thr Val Ser Asn Arg Phe Ser
1 5

<210> 212
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 212
Ser Gln Thr Thr His Val Pro Trp Thr
1 5

<210> 213
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 213
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 Gly 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 Asp 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 Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

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

Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
        115   120   125

<210> 214
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 214
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 Tyr Ser Trp
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile

35 40 45

Tyr Thr Ala Ser Thr 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 Ile Phe Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 215
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 215
Gly Tyr Thr Phe Thr Gly Tyr
1 5

<210> 216
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 216
Asn Pro Asp Ser Gly Gly
1 5

<210> 217
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 217
Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr Phe Asp
1 5 10 15

Tyr

<210> 218
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 218
Gln Gly Ile Tyr Ser Trp Leu Ala
1 5

<210> 219
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 219
Thr Ala Ser Thr Leu Gln Ser
1 5

<210> 220
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 220
Gln Gln Ala Asn Ile Phe Pro Leu Thr

1 5

<210> 221
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 221
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 Ser Tyr Glu Glu Ser Asn Arg Tyr His Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Ile Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Gly Gly Ile Ala Ala Pro Gly Pro Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala
115 120

<210> 222
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

polypeptide

<400> 222
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Thr Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Ser Leu Gly Ser Asn Arg Ala 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 Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Arg Gln Thr Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Arg
100 105 110

Arg

<210> 223
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 223
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 224
<211> 6
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 224
Ser Tyr Glu Glu Ser Asn
1 5

<210> 225
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 225
Asp Gly Gly Ile Ala Ala Pro Gly Pro Asp Tyr
1 5 10

<210> 226
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 226
Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10

<210> 227
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 227
Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 228
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 228
Met Gln Ala Arg Gln Thr Pro Phe Thr
1 5

<210> 229
<211> 128
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 229
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 Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Asp Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Arg Asp Tyr Val
50 55 60

Gly Ser Val Lys Ser Arg Ile Ile Ile Asn Pro Asp Thr Ser Asn Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Ile
85 90 95

Tyr Tyr Cys Thr Arg Ala Gln Trp Leu Gly Gly Asp Tyr Pro Tyr Tyr
100 105 110

Tyr Ser Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120   125

<210> 230
<211> 104
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 230
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Thr Phe Gly
                85   90   95

Pro Gly Thr Lys Val Asp Ile Lys
            100

<210> 231
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 231
Gly Asp Ser Val Ser Ser Asn Ser Ala
1 5

<210> 232
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 232
Tyr Tyr Arg Ser Lys Trp Tyr
1 5

<210> 233
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 233
Ala Gln Trp Leu Gly Gly Asp Tyr Pro Tyr Tyr Tyr Ser Met Asp Val
1 5 10 15

<210> 234
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 234
Gln Ser Val Ser Ser Tyr Leu Ala
1 5

<210> 235
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 235
Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 236
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 236
Gln Gln Arg Ser Asn Thr
1 5

<210> 237
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 237
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 Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Ala Phe
50 55 60

Lys 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 Arg Asp Tyr Gly Asp Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Thr Val Thr Val Ser Ser Ala
        115


<210> 238
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 238
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Ser Thr Ser
            20                  25                  30


Gly Tyr Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45


Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
    50                  55                  60


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80


Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln His Ser Arg
                85                  90                  95


Glu Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110


<210> 239
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<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 239
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 240
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 240
Asn Thr Tyr Thr Gly Glu
1 5

<210> 241
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 241
Asp Tyr Gly Asp Tyr Gly Met Asp Tyr
1 5

<210> 242
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 242
Lys Ser Val Ser Thr Ser Gly Tyr Ser Phe Met His

1 5 10

<210> 243
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 243
Leu Ala Ser Asn Leu Glu Ser
1 5

<210> 244
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 244
Gln His Ser Arg Glu Val Pro Trp Thr
1 5

<210> 245
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 245
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 Thr Phe Ser Ser Tyr
20 25 30

Trp Ile Glu Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

```
Gly Glu Ile Leu Pro Gly Gly Gly Asp Thr Asn Tyr Asn Glu Ile Phe
    50                  55                  60

Lys Gly Arg Ala Thr Phe Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Thr Arg Arg Val Pro Ile Arg Leu Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala
        115


<210> 246
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 246
Asp 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 Lys Ala Ser Gln Ser Val Asp Tyr Glu
            20                  25                  30

Gly Asp Ser Phe Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Val Pro Ser
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
```

85 90 95

Glu Asp Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

<210> 247
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 247
Gly Tyr Thr Phe Ser Ser Tyr
1 5

<210> 248
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 248
Leu Pro Gly Gly Gly Asp
1 5

<210> 249
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 249
Arg Val Pro Ile Arg Leu Asp Tyr
1 5

<210> 250
<211> 12
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 250
Gln Ser Val Asp Tyr Glu Gly Asp Ser Phe Leu Asn
1 5 10

<210> 251
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 251
Ala Ala Ser Asn Leu Glu Ser
1 5

<210> 252
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 252
Gln Gln Ser Asn Glu Asp Pro Leu Thr
1 5

<210> 253
<211> 128
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 253
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 Ala Val Ser Gly Gly Ser Ile Ser Gly Gly
            20   25   30

Tyr Gly Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35   40   45

Ile Gly Ser Phe Tyr Ser Ser Ser Gly Asn Thr Tyr Tyr Asn Pro Ser
    50   55   60

Leu Lys Ser Gln Val Thr Ile Ser Thr Asp Thr Ser Lys Asn Gln Phe
65   70   75   80

Ser Leu Lys Leu Asn Ser Met Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85   90   95

Cys Val Arg Asp Arg Leu Phe Ser Val Val Gly Met Val Tyr Asn Asn
            100   105   110

Trp Phe Asp Val Trp Gly Pro Gly Val Leu Val Thr Val Ser Ser Ala
        115   120   125

<210> 254
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 254
Glu Ser Ala Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1   5   10   15

Lys Val Thr Ile Ser Cys Thr Gly Ser Thr Ser Asn Ile Gly Gly Tyr
            20   25   30

Asp Leu His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35   40   45

Ile Tyr Asp Ile Asn Lys Arg Pro Ser Gly Ile Ser Asp Arg Phe Ser

50 55 60

Gly Ser Lys Ser Gly Thr Ala Ala Ser Leu Ala Ile Thr Gly Leu Gln
65 70 75 80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Leu
85 90 95

Asn Ala Gln Val Phe Gly Gly Gly Thr Arg Leu Thr Val Leu Gly
100 105 110

<210> 255
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 255
Gly Gly Ser Ile Ser Gly Gly Tyr
1 5

<210> 256
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 256
Tyr Ser Ser Ser Gly Asn
1 5

<210> 257
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 257
Asp Arg Leu Phe Ser Val Val Gly Met Val Tyr Asn Asn Trp Phe Asp
1   5   10   15

Val

<210> 258
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 258
Thr Ser Asn Ile Gly Gly Tyr Asp Leu His
1   5   10

<210> 259
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 259
Asp Ile Asn Lys Arg Pro Ser
1   5

<210> 260
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 260
Gln Ser Tyr Asp Ser Ser Leu Asn Ala Gln Val
1   5   10

<210> 261

<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 261
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 Arg Ser Ser
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Lys Trp Val
35 40 45

Ser Ser Val Ser Gly Ser Gly Ala Gly Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro 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

Val Lys Glu Gly Gly Ser Arg Gly Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 262
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 262
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 Asp Ile Ser Asn Tyr
20 25 30

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
35 40 45

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 263
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 263
Gly Phe Thr Phe Arg Ser Ser
1 5

<210> 264
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 264
Ser Val Ser Gly Ser Gly Ala Gly Thr Tyr Tyr Ala Asp Ser Val Lys

1 5 10 15

Gly

<210> 265
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 265
Glu Gly Gly Ser Arg Gly Phe Asp Tyr
1 5

<210> 266
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 266
Gln Asp Ile Ser Asn Tyr Leu Ala
1 5

<210> 267
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 267
Tyr Thr Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Lys Phe Ser
1 5 10 15

<210> 268
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 268
Gln Gln Tyr Asn Leu Tyr Pro Pro Thr
1 5

<210> 269
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 269
Met Ala Gly Ser Pro Thr Cys Leu Thr Leu Ile Tyr Ile Leu Trp Gln
1 5 10 15

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

Val Gly Gly Ala Val Thr Phe Pro Leu Lys Ser Lys Val Lys Gln Val
35 40 45

Asp Ser Ile Val Trp Thr Phe Asn Thr Thr Pro Leu Val Thr Ile Gln
50 55 60

Pro Glu Gly Gly Thr Ile Ile Val Thr Gln Asn Arg Asn Arg Glu Arg
65 70 75 80

Val Asp Phe Pro Asp Gly Gly Tyr Ser Leu Lys Leu Ser Lys Leu Lys
85 90 95

Lys Asn Asp Ser Gly Ile Tyr Tyr Val Gly Ile Tyr Ser Ser Ser Leu
100 105 110

Gln Gln Pro Ser Thr Gln Glu Tyr Val Leu His Val Tyr Glu His Leu
115 120 125

```
Ser Lys Pro Lys Val Thr Met Gly Leu Gln Ser Asn Lys Asn Gly Thr
    130                 135                 140

Cys Val Thr Asn Leu Thr Cys Cys Met Glu His Gly Glu Glu Asp Val
145                 150                 155                 160

Ile Tyr Thr Trp Lys Ala Leu Gly Gln Ala Ala Asn Glu Ser His Asn
                165                 170                 175

Gly Ser Ile Leu Pro Ile Ser Trp Arg Trp Gly Glu Ser Asp Met Thr
            180                 185                 190

Phe Ile Cys Val Ala Arg Asn Pro Val Ser Arg Asn Phe Ser Ser Pro
        195                 200                 205

Ile Leu Ala Arg Lys Leu Cys Glu Gly Ala Ala Asp Asp Pro Asp Ser
    210                 215                 220

Ser Met Val Leu Leu Cys Leu Leu Leu Val Pro Leu Leu Leu Ser Leu
225                 230                 235                 240

Phe Val Leu Gly Leu Phe Leu Trp Phe Leu Lys Arg Glu Arg Gln Glu
                245                 250                 255

Glu Tyr Ile Glu Glu Lys Lys Arg Val Asp Ile Cys Arg Glu Thr Pro
            260                 265                 270

Asn Ile Cys Pro His Ser Gly Glu Asn Thr Glu Tyr Asp Thr Ile Pro
        275                 280                 285

His Thr Asn Arg Thr Ile Leu Lys Glu Asp Pro Ala Asn Thr Val Tyr
    290                 295                 300

Ser Thr Val Glu Ile Pro Lys Lys Met Glu Asn Pro His Ser Leu Leu
305                 310                 315                 320

Thr Met Pro Asp Thr Pro Arg Leu Phe Ala Tyr Glu Asn Val Ile
                325                 330                 335
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<210> 270
<211> 300
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 270
Met Ala Asn Cys Glu Phe Ser Pro Val Ser Gly Asp Lys Pro Cys Cys
1 5 10 15

Arg Leu Ser Arg Arg Ala Gln Leu Cys Leu Gly Val Ser Ile Leu Val
20 25 30

Leu Ile Leu Val Val Val Leu Ala Val Val Val Pro Arg Trp Arg Gln
35 40 45

Gln Trp Ser Gly Pro Gly Thr Thr Lys Arg Phe Pro Glu Thr Val Leu
50 55 60

Ala Arg Cys Val Lys Tyr Thr Glu Ile His Pro Glu Met Arg His Val
65 70 75 80

Asp Cys Gln Ser Val Trp Asp Ala Phe Lys Gly Ala Phe Ile Ser Lys
85 90 95

His Pro Cys Asn Ile Thr Glu Glu Asp Tyr Gln Pro Leu Met Lys Leu
100 105 110

Gly Thr Gln Thr Val Pro Cys Asn Lys Ile Leu Leu Trp Ser Arg Ile
115 120 125

Lys Asp Leu Ala His Gln Phe Thr Gln Val Gln Arg Asp Met Phe Thr
130 135 140

Leu Glu Asp Thr Leu Leu Gly Tyr Leu Ala Asp Asp Leu Thr Trp Cys
145 150 155 160

Gly Glu Phe Asn Thr Ser Lys Ile Asn Tyr Gln Ser Cys Pro Asp Trp

```
                165                 170                 175

Arg Lys Asp Cys Ser Asn Asn Pro Val Ser Val Phe Trp Lys Thr Val
            180                 185                 190

Ser Arg Arg Phe Ala Glu Ala Ala Cys Asp Val Val His Val Met Leu
        195                 200                 205

Asn Gly Ser Arg Ser Lys Ile Phe Asp Lys Asn Ser Thr Phe Gly Ser
    210                 215                 220

Val Glu Val His Asn Leu Gln Pro Glu Lys Val Gln Thr Leu Glu Ala
225                 230                 235                 240

Trp Val Ile His Gly Gly Arg Glu Asp Ser Arg Asp Leu Cys Gln Asp
                245                 250                 255

Pro Thr Ile Lys Glu Leu Glu Ser Ile Ile Ser Lys Arg Asn Ile Gln
            260                 265                 270

Phe Ser Cys Lys Asn Ile Tyr Arg Pro Asp Lys Phe Leu Gln Cys Val
        275                 280                 285

Lys Asn Pro Glu Asp Ser Ser Cys Thr Ser Glu Ile
    290                 295                 300


<210> 271
<211> 310
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 271
Met Arg Arg Ala Ala Leu Trp Leu Trp Leu Cys Ala Leu Ala Leu Ser
1               5                   10                  15

Leu Gln Pro Ala Leu Pro Gln Ile Val Ala Thr Asn Leu Pro Pro Glu
            20                  25                  30
```

```
Asp Gln Asp Gly Ser Gly Asp Asp Ser Asp Asn Phe Ser Gly Ser Gly
        35                  40                  45

Ala Gly Ala Leu Gln Asp Ile Thr Leu Ser Gln Gln Thr Pro Ser Thr
    50                  55                  60

Trp Lys Asp Thr Gln Leu Leu Thr Ala Ile Pro Thr Ser Pro Glu Pro
65                  70                  75                  80

Thr Gly Leu Glu Ala Thr Ala Ala Ser Thr Ser Thr Leu Pro Ala Gly
                85                  90                  95

Glu Gly Pro Lys Glu Gly Glu Ala Val Val Leu Pro Glu Val Glu Pro
            100                 105                 110

Gly Leu Thr Ala Arg Glu Gln Glu Ala Thr Pro Arg Pro Arg Glu Thr
        115                 120                 125

Thr Gln Leu Pro Thr Thr His Leu Ala Ser Thr Thr Thr Ala Thr Thr
    130                 135                 140

Ala Gln Glu Pro Ala Thr Ser His Pro His Arg Asp Met Gln Pro Gly
145                 150                 155                 160

His His Glu Thr Ser Thr Pro Ala Gly Pro Ser Gln Ala Asp Leu His
                165                 170                 175

Thr Pro His Thr Glu Asp Gly Gly Pro Ser Ala Thr Glu Arg Ala Ala
            180                 185                 190

Glu Asp Gly Ala Ser Ser Gln Leu Pro Ala Ala Glu Gly Ser Gly Glu
        195                 200                 205

Gln Asp Phe Thr Phe Glu Thr Ser Gly Glu Asn Thr Ala Val Val Ala
    210                 215                 220

Val Glu Pro Asp Arg Arg Asn Gln Ser Pro Val Asp Gln Gly Ala Thr
225                 230                 235                 240
```

Gly Ala Ser Gln Gly Leu Leu Asp Arg Lys Glu Val Leu Gly Gly Val
245 250 255

Ile Ala Gly Gly Leu Val Gly Leu Ile Phe Ala Val Cys Leu Val Gly
260 265 270

Phe Met Leu Tyr Arg Met Lys Lys Lys Asp Glu Gly Ser Tyr Ser Leu
275 280 285

Glu Glu Pro Lys Gln Ala Asn Gly Gly Ala Tyr Gln Lys Pro Thr Lys
290 295 300

Gln Glu Glu Phe Tyr Ala
305 310

<210> 272
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 272
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 Asp Phe Ser Arg Tyr
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Pro Ser Leu
50 55 60

Lys Asp Lys Phe Ile 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 Pro Asp Gly Asn Tyr Trp Tyr Phe Asp Val Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Ala
115 120

<210> 273
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 273
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 Lys Ala Ser Gln Asp Val Gly Ile Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Asp 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 Val Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Ser Tyr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 274
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 274
Gly Phe Asp Phe Ser Arg Tyr
1 5

<210> 275
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 275
Asn Pro Asp Ser Ser Thr
1 5

<210> 276
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 276
Pro Asp Gly Asn Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 277
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 277
Gln Asp Val Gly Ile Ala Val Ala
1 5

<210> 278
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 278
Trp Ala Ser Thr Arg His Thr
1 5

<210> 279
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 279
Gln Gln Tyr Ser Ser Tyr Pro Tyr Thr
1 5

<210> 280
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 280
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 Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Asn Tyr Asp Gly Ser Ser Thr Tyr Tyr Val 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 Gly Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Ala
115

<210> 281
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 281
Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln 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 Val Gly Val Tyr Phe Cys Ser Gln Ser
85 90 95

Thr His Val Pro Pro Phe Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg

<210> 282
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 282
Gly Phe Thr Phe Ser Asp Tyr Tyr Met Ala
1 5 10

<210> 283
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 283
Ser Ile Asn Tyr Asp Gly Ser Ser Thr Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
20 25

<210> 284
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 284
Asp Arg Gly Tyr Tyr Phe Asp Tyr

1 5

<210> 285
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 285
Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu
1 5 10 15

His

<210> 286
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 286
Lys Val Ser Asn Arg Phe Ser
1 5

<210> 287
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 287
Ser Gln Ser Thr His Val Pro Pro Phe Thr
1 5 10

<210> 288
<211> 123
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 288
Gln Val Gln Leu Gln Gln Ser Gly Ser Glu Leu Met Met Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Thr Gly Tyr Thr Phe Ser Asn Tyr
20 25 30

Trp Ile Glu Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Leu Pro Gly Thr Gly Arg Thr Ile Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Phe Thr Ala Asp Ile Ser Ser Asn Thr Val Gln
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Asp Tyr Tyr Gly Asn Phe Tyr Tyr Ala Met Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala
115 120

<210> 289
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 289
Asp Ile Gln Met Thr Gln Ser Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

```
Asp Arg Val Thr Ile Ser Cys Ser Ala Ser Gln Gly Ile Asn Asn Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Glu Leu Leu Ile
        35                  40                  45


Tyr Tyr Thr Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Pro
65                  70                  75                  80


Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Ser Lys Leu Pro Arg
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105


<210> 290
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 290
Gly Tyr Thr Phe Ser Asn Tyr
1               5


<210> 291
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 291
Leu Pro Gly Thr Gly Arg
1               5
```

<210> 292
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 292
Arg Asp Tyr Tyr Gly Asn Phe Tyr Tyr Ala Met Asp Tyr
1 5 10

<210> 293
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 293
Gln Gly Ile Asn Asn Tyr Leu Asn
1 5

<210> 294
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 294
Tyr Thr Ser Thr Leu Gln Ser
1 5

<210> 295
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 295
Gln Gln Tyr Ser Lys Leu Pro Arg Thr
1 5

<210> 296
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 296
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 Val Ser Gly Phe Thr Phe Asn Ser Phe
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 Gly 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 Phe Cys
85 90 95

Ala Lys Asp Lys Ile Leu Trp Phe Gly Glu Pro Val Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
115 120

<210> 297
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 297
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 298
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 298
Gly Phe Thr Phe Asn Ser Phe
1 5

<210> 299
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 299
Ser Gly Ser Gly Gly Gly
1 5

<210> 300
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 300
Asp Lys Ile Leu Trp Phe Gly Glu Pro Val Phe Asp Tyr
1 5 10

<210> 301
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 301
Gln Ser Val Ser Ser Tyr Leu Ala
1 5

<210> 302
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 302
Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 303

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 303
Gln Gln Arg Ser Asn Trp Pro Pro Thr
1 5

<210> 304
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 304
Gln 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

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Gly Asp Pro Ser Asn 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 Asp Leu Pro Leu Val Tyr Thr Gly Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 305
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 305
Asp Ile Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Ser Cys Ser Gly Asp Asn Leu Arg His Tyr Tyr Trp
20 25 30

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly
35 40 45

Asp Ser Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn
50 55 60

Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu Asp
65 70 75 80

Glu Ala Asp Tyr Tyr Cys Gln Thr Tyr Thr Gly Gly Ala Ser Leu Val
85 90 95

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105

<210> 306
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 306
Gly Phe Thr Phe Ser Ser Tyr Tyr Met Asn

1 5 10

<210> 307
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 307
Gly Ile Ser Gly Asp Pro Ser Asn Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
20 25

<210> 308
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 308
Asp Leu Pro Leu Val Tyr Thr Gly Phe Ala Tyr
1 5 10

<210> 309
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 309
Ser Gly Asp Asn Leu Arg His Tyr Tyr Trp
1 5 10

<210> 310
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 310
Gly Asp Ser Lys Arg Pro Ser
1 5

<210> 311
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 311
Gln Thr Tyr Thr Gly Gly Ala Ser Leu Val
1 5 10

<210> 312
<211> 177
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 312
Glu Asp Leu Asn Lys Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro
1 5 10 15

Ser Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu
20 25 30

Ala Thr Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn
35 40 45

Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys
50 55 60

Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu

65 70 75 80

Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys
85 90 95

Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp
100 105 110

Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg
115 120 125

Ala Asp Cys Gly Phe Thr Ser Val Ser Tyr Gln Gln Gly Val Leu Ser
130 135 140

Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala
145 150 155 160

Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp
165 170 175

Phe

<210> 313
<211> 178
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 313
Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro Ser
1 5 10 15

Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu Ala
20 25 30

Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly
35 40 45

```
Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys Glu
    50                  55                  60


Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu Arg
65                  70                  75                  80


Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys Gln
                85                  90                  95


Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp Arg
            100                 105                 110


Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg Ala
        115                 120                 125


Asp Cys Gly Phe Thr Ser Glu Ser Tyr Gln Gln Gly Val Leu Ser Ala
    130                 135                 140


Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
145                 150                 155                 160


Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp Ser
                165                 170                 175


Arg Gly



<210> 314
<211> 598
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 314
Met Thr Pro Ile Val Thr Val Leu Ile Cys Leu Gly Leu Ser Leu Gly
1               5                   10                  15


Pro Arg Thr His Val Gln Thr Gly Thr Ile Pro Lys Pro Thr Leu Trp
```

```
            20                  25                  30

Ala Glu Pro Asp Ser Val Ile Thr Gln Gly Ser Pro Val Thr Leu Ser
        35                  40                  45

Cys Gln Gly Ser Leu Glu Ala Gln Glu Tyr Arg Leu Tyr Arg Glu Lys
    50                  55                  60

Lys Ser Ala Ser Trp Ile Thr Arg Ile Arg Pro Glu Leu Val Lys Asn
65                  70                  75                  80

Gly Gln Phe His Ile Pro Ser Ile Thr Trp Glu His Thr Gly Arg Tyr
                85                  90                  95

Gly Cys Gln Tyr Tyr Ser Arg Ala Arg Trp Ser Glu Leu Ser Asp Pro
            100                 105                 110

Leu Val Leu Val Met Thr Gly Ala Tyr Pro Lys Pro Thr Leu Ser Ala
        115                 120                 125

Gln Pro Ser Pro Val Val Thr Ser Gly Gly Arg Val Thr Leu Gln Cys
    130                 135                 140

Glu Ser Gln Val Ala Phe Gly Gly Phe Ile Leu Cys Lys Glu Gly Glu
145                 150                 155                 160

Glu Glu His Pro Gln Cys Leu Asn Ser Gln Pro His Ala Arg Gly Ser
                165                 170                 175

Ser Arg Ala Ile Phe Ser Val Gly Pro Val Ser Pro Asn Arg Arg Trp
            180                 185                 190

Ser His Arg Cys Tyr Gly Tyr Asp Leu Asn Ser Pro Tyr Val Trp Ser
        195                 200                 205

Ser Pro Ser Asp Leu Leu Glu Leu Leu Val Pro Gly Val Ser Lys Lys
    210                 215                 220

Pro Ser Leu Ser Val Gln Pro Gly Pro Val Val Ala Pro Gly Glu Ser
```

```
225                 230                 235                 240

Leu Thr Leu Gln Cys Val Ser Asp Val Gly Tyr Asp Arg Phe Val Leu
                245                 250                 255

Tyr Lys Glu Gly Glu Arg Asp Leu Arg Gln Leu Pro Gly Arg Gln Pro
            260                 265                 270

Gln Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Gly Pro Val Ser Arg
        275                 280                 285

Ser Tyr Gly Gly Gln Tyr Arg Cys Tyr Gly Ala His Asn Leu Ser Ser
    290                 295                 300

Glu Cys Ser Ala Pro Ser Asp Pro Leu Asp Ile Leu Ile Thr Gly Gln
305                 310                 315                 320

Ile Arg Gly Thr Pro Phe Ile Ser Val Gln Pro Gly Pro Thr Val Ala
                325                 330                 335

Ser Gly Glu Asn Val Thr Leu Leu Cys Gln Ser Trp Arg Gln Phe His
            340                 345                 350

Thr Phe Leu Leu Thr Lys Ala Gly Ala Ala Asp Ala Pro Leu Arg Leu
        355                 360                 365

Arg Ser Ile His Glu Tyr Pro Lys Tyr Gln Ala Glu Phe Pro Met Ser
    370                 375                 380

Pro Val Thr Ser Ala His Ala Gly Thr Tyr Arg Cys Tyr Gly Ser Leu
385                 390                 395                 400

Asn Ser Asp Pro Tyr Leu Leu Ser His Pro Ser Glu Pro Leu Glu Leu
                405                 410                 415

Val Val Ser Gly Pro Ser Met Gly Ser Ser Pro Pro Pro Thr Gly Pro
            420                 425                 430

Ile Ser Thr Pro Ala 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 Val 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 Asp Thr Gln Pro Glu Asp Gly
530 535 540

Val Glu Met Asp Thr Arg Ala Ala Ala Ser Glu Ala Pro Gln Asp Val
545 550 555 560

Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Lys Ala Thr Glu
565 570 575

Pro Pro Pro Ser Gln Glu Arg Glu Pro Pro Ala Glu Pro Ser Ile Tyr
580 585 590

Ala Thr Leu Ala Ile His
595

<210> 315
<211> 650
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 315

```
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
645 650

<210> 316
<211> 631
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 316
Met Thr Pro Ala Leu Thr Ala Leu Leu Cys Leu Gly Leu Ser Leu Gly
1 5 10 15

Pro Arg Thr Arg Val Gln Ala Gly Pro Phe Pro Lys Pro Thr Leu Trp
20 25 30

Ala Glu Pro Gly Ser Val Ile Ser Trp Gly Ser Pro Val Thr Ile Trp
35 40 45

Cys Gln Gly Ser Gln Glu Ala Gln Glu Tyr Arg Leu His Lys Glu Gly
50 55 60

Ser Pro Glu Pro Leu Asp Arg Asn Asn Pro Leu Glu Pro Lys Asn Lys
65 70 75 80

Ala Arg Phe Ser Ile Pro Ser Met Thr Glu His His Ala Gly Arg Tyr
85 90 95

Arg Cys His Tyr Tyr Ser Ser Ala Gly Trp Ser Glu Pro Ser Asp Pro
100 105 110

Leu Glu Met Val Met Thr Gly Ala Tyr Ser Lys Pro Thr Leu Ser Ala
115 120 125

Leu Pro Ser Pro Val Val Ala Ser Gly Gly Asn Met Thr Leu Arg Cys

```
    130                 135                 140

Gly Ser Gln Lys Gly Tyr His His Phe Val Leu Met Lys Glu Gly Glu
145                 150                 155                 160

His Gln Leu Pro Arg Thr Leu Asp Ser Gln Gln Leu His Ser Arg Gly
                165                 170                 175

Phe Gln Ala Leu Phe Pro Val Gly Pro Val Thr Pro Ser His Arg Trp
            180                 185                 190

Arg Phe Thr Cys Tyr Tyr Tyr Tyr Thr Asn Thr Pro Trp Val Trp Ser
        195                 200                 205

His Pro Ser Asp Pro Leu Glu Ile Leu Pro Ser Gly Val Ser Arg Lys
    210                 215                 220

Pro Ser Leu Leu Thr Leu Gln Gly Pro Val Leu Ala Pro Gly Gln Ser
225                 230                 235                 240

Leu Thr Leu Gln Cys Gly Ser Asp Val Gly Tyr Asn Arg Phe Val Leu
                245                 250                 255

Tyr Lys Glu Gly Glu Arg Asp Phe Leu Gln Arg Pro Gly Gln Gln Pro
            260                 265                 270

Gln Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Gly Pro Val Ser Pro
        275                 280                 285

Ser Asn Gly Gly Gln Tyr Arg Cys Tyr Gly Ala His Asn Leu Ser Ser
    290                 295                 300

Glu Trp Ser Ala Pro Ser Asp Pro Leu Asn Ile Leu Met Ala Gly Gln
305                 310                 315                 320

Ile Tyr Asp Thr Val Ser Leu Ser Ala Gln Pro Gly Pro Thr Val Ala
                325                 330                 335

Ser Gly Glu Asn Val Thr Leu Leu Cys Gln Ser Trp Trp Gln Phe Asp
```

```
            340                 345                 350

Thr Phe Leu Leu Thr Lys Glu Gly Ala Ala His Pro Pro Leu Arg Leu
        355                 360                 365

Arg Ser Met Tyr Gly Ala His Lys Tyr Gln Ala Glu Phe Pro Met Ser
    370                 375                 380

Pro Val Thr Ser Ala His Ala Gly Thr Tyr Arg Cys Tyr Gly Ser Tyr
385                 390                 395                 400

Ser Ser Asn Pro His Leu Leu Ser His Pro Ser Glu Pro Leu Glu Leu
                405                 410                 415

Val Val Ser Gly His Ser Gly Gly Ser Ser Leu Pro Pro Thr Gly Pro
            420                 425                 430

Pro Ser Thr Pro Gly Leu Gly Arg Tyr Leu Glu Val Leu Ile Gly Val
        435                 440                 445

Ser Val Ala Phe Val Leu Leu Leu Phe Leu Leu Leu Phe Leu Leu Leu
    450                 455                 460

Arg Arg Gln Arg His Ser Lys His Arg Thr Ser Asp Gln Arg Lys Thr
465                 470                 475                 480

Asp Phe Gln Arg Pro Ala Gly Ala Ala Glu Thr Glu Pro Lys Asp Arg
                485                 490                 495

Gly Leu Leu Arg Arg Ser Ser Pro Ala Ala Asp Val Gln Glu Glu Asn
            500                 505                 510

Leu Tyr Ala Ala Val Lys Asp Thr Gln Ser Glu Asp Arg Val Glu Leu
        515                 520                 525

Asp Ser Gln Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr Ala
    530                 535                 540

Pro Val Lys His Ser Ser Pro Arg Arg Glu Met Ala Ser Pro Pro Ser
```

545 550 555 560

Ser Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Val Glu Glu
565 570 575

Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Ser Gln Asp
580 585 590

Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Lys Ala Thr
595 600 605

Glu Pro Pro Pro Ser Gln Glu Gly Glu Pro Pro Ala Glu Pro Ser Ile
610 615 620

Tyr Ala Thr Leu Ala Ile His
625 630

<210> 317
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 317
Met Ile Pro Thr Phe Thr Ala Leu Leu Cys Leu Gly Leu Ser Leu Gly
1 5 10 15

Pro Arg Thr His Met Gln Ala Gly Pro Leu Pro Lys Pro Thr Leu Trp
20 25 30

Ala Glu Pro Gly Ser Val Ile Ser Trp Gly Asn Ser Val Thr Ile Trp
35 40 45

Cys Gln Gly Thr Leu Glu Ala Arg Glu Tyr Arg Leu Asp Lys Glu Glu
50 55 60

Ser Pro Ala Pro Trp Asp Arg Gln Asn Pro Leu Glu Pro Lys Asn Lys
65 70 75 80

```
Ala Arg Phe Ser Ile Pro Ser Met Thr Glu Asp Tyr Ala Gly Arg Tyr
                85                  90                  95

Arg Cys Tyr Tyr Arg Ser Pro Val Gly Trp Ser Gln Pro Ser Asp Pro
            100                 105                 110

Leu Glu Leu Val Met Thr Gly Ala Tyr Ser Lys Pro Thr Leu Ser Ala
        115                 120                 125

Leu Pro Ser Pro Leu Val Thr Ser Gly Lys Ser Val Thr Leu Leu Cys
    130                 135                 140

Gln Ser Arg Ser Pro Met Asp Thr Phe Leu Leu Ile Lys Glu Arg Ala
145                 150                 155                 160

Ala His Pro Leu Leu His Leu Arg Ser Glu His Gly Ala Gln Gln His
                165                 170                 175

Gln Ala Glu Phe Pro Met Ser Pro Val Thr Ser Val His Gly Gly Thr
            180                 185                 190

Tyr Arg Cys Phe Ser Ser His Gly Phe Ser His Tyr Leu Leu Ser His
        195                 200                 205

Pro Ser Asp Pro Leu Glu Leu Ile Val Ser Gly Ser Leu Glu Asp Pro
    210                 215                 220

Arg Pro Ser Pro Thr Arg Ser Val Ser Thr Ala Ala Gly Pro Glu Asp
225                 230                 235                 240

Gln Pro Leu Met Pro Thr Gly Ser Val Pro His Ser Gly Leu Arg Arg
                245                 250                 255

His Trp Glu Val Leu Ile Gly Val Leu Val Val Ser Ile Leu Leu Leu
            260                 265                 270

Ser Leu Leu Leu Phe Leu Leu Leu Gln His Trp Arg Gln Gly Lys His
        275                 280                 285
```

```
Arg Thr Leu Ala Gln Arg Gln Ala Asp Phe Gln Arg Pro Pro Gly Ala
    290                 295                 300

Ala Glu Pro Glu Pro Lys Asp Gly Gly Leu Gln Arg Arg Ser Ser Pro
305                 310                 315                 320

Ala Ala Asp Val Gln Gly Glu Asn Phe Cys Ala Ala Val Lys Asn Thr
                325                 330                 335

Gln Pro Glu Asp Gly Val Glu Met Asp Thr Arg Gln Ser Pro His Asp
            340                 345                 350

Glu Asp Pro Gln Ala Val Thr Tyr Ala Lys Val Lys His Ser Arg Pro
        355                 360                 365

Arg Arg Glu Met Ala Ser Pro Pro Ser Pro Leu Ser Gly Glu Phe Leu
    370                 375                 380

Asp Thr Lys Asp Arg Gln Ala Glu Glu Asp Arg Gln Met Asp Thr Glu
385                 390                 395                 400

Ala Ala Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr Ala Gln Leu His
                405                 410                 415

Ser Phe Thr Leu Arg Gln Lys Ala Thr Glu Pro Pro Pro Ser Gln Glu
            420                 425                 430

Gly Ala Ser Pro Ala Glu Pro Ser Val Tyr Ala Thr Leu Ala Ile His
        435                 440                 445


<210> 318
<211> 590
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 318
Met Thr Leu Thr Leu Ser Val Leu Ile Cys Leu Gly Leu Ser Val Gly
```

```
1               5                   10                  15

Pro Arg Thr Cys Val Gln Ala Gly Thr Leu Pro Lys Pro Thr Leu Trp
            20                  25                  30

Ala Glu Pro Ala Ser Val Ile Ala Arg Gly Lys Pro Val Thr Leu Trp
        35                  40                  45

Cys Gln Gly Pro Leu Glu Thr Glu Glu Tyr Arg Leu Asp Lys Glu Gly
    50                  55                  60

Leu Pro Trp Ala Arg Lys Arg Gln Asn Pro Leu Glu Pro Gly Ala Lys
65                  70                  75                  80

Ala Lys Phe His Ile Pro Ser Thr Val Tyr Asp Ser Ala Gly Arg Tyr
                85                  90                  95

Arg Cys Tyr Tyr Glu Thr Pro Ala Gly Trp Ser Glu Pro Ser Asp Pro
            100                 105                 110

Leu Glu Leu Val Ala Thr Gly Phe Tyr Ala Glu Pro Thr Leu Leu Ala
        115                 120                 125

Leu Pro Ser Pro Val Val Ala Ser Gly Gly Asn Val Thr Leu Gln Cys
    130                 135                 140

Asp Thr Leu Asp Gly Leu Leu Thr Phe Val Leu Val Glu Glu Glu Gln
145                 150                 155                 160

Lys Leu Pro Arg Thr Leu Tyr Ser Gln Lys Leu Pro Lys Gly Pro Ser
                165                 170                 175

Gln Ala Leu Phe Pro Val Gly Pro Val Thr Pro Ser Cys Arg Trp Arg
            180                 185                 190

Phe Arg Cys Tyr Tyr Tyr Tyr Arg Lys Asn Pro Gln Val Trp Ser Asn
        195                 200                 205

Pro Ser Asp Leu Leu Glu Ile Leu Val Pro Gly Val Ser Arg Lys Pro
```

```
    210                 215                 220

Ser Leu Leu Ile Pro Gln Gly Ser Val Val Ala Arg Gly Gly Ser Leu
225                 230                 235                 240

Thr Leu Gln Cys Arg Ser Asp Val Gly Tyr Asp Ile Phe Val Leu Tyr
                245                 250                 255

Lys Glu Gly Glu His Asp Leu Val Gln Gly Ser Gly Gln Gln Pro Gln
            260                 265                 270

Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Gly Pro Val Ser Arg Ser
        275                 280                 285

His Gly Gly Gln Tyr Arg Cys Tyr Gly Ala His Asn Leu Ser Pro Arg
    290                 295                 300

Trp Ser Ala Pro Ser Asp Pro Leu Asp Ile Leu Ile Ala Gly Leu Ile
305                 310                 315                 320

Pro Asp Ile Pro Ala Leu Ser Val Gln Pro Gly Pro Lys Val Ala Ser
                325                 330                 335

Gly Glu Asn Val Thr Leu Leu Cys Gln Ser Trp His Gln Ile Asp Thr
            340                 345                 350

Phe Phe Leu Thr Lys Glu Gly Ala Ala His Pro Pro Leu Cys Leu Lys
        355                 360                 365

Ser Lys Tyr Gln Ser Tyr Arg His Gln Ala Glu Phe Ser Met Ser Pro
    370                 375                 380

Val Thr Ser Ala Gln Gly Gly Thr Tyr Arg Cys Tyr Ser Ala Ile Arg
385                 390                 395                 400

Ser Tyr Pro Tyr Leu Leu Ser Ser Pro Ser Tyr Pro Gln Glu Leu Val
                405                 410                 415

Val Ser Gly Pro Ser Gly Asp Pro Ser Leu Ser Pro Thr Gly Ser Thr
```

420 425 430

Pro Thr Pro Gly Pro Glu Asp Gln Pro Leu Thr Pro Thr Gly Leu Asp
435 440 445

Pro Gln Ser Gly Leu Gly Arg His Leu Gly Val Val Thr Gly Val Ser
450 455 460

Val Ala Phe Val Leu Leu Leu Phe Leu Leu Leu Phe Leu Leu Leu Arg
465 470 475 480

His Arg His Gln Ser Lys His Arg Thr Ser Ala His Phe Tyr Arg Pro
485 490 495

Ala Gly Ala Ala Gly Pro Glu Pro Lys Asp Gln Gly Leu Gln Lys Arg
500 505 510

Ala Ser Pro Val Ala Asp Ile Gln Glu Glu Ile Leu Asn Ala Ala Val
515 520 525

Lys Asp Thr Gln Pro Lys Asp Gly Val Glu Met Asp Ala Arg Ala Ala
530 535 540

Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr Ala Gln Leu His Ser Leu
545 550 555 560

Thr Leu Arg Arg Glu Ala Thr Glu Pro Pro Pro Ser Gln Glu Arg Glu
565 570 575

Pro Pro Ala Glu Pro Ser Ile Tyr Ala Pro Leu Ala Ile His
580 585 590

<210> 319
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 319

```
Met Thr Pro Ile Val Thr Val Leu Ile Cys Leu Arg Leu Ser Leu Gly
1               5                  10                  15

Pro Arg Thr His Val Gln Ala Gly Thr 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 Trp
        35                  40                  45

Cys Gln Gly Ile Leu Glu Thr Gln Glu Tyr Arg Leu Tyr Arg Glu Lys
    50                  55                  60

Lys Thr Ala Pro Trp Ile Thr Arg Ile Pro Gln Glu Ile Val Lys Lys
65                  70                  75                  80

Gly Gln Phe Pro Ile Pro Ser Ile Thr Trp Glu His Thr Gly Arg Tyr
                85                  90                  95

Arg Cys Phe Tyr Gly Ser His Thr Ala Gly Trp Ser Glu Pro 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 Leu Pro Ser Pro Val Val Thr Ser Gly Gly Asn Val Thr Leu His
    130                 135                 140

Cys Val Ser Gln Val Ala Phe Gly Ser Phe Ile Leu Cys Lys Glu Gly
145                 150                 155                 160

Glu Asp Glu His Pro Gln Cys Leu Asn Ser Gln Pro Arg Thr His Gly
                165                 170                 175

Trp Ser Arg Ala Ile Phe Ser Val Gly Pro Val Ser Pro Ser Arg Arg
            180                 185                 190

Trp Ser Tyr Arg Cys Tyr Ala Tyr Asp Ser Asn Ser Pro His Val 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 Gly Glu
225                 230                 235                 240

Ser Leu Thr Leu Gln Cys Val Ser Asp Val Ser Tyr Asp Arg Phe Val
                245                 250                 255

Leu Tyr Lys Glu Gly Glu Arg Asp Phe Leu Gln Leu Pro Gly Pro 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 Ser Gly Ala Tyr 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 Arg Gly Arg Pro Phe Ile Ser Val His Pro Gly Pro Thr Val
                325                 330                 335

Ala Ser Gly Glu Asn Val Thr Leu Leu Cys Gln Ser Trp Gly Pro Phe
            340                 345                 350

His Thr Phe Leu Leu Thr Lys Ala Gly Ala Ala Asp Ala Pro Leu Arg
        355                 360                 365

Leu Arg Ser Ile His Glu Tyr Pro Lys Tyr Gln Ala Glu Phe Pro Met
    370                 375                 380

Ser Pro Val Thr Ser Ala His Ser Gly Thr Tyr Arg Cys Tyr Gly Ser
385                 390                 395                 400

Leu Ser Ser Asn Pro Tyr Leu Leu Ser His Pro Ser Asp Ser Leu Glu
                405                 410                 415
```

Leu Met Val Ser Gly Ala Ala Glu Thr Leu Ser Pro Pro Gln Asn Lys
420 425 430

Ser Asp Ser Lys Ala Gly Ala Ala Asn Thr Leu Ser Pro Ser Gln Asn
435 440 445

Lys Thr Ala Ser His Pro Gln Asp Tyr Thr Val Glu Asn Leu Ile Arg
450 455 460

Met Gly Ile Ala Gly Leu Val Leu Val Val Leu Gly Ile Leu Leu Phe
465 470 475 480

Glu Ala Gln His Ser Gln Arg Ser Leu
485

<210> 320
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 320
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 Ile Gln Gly Ser Pro Val Thr Leu Arg
35 40 45

Cys Gln Gly Ser Leu Gln Ala Glu Glu Tyr His Leu Tyr Arg Glu Asn
50 55 60

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

Gln Phe Pro Ile Pro Ser Ile Thr Trp Glu His Ala Gly Arg Tyr His

```
                85                  90                  95

Cys Gln Tyr Tyr Ser His Asn His Ser Ser Glu Tyr Ser Asp Pro Leu
            100                 105                 110

Glu Leu Val Val Thr Gly Ala Tyr Ser Lys Pro Thr Leu Ser Ala Leu
        115                 120                 125

Pro Ser Pro Val Val Thr Leu Gly Gly Asn Val Thr Leu Gln Cys Val
    130                 135                 140

Ser Gln Val Ala Phe Asp Gly Phe Ile Leu Cys Lys Glu Gly Glu Asp
145                 150                 155                 160

Glu His Pro Gln Arg Leu Asn Ser His Ser His Ala Arg Gly Trp Ser
                165                 170                 175

Trp Ala Ile Phe Ser Val Gly Pro Val Ser Pro Ser Arg Arg Trp Ser
            180                 185                 190

Tyr Arg Cys Tyr Ala Tyr Asp Ser Asn Ser Pro Tyr Val Trp Ser Leu
        195                 200                 205

Pro Ser Asp Leu Leu Glu Leu Leu Val Pro Gly Val Ser Lys Lys Pro
    210                 215                 220

Ser Leu Ser Val Gln Pro Gly Pro Met Val Ala Pro Gly Glu Ser Leu
225                 230                 235                 240

Thr Leu Gln Cys Val Ser Asp Val Gly Tyr Asp Arg Phe Val Leu Tyr
                245                 250                 255

Lys Glu Gly Glu Arg Asp Phe Leu Gln Arg Pro Gly Trp Gln Pro Gln
            260                 265                 270

Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Gly Pro Val Ser Pro Ser
        275                 280                 285

His Gly Gly Gln Tyr Arg Cys Tyr Ser Ala His Asn Leu Ser Ser Glu
```

```
    290                 295                 300

Trp Ser Ala Pro Ser Asp Pro Leu Asp Ile Leu Ile Thr Gly Gln Phe
305                 310                 315                 320

Tyr Asp Arg Pro Ser Leu Ser Val Gln Pro Val Pro Thr Val Ala Pro
                325                 330                 335

Gly Lys Asn Val Thr Leu Leu Cys Gln Ser Arg Gly Gln Phe His Thr
            340                 345                 350

Phe Leu Leu Thr Lys Glu Gly Ala Gly His Pro Pro Leu His Leu Arg
        355                 360                 365

Ser Glu His Gln Ala Gln Gln Asn Gln Ala Glu Phe Arg Met Gly Pro
    370                 375                 380

Val Thr Ser Ala His Val Gly Thr Tyr Arg Cys Tyr Ser Ser Leu Ser
385                 390                 395                 400

Ser Asn Pro Tyr Leu Leu Ser Leu Pro Ser Asp Pro Leu Glu Leu Val
                405                 410                 415

Val Ser Glu Ala Ala Glu Thr Leu Ser Pro Ser Gln Asn Lys Thr Asp
            420                 425                 430

Ser Thr Thr Thr Ser Leu Gly Gln His Pro Gln Asp Tyr Thr Val Glu
        435                 440                 445

Asn Leu Ile Arg Met Gly Val Ala Gly Leu Val Leu Val Val Leu Gly
    450                 455                 460

Ile Leu Leu Phe Glu Ala Gln His Ser Gln Arg Ser Leu Gln Asp Ala
465                 470                 475                 480

Ala Gly Arg
```

<210> 321

<211> 439
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 321

```
Met Thr Pro Ile Leu Thr Val Leu Ile Cys Leu Gly Leu Ser Leu Asp
1               5                  10                  15

Pro Arg Thr His Val Gln Ala Gly Pro 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 Ser Leu Glu Thr Gln Glu Tyr His 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 Leu Ser Ile Thr Trp Glu His Ala Gly Arg Tyr
                85                  90                  95

Cys Cys Ile Tyr Gly Ser His Thr Ala Gly Leu Ser Glu Ser Ser Asp
            100                 105                 110

Pro Leu Glu Leu Val Val Thr Gly Ala Tyr Ser Lys Pro Thr Leu Ser
        115                 120                 125

Ala Leu Pro Ser Pro Val Val Thr Ser Gly Gly Asn Val Thr Ile Gln
    130                 135                 140

Cys Asp Ser Gln Val Ala Phe Asp Gly Phe Ile Leu Cys Lys Glu Gly
145                 150                 155                 160

Glu Asp Glu His Pro Gln Cys Leu Asn Ser His Ser 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 Ser Tyr Arg Cys Tyr Gly Tyr Asp Ser Arg Ala Pro Tyr Val Trp
        195                 200                 205

Ser Leu Pro Ser Asp Leu Leu Gly Leu Leu Val Pro Gly Val Ser Lys
    210                 215                 220

Lys Pro Ser Leu Ser Val Gln Pro Gly Pro Val Val Ala Pro Gly Glu
225                 230                 235                 240

Lys Leu Thr Phe Gln Cys Gly Ser Asp Ala Gly Tyr Asp Arg Phe Val
                245                 250                 255

Leu Tyr Lys Glu Trp Gly Arg Asp Phe Leu Gln Arg Pro Gly Arg 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 Thr Cys Ser Gly Ala Tyr Asn Leu Ser
    290                 295                 300

Ser Glu Trp Ser Ala Pro Ser Asp Pro Leu Asp Ile Leu Ile Thr Gly
305                 310                 315                 320

Gln Ile Arg Ala Arg Pro Phe Leu Ser Val Arg Pro Gly Pro Thr Val
                325                 330                 335

Ala Ser Gly Glu Asn Val Thr Leu Leu Cys Gln Ser Gln Gly Gly Met
            340                 345                 350

His Thr Phe Leu Leu Thr Lys Glu Gly Ala Ala Asp Ser Pro Leu Arg
        355                 360                 365

Leu Lys Ser Lys Arg Gln Ser His Lys Tyr Gln Ala Glu Phe Pro Met
    370                 375                 380
```

```
Ser Pro Val Thr Ser Ala His Ala Gly Thr Tyr Arg Cys Tyr Gly Ser
385                 390                 395                 400


Leu Ser Ser Asn Pro Tyr Leu Leu Thr His Pro Ser Asp Pro Leu Glu
                405                 410                 415


Leu Val Val Ser Gly Ala Ala Glu Thr Leu Ser Pro Pro Gln Asn Lys
            420                 425                 430


Ser Asp Ser Lys Ala Gly Glu
        435


<210> 322
<211> 499
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 322
Met Thr Leu Ile Leu Thr Ser Leu Leu Phe Phe Gly Leu Ser Leu Gly
1               5                   10                  15


Pro Arg Thr Arg Val Gln Ala Glu Asn Leu Pro Lys Pro Ile Leu Trp
            20                  25                  30


Ala Glu Pro Gly Pro Val Ile Thr Trp His Asn Pro Val Thr Ile Trp
        35                  40                  45


Cys Gln Gly Thr Leu Glu Ala Gln Gly Tyr Arg Leu Asp Lys Glu Gly
    50                  55                  60


Asn Ser Met Ser Arg His Ile Leu Lys Thr Leu Glu Ser Glu Asn Lys
65                  70                  75                  80


Val Lys Leu Ser Ile Pro Ser Met Met Trp Glu His Ala Gly Arg Tyr
                85                  90                  95


His Cys Tyr Tyr Gln Ser Pro Ala Gly Trp Ser Glu Pro Ser Asp Pro
```

```
            100                 105                 110

Leu Glu Leu Val Val Thr Ala Tyr Ser Arg Pro Thr Leu Ser Ala Leu
        115                 120                 125

Pro Ser Pro Val Val Thr Ser Gly Val Asn Val Thr Leu Arg Cys Ala
    130                 135                 140

Ser Arg Leu Gly Leu Gly Arg Phe Thr Leu Ile Glu Glu Gly Asp His
145                 150                 155                 160

Arg Leu Ser Trp Thr Leu Asn Ser His Gln His Asn His Gly Lys Phe
                165                 170                 175

Gln Ala Leu Phe Pro Met Gly Pro Leu Thr Phe Ser Asn Arg Gly Thr
            180                 185                 190

Phe Arg Cys Tyr Gly Tyr Glu Asn Asn Thr Pro Tyr Val Trp Ser Glu
        195                 200                 205

Pro Ser Asp Pro Leu Gln Leu Leu Val Ser Gly Val Ser Arg Lys Pro
    210                 215                 220

Ser Leu Leu Thr Leu Gln Gly Pro Val Val Thr Pro Gly Glu Asn Leu
225                 230                 235                 240

Thr Leu Gln Cys Gly Ser Asp Val Gly Tyr Ile Arg Tyr Thr Leu Tyr
                245                 250                 255

Lys Glu Gly Ala Asp Gly Leu Pro Gln Arg Pro Gly Arg Gln Pro Gln
            260                 265                 270

Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Ser Pro Val Ser Arg Ser
        275                 280                 285

Tyr Gly Gly Gln Tyr Arg Cys Tyr Gly Ala His Asn Val Ser Ser Glu
    290                 295                 300

Trp Ser Ala Pro Ser Asp Pro Leu Asp Ile Leu Ile Ala Gly Gln Ile
```

305 310 315 320

Ser Asp Arg Pro Ser Leu Ser Val Gln Pro Gly Pro Thr Val Thr Ser
325 330 335

Gly Glu Lys Val Thr Leu Leu Cys Gln Ser Trp Asp Pro Met Phe Thr
340 345 350

Phe Leu Leu Thr Lys Glu Gly Ala Ala His Pro Pro Leu Arg Leu Arg
355 360 365

Ser Met Tyr Gly Ala His Lys Tyr Gln Ala Glu Phe Pro Met Ser Pro
370 375 380

Val Thr Ser Ala His Ala Gly Thr Tyr Arg Cys Tyr Gly Ser Arg Ser
385 390 395 400

Ser Asn Pro Tyr Leu Leu Ser His Pro Ser Glu Pro Leu Glu Leu Val
405 410 415

Val Ser Gly Ala Thr Glu Thr Leu Asn Pro Ala Gln Lys Lys Ser Asp
420 425 430

Ser Lys Thr Ala Pro His Leu Gln Asp Tyr Thr Val Glu Asn Leu Ile
435 440 445

Arg Met Gly Val Ala Gly Leu Val Leu Leu Phe Leu Gly Ile Leu Leu
450 455 460

Phe Glu Ala Gln His Ser Gln Arg Ser Pro Pro Arg Cys Ser Gln Glu
465 470 475 480

Ala Asn Ser Arg Lys Asp Asn Ala Pro Phe Arg Val Val Glu Pro Trp
485 490 495

Glu Gln Ile

<210> 323

<211> 299
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 323
Met Ala Pro Trp Ser His Pro Ser Ala Gln Leu Gln Pro Val Gly Gly
1 5 10 15

Asp Ala Val Ser Pro Ala Leu Met Val Leu Leu Cys Leu Gly Leu Ser
20 25 30

Leu Gly Pro Arg Thr His Val Gln Ala Gly Asn Leu Ser Lys Ala Thr
35 40 45

Leu Trp Ala Glu Pro Gly Ser Val Ile Ser Arg Gly Asn Ser Val Thr
50 55 60

Ile Arg Cys Gln Gly Thr Leu Glu Ala Gln Glu Tyr Arg Leu Val Lys
65 70 75 80

Glu Gly Ser Pro Glu Pro Trp Asp Thr Gln Asn Pro Leu Glu Pro Lys
85 90 95

Asn Lys Ala Arg Phe Ser Ile Pro Ser Met Thr Glu His His Ala Gly
100 105 110

Arg Tyr Arg Cys Tyr Tyr Tyr Ser Pro Ala Gly Trp Ser Glu Pro Ser
115 120 125

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

Ser Ala Leu Pro Ser Pro Val Val Thr Ser Gly Glu Asn Val Thr Leu
145 150 155 160

Gln Cys Gly Ser Arg Leu Arg Phe Asp Arg Phe Ile Leu Thr Glu Glu
165 170 175

```
Gly Asp His Lys Leu Ser Trp Thr Leu Asp Ser Gln Leu Thr Pro Ser
            180                 185                 190


Gly Gln Phe Gln Ala Leu Phe Pro Val Gly Pro Val Thr Pro Ser His
        195                 200                 205


Arg Trp Met Leu Arg Cys Tyr Gly Ser Arg Arg His Ile Leu Gln Val
    210                 215                 220


Trp Ser Glu Pro Ser Asp Leu Leu Glu Ile Pro Val Ser Gly Ala Ala
225                 230                 235                 240


Asp Asn Leu Ser Pro Ser Gln Asn Lys Ser Asp Ser Gly Thr Ala Ser
                245                 250                 255


His Leu Gln Asp Tyr Ala Val Glu Asn Leu Ile Arg Met Gly Met Ala
            260                 265                 270


Gly Leu Ile Leu Val Val Leu Gly Ile Leu Ile Phe Gln Asp Trp His
        275                 280                 285


Ser Gln Arg Ser Pro Gln Ala Ala Ala Gly Arg
    290                 295


<210> 324
<211> 481
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 324
Met Thr Pro Ala Leu Thr Ala Leu Leu Cys Leu Gly Leu Ser Leu Gly
1               5                   10                  15


Pro Arg Thr Arg Val Gln Ala Gly Pro Phe Pro Lys Pro Thr Leu Trp
            20                  25                  30


Ala Glu Pro Gly Ser Val Ile Ser Trp Gly Ser Pro Val Thr Ile Trp
```

```
        35                  40                  45

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

Ser Pro Glu Pro Leu Asp Arg Asn Asn Pro Leu Glu Pro Lys Asn Lys
65                  70                  75                  80

Ala Arg Phe Ser Ile Pro Ser Met Thr Gln His His Ala Gly Arg Tyr
                85                  90                  95

Arg Cys His Tyr Tyr Ser Ser Ala Gly Trp Ser Glu Pro Ser Asp Pro
            100                 105                 110

Leu Glu Leu Val Met Thr Gly Phe Tyr Asn Lys Pro Thr Leu Ser Ala
        115                 120                 125

Leu Pro Ser Pro Val Val Ala Ser Gly Gly Asn Met Thr Leu Arg Cys
    130                 135                 140

Gly Ser Gln Lys Gly Tyr His His Phe Val Leu Met Lys Glu Gly Glu
145                 150                 155                 160

His Gln Leu Pro Arg Thr Leu Asp Ser Gln Gln Leu His Ser Gly Gly
                165                 170                 175

Phe Gln Ala Leu Phe Pro Val Gly Pro Val Thr Pro Ser His Arg Trp
            180                 185                 190

Arg Phe Thr Cys Tyr Tyr Tyr Tyr Thr Asn Thr Pro Arg Val Trp Ser
        195                 200                 205

His Pro Ser Asp Pro Leu Glu Ile Leu Pro Ser Gly Val Ser Arg Lys
    210                 215                 220

Pro Ser Leu Leu Thr Leu Gln Gly Pro Val Leu Ala Pro Gly Gln Ser
225                 230                 235                 240

Leu Thr Leu Gln Cys Gly Ser Asp Val Gly Tyr Asp Arg Phe Val Leu
```

```
                245                 250                 255

Tyr Lys Glu Gly Glu Arg Asp Phe Leu Gln Arg Pro Gly Gln Gln Pro
            260                 265                 270

Gln Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Gly Pro Val Ser Pro
        275                 280                 285

Ser His Gly Gly Gln Tyr Arg Cys Tyr Gly Ala His Asn Leu Ser Ser
    290                 295                 300

Glu Trp Ser Ala Pro Ser Asp Pro Leu Asn Ile Leu Met Ala Gly Gln
305                 310                 315                 320

Ile Tyr Asp Thr Val Ser Leu Ser Ala Gln Pro Gly Pro Thr Val Ala
                325                 330                 335

Ser Gly Glu Asn Val Thr Leu Leu Cys Gln Ser Arg Gly Tyr Phe Asp
            340                 345                 350

Thr Phe Leu Leu Thr Lys Glu Gly Ala Ala His Pro Pro Leu Arg Leu
        355                 360                 365

Arg Ser Met Tyr Gly Ala His Lys Tyr Gln Ala Glu Phe Pro Met Ser
    370                 375                 380

Pro Val Thr Ser Ala His Ala Gly Thr Tyr Arg Cys Tyr Gly Ser Tyr
385                 390                 395                 400

Ser Ser Asn Pro His Leu Leu Ser Phe Pro Ser Glu Pro Leu Glu Leu
                405                 410                 415

Met Val Ser Gly His Ser Gly Gly Ser Ser Leu Pro Pro Thr Gly Pro
            420                 425                 430

Pro Ser Thr Pro Ala Ser His Ala Lys Asp Tyr Thr Val Glu Asn Leu
        435                 440                 445

Ile Arg Met Gly Met Ala Gly Leu Val Leu Val Phe Leu Gly Ile Leu
```

450 455 460

Leu Phe Glu Ala Gln His Ser Gln Arg Asn Pro Gln Asp Ala Ala Gly
465 470 475 480

Arg

<210> 325
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 325
Met Asp Val Gln Leu Gln Glu Ser Gly Gly Gly Ser Val Gln Ala Gly
1 5 10 15

Gly Ser Leu Arg Leu Ser Cys Pro Ala Ser Gly Tyr Thr Phe Ser His
20 25 30

Tyr Cys Met Gly Trp Asn Arg Gln Ala Pro Gly Lys Glu Arg Glu Glu
35 40 45

Val Ala Thr Ile Asp Thr Asp Asp Thr Pro Thr Tyr Ala Asp Ser Val
50 55 60

Met Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Asn Asn Ala Leu Tyr
65 70 75 80

Leu Gln Met Asn Asp Leu Lys Pro Glu Asp Thr Ser Met Tyr Tyr Cys
85 90 95

Ala Ile Trp Met Lys Leu Arg Gly Ser Cys His Asp Arg Arg Leu Glu
100 105 110

Val Arg Gly Gln Gly Thr Gln Val Thr Val Ser Ile Asn
115 120 125

<210> 326
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 326
Gly Tyr Thr Phe Ser His Tyr Cys Met
1 5

<210> 327
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 327
Thr Ile Asp Thr Asp Asp Thr Pro Thr
1 5

<210> 328
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 328
Ala Ile Trp Met Lys Leu Arg Gly Ser Cys His Asp Arg Arg Leu Glu
1 5 10 15

<210> 329
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 329
Met Asp Val Gln Leu Gln Glu Ser Gly Gly Gly Ser Val Gln Ala Gly
1   5   10   15

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr His Ser Ser
            20   25   30

Tyr Cys Met Ala Trp Phe Arg Gln Ala Pro Gly Arg Glu Arg Glu Gly
        35   40   45

Val Ala Ser Ile Asp Ser Asp Gly Thr Thr Ser Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Gln Asp Asn Ala Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Met Tyr Tyr Cys
                85   90   95

Ala Ala Arg Phe Gly Pro Met Gly Cys Val Asp Leu Ser Thr Leu Ser
            100   105   110

Phe Gly His Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ile Thr
        115   120   125

<210> 330
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 330
Gly Tyr Thr His Ser Ser Tyr Cys Met
1   5

<210> 331
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 331
Ser Ile Asp Ser Asp Gly Thr Thr Ser
1 5

<210> 332
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 332
Ala Ala Arg Phe Gly Pro Met Gly Cys Val Asp Leu Ser Thr Leu Ser
1 5 10 15

Phe Gly His

<210> 333
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 333
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

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Thr Phe Ile Ser Tyr Asp Gly Asn 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 Ile Tyr Tyr Cys
                85                  90                  95


Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210> 334
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 334
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Ser
            20                  25                  30


Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45


Ile Tyr Gly Ala Phe Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95


Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
```

100 105

<210> 335
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 335
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 336
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 336
Ser Tyr Asp Gly Asn Asn
1 5

<210> 337
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 337
Thr Gly Trp Leu Gly Pro Phe Asp Tyr
1 5

<210> 338
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 338
Gln Ser Val Gly Ser Ser Tyr Leu Ala
1 5

<210> 339
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 339
Gly Ala Phe Ser Arg Ala Thr
1 5

<210> 340
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 340
Gln Gln Tyr Gly Ser Ser Pro Trp Thr
1 5

<210> 341
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 341
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 Asp Pro Arg Gly Ala Thr Leu Tyr Tyr Tyr Tyr Tyr Gly Met
            100                 105                 110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
    130                 135                 140

Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys
        195                 200                 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu
    210                 215                 220

Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala
225                 230                 235                 240
```

```
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445
```

Pro Gly Lys
450

<210> 342
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 342
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 Asn Ser Tyr
20 25 30

Leu Asp 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 Tyr Tyr Ser Thr Pro Phe
85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 343
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 343
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 344
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 344
Trp Tyr Asp Gly Ser Asn
1 5

<210> 345
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 345
Asp Pro Arg Gly Ala Thr Leu Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 346
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 346
Gln Ser Ile Asn Ser Tyr Leu Asp
1 5

<210> 347
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 347
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 348
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 348
Gln Gln Tyr Tyr Ser Thr Pro Phe Thr
1 5

<210> 349

<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 349
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Ser Val Gln Ala Gly Glu
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Ile Phe Ser Ser Asn
20 25 30

Ala Met Ala Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Asp Leu Val
35 40 45

Ala Gly Ile Asn Ser Val Gly Ile Thr Lys Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr
85 90 95

Ser Asp Pro Arg Arg Gly Trp Asp Thr Arg Tyr Trp Gly Gln Gly Thr
100 105 110

Gln Val Thr Val Ser Ser
115

<210> 350
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 350
Gly Ser Ile Phe Ser Ser Asn Ala Met Ala

1 5 10

<210> 351
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 351
Ala Ile Asn Ser Val Gly Val Thr Lys
1 5

<210> 352
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 352
Asp Pro Arg Arg Gly Trp Asp Thr Arg Tyr
1 5 10

<210> 353
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 353
Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
1 5 10 15

Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Ile Phe Ser Ser Thr Ala
20 25 30

Met Ala Trp Tyr Arg Gln Ala Pro Gly Lys Arg Arg Asp Leu Val Ala
35 40 45

Ala Ile Ser Ser Val Gly Val Thr Lys Tyr Ala Asp Ser Val Lys Gly
    50   55   60

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr Leu Gln
65   70   75   80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ser
                85   90   95

Asp Pro Arg Arg Gly Trp Asp Thr Arg Tyr Trp Gly Gln Gly Thr Leu
            100   105   110

Val Thr Val Ser Ser
        115

<210> 354
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 354
Gly Ser Ile Phe Ser Ser Thr Ala Met Ala
1   5   10

<210> 355
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 355
Gln Asn Asp Tyr Ser Tyr Pro Tyr Thr
1   5

<210> 356
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 356
Ala Ile Ser Ser Val Gly Val Thr Lys
1 5

<210> 357
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 357
Asp Pro Arg Arg Gly Trp Asp Thr Arg Tyr
1 5 10

<210> 358
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 358
Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Phe Gly Phe Thr Phe Ser Arg Tyr
20 25 30

Gly Met Ser Trp Val Arg Gln Thr Pro Asp Lys Arg Leu Glu Trp Val
35 40 45

Ala Thr Ile Thr Ser Gly Gly Ile Tyr Thr Tyr Tyr Pro 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 Ser Ser Leu Lys Ser Glu Glu Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg His Gly Gln Phe Gly Asp Tyr Tyr Gly Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 359
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 359
Asp Val Val 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 Leu Leu His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu His 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 Phe Cys Ser Gln Ser
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 360
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 360
Gly Phe Thr Phe Ser Arg Tyr Gly Met Ser
1 5 10

<210> 361
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 361
Thr Ile Thr Ser Gly Gly Ile Tyr Thr Tyr Tyr Pro Asp Ser Val Lys
1 5 10 15

Gly

<210> 362
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 362
His Gly Gln Phe Gly Asp Tyr Tyr Gly Met Asp Tyr
1 5 10

<210> 363
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 363
Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Asn Thr Tyr Leu His
1 5 10 15

<210> 364
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 364
Lys Val Ser Asn Arg Phe Ser
1 5

<210> 365
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 365
Ser Gln Ser Thr His Val Pro Tyr Thr
1 5

<210> 366
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 366
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 His Tyr

20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

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

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Arg Tyr Glu Gly Asn Tyr Val Phe Tyr Tyr Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 367
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 367
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 Glu Asn Ile Tyr Ser Tyr
20 25 30

Phe Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Thr Ala Lys Thr Leu Ala Glu 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 His His Tyr Val Thr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 368
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 368
Gly Tyr Thr Phe Thr His Tyr Gly
1 5

<210> 369
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 369
Asn Thr Tyr Thr Gly Glu Pro
1 5

<210> 370
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 370
Ala Arg Arg Arg Tyr Glu Gly Asn Tyr Val Phe Tyr Tyr Phe Asp Tyr

1 5 10 15

<210> 371
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 371
Arg Ala Ser Glu Asn Ile Tyr Ser Tyr Phe Ser
1 5 10

<210> 372
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 372
Thr Ala Lys Thr Leu Ala Glu
1 5

<210> 373
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 373
Gln His His Tyr Val Thr Pro Tyr Thr
1 5

<210> 374
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

polypeptide

<400> 374
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 Ala Ser Gly Phe Thr Phe Ser Ser
20 25 30

Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp
35 40 45

Val Ser Thr Ile Ser Gly Gly Gly Thr Tyr Thr Tyr Tyr Gln Asp Ser
50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Ser Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
100 105 110

Ser Ala

<210> 375
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 375
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 Arg Arg Tyr
20 25 30

```
Leu Asn Trp Tyr His Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Gly Ala Ser Thr 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 Val Tyr Tyr Cys Gln Gln Ser His Ser Ala Pro Leu
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 376
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 376
Ser Gly Phe Thr Phe Ser Ser Tyr Asp
1               5


<210> 377
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 377
Ser Gly Gly Gly Thr Tyr Thr
1               5


<210> 378
<211> 5
<212> PRT
```

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 378
Ala Ser Met Asp Tyr
1 5

<210> 379
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 379
Arg Ala Ser Gln Ser Ile Arg Arg Tyr Leu Asn
1 5 10

<210> 380
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 380
Gly Ala Ser Thr Leu Gln Ser
1 5

<210> 381
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 381
Gln Gln Ser His Ser Ala Pro Leu Thr
1 5

<210> 382
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 382
Gln Val Gln Leu Gln Gln Pro Gly Ala 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

Asn Met His Trp Ile Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asp Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Val Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Val Thr Val Ser Ser
115

<210> 383
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 383
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
            20   25   30

Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35   40   45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Ala
    50   55   60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65   70   75   80

Pro Val Glu Glu Asp Asp Ile Ala Ile Tyr Phe Cys Gln Gln Ser Arg
                85   90   95

Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100   105   110

<210> 384
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 384
Ser Tyr Asn Met His
1   5

<210> 385
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 385
Asp Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 386
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 386
Val Gly Gly Ala Phe Pro Met Asp Tyr
1 5

<210> 387
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 387
Arg Ala Ser Glu Ser Val Glu Tyr Tyr Gly Thr Ser Leu Met Gln
1 5 10 15

<210> 388
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 388
Ala Ala Ser Asn Val Glu Ser
1 5

<210> 389

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 389
Gln Gln Ser Arg Lys Asp Pro Ser Thr
1 5

<210> 390
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 390
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 Gly Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Arg Ser Gly Tyr Thr Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Thr Thr Leu 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 Pro Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
100 105 110

Ser Ser

<210> 391
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 391
Asp Ile Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 392
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 392
Gly Tyr Thr Phe Thr Gly Tyr Thr
1 5

<210> 393
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 393
Asn Pro Arg Ser Gly Tyr Thr
1 5

<210> 394
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 394
Ala Arg Pro Trp Phe Ala Tyr
1 5

<210> 395
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 395
Lys Ser Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
1 5 10 15

Thr

<210> 396
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 396
Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 397
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 397
Gln Asn Asp Tyr Ser Tyr Pro Leu Thr
1 5

<210> 398
<211> 136
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 398
Met Asn Phe Gly Leu Ser Leu Ile Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys
20 25 30

Ser Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ile Phe
35 40 45

Ser Ser Phe Gly Met Ser Trp Val Arg Gln Thr Pro Asp Lys Arg Leu

50 55 60

Glu Trp Val Ala Thr Ile Ser Ser Gly Gly Arg Asn Ile Tyr Tyr Leu
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Val Lys Asn
85 90 95

Ile Leu Tyr Leu Gln Met Ser Gly Leu Lys Ser Glu Asp Ser Ala Met
100 105 110

Tyr Tyr Cys Ala Arg Glu Gly His Tyr Ala Leu Asp Tyr Cys Gly Gln
115 120 125

Gly Thr Ser Val Thr Val Ser Ser
130 135

<210> 399
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 399
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Thr Ser Val Gly
1 5 10 15

Gln Arg Val Thr Met Ser Cys Lys Ser Ser Gln Asn Leu Leu Tyr Ser
20 25 30

Thr Asp Gln Lys Asn Tyr Leu Ala Trp Phe Gln Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Leu Tyr Phe Ala Ser Ile Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln
85 90 95

His Tyr Asn Thr Pro Pro Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile
100 105 110

Lys

<210> 400
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 400
Ser Phe Gly Met Ser
1 5

<210> 401
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 401
Thr Ile Ser Ser Gly Gly Arg Asn Ile Tyr Tyr Leu Asp Ser Val Lys
1 5 10 15

Gly

<210> 402
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 402
Glu Gly His Tyr Ala Leu Asp Tyr
1 5

<210> 403
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 403
Lys Ser Ser Gln Asn Leu Leu Tyr Ser Thr Asp Gln Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 404
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 404
Phe Ala Ser Ile Arg Glu Ser
1 5

<210> 405
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 405
Gln Gln His Tyr Asn Thr Pro Pro Thr
1 5

<210> 406
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 406
Glu Val Gln Leu Val Gln Ser Gly Ser Asp Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Pro Met Asn Trp Val Arg Gln Ala Pro Gly His Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Val Gln Gly Phe
50 55 60

Thr Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Asn Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Thr Gly Gly His Thr Tyr Asp Ser Tyr Ala Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 407
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 407
Asp Ile Gln Leu Thr Gln Ser Pro Thr Phe Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Val Ile Ser Ser Ser
            20   25   30

Leu Ala Trp Tyr Gln Gln Asn Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

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

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Val Thr Tyr Tyr Cys Gln His Leu His Gly Tyr Pro Ser
                85   90   95

Asn Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 408
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 408
Ser Tyr Pro Met Asn
1   5

<210> 409
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 409
Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Val Gln Gly Phe Thr
1   5   10   15

Gly

<210> 410
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 410
Thr Gly Gly His Thr Tyr Asp Ser Tyr Ala Phe Asp Val
1   5   10

<210> 411
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 411
Arg Ala Ser Gln Val Ile Ser Ser Ser Leu Ala
1   5   10

<210> 412
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 412
Ala Ala Ser Thr Leu Gln Ser
1   5

<210> 413

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 413
Gln His Leu His Gly Tyr Pro Ser Asn
1 5

<210> 414
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 414
Asp Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Tyr Ala Trp Asn Trp Val Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45

Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Arg Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Arg Gln Val Gly Leu Gly Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser

115

<210> 415
<211> 99
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 415
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

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

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly

<210> 416
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 416
Thr Ser Asp Tyr Ala Trp Asn

1 5

<210> 417
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 417
Tyr Ile Ser Tyr Ser Gly Ser Thr Ser Tyr Asn Pro Ser Leu Arg Ser
1 5 10 15

<210> 418
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 418
Ala Arg Arg Gln Val Gly Leu Gly Phe Ala Tyr
1 5 10

<210> 419
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 419
Lys Ala Ser Gln Asp Val Ser Thr Ala Val Ala
1 5 10

<210> 420
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 420
Ser Ala Ser Tyr Arg Tyr Thr
1 5

<210> 421
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 421
Gln Gln His Tyr Ser Thr Pro
1 5

<210> 422
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 422
Glu 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 Asp Ser
20 25 30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asp Met Tyr Pro Asp Asn Gly Asp Ser Ser Tyr Asn Gln Lys Phe
50 55 60

Arg Glu Arg Val Thr Ile Thr Arg Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

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                85                  90                  95

Val Leu Ala Pro Arg Trp Tyr Phe Ser Val Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
```

290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 423
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 423
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 Asp Ile Ser Asn Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu Arg 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 Gly His Thr Leu Pro Pro
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
```

<210> 424
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 424
Gly Tyr Thr Phe Thr Asp Ser Tyr
1 5

<210> 425
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 425
Asp Asn Gly Asp Ser
1 5

<210> 426
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 426
Val Leu Ala Pro Arg Trp Tyr Phe Ser Val
1 5 10

<210> 427
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 427
Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 428
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 428
Thr Ser Arg Leu Arg Ser
1 5

<210> 429
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 429
Gln Gln Gly His Thr Leu Pro Pro Thr
1 5

<210> 430
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 430
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 Ala Val Tyr Gly Gly Ser Phe Ser Ser Gly
20 25 30

Tyr Trp Asn Trp Ile Arg Lys His Pro Gly Lys Gly Leu Glu Tyr Ile

```
        35                  40                  45

Gly Tyr Ile Ser Tyr Asn Gly Ile Thr Tyr His Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Ile Thr Ile Asn Arg Asp Thr Ser Lys Asn Gln Tyr Ser Leu
65                  70                  75                  80

Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Tyr Lys Tyr Asp Tyr Asp Gly Gly His Ala Met Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
```

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                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
```

450

<210> 431
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 431
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 Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Lys Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Ser Ala Leu Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 432
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 432
Gly Gly Ser Phe Ser Ser Gly Tyr
1 5

<210> 433
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 433
Ser Tyr Asn Gly Ile Thr Tyr His
1 5

<210> 434
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 434
Ala Arg Tyr Lys Tyr Asp Tyr Asp Gly Gly His Ala Met Asp Tyr
1 5 10 15

<210> 435
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 435
Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 436
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 436
Thr Ser Lys Leu His
1 5

<210> 437
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 437
Gln Gln Gly Ser Ala Leu Pro Trp Thr
1 5

<210> 438
<211> 446
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 438

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Gln Ile Gln Leu Gln Gln Ser Gly Pro Glu Val Val Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Tyr Ile Thr Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Trp Ile Tyr Pro Gly Ser Gly Asn Thr Lys Tyr Asn Glu Lys Phe
    50                  55                  60

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

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95

Ala Asn Tyr Gly Asn Tyr Trp Phe Ala Tyr Trp Gly Gln Gly Thr Gln
            100                 105                 110

Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
```

```
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
```

385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

<210> 439
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 439
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Phe Asp
20 25 30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Val Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

```
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125


Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140


Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160


Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175


Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190


His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 440
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 440
Gly Tyr Thr Phe Thr Asp Tyr Tyr
1               5


<210> 441
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide
```

<400> 441
Tyr Pro Gly Ser Gly Asn Thr
1 5

<210> 442
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 442
Ala Asn Tyr Gly Asn Tyr Trp Phe Ala Tyr
1 5 10

<210> 443
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 443
Lys Ala Ser Gln Ser Val Asp Phe Asp Gly Asp Ser Tyr Met Asn
1 5 10 15

<210> 444
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 444
Ala Ala Ser Asn Leu Glu Ser
1 5

<210> 445
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 445
Gln Gln Ser Asn Glu Asp Pro Trp Thr
1 5

<210> 446
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 446
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 Asp Tyr
20 25 30

Tyr Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Tyr Pro Gly Ser Gly Asn Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Val 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 Phe Cys
85 90 95

Ala Asn Tyr Gly Asn Tyr Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 447

<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 447
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ala Ser Gln Ser Val Asp Phe Asp
20 25 30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 448
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 448
Gly Tyr Thr Phe Thr Asp Tyr Tyr
1 5

<210> 449

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 449
Tyr Pro Gly Ser Gly Asn Thr
1 5

<210> 450
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 450
Ala Asn Tyr Gly Asn Tyr Trp Phe Ala Tyr
1 5 10

<210> 451
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 451
Lys Ala Ser Gln Ser Val Asp Phe Asp Gly Asp Ser Tyr Met Asn
1 5 10 15

<210> 452
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 452
Ala Ala Ser Asn Leu Glu Ser

1 5

<210> 453
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 453
Gln Gln Ser Asn Glu Asp Pro Trp Thr
1 5

<210> 454
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 454
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 Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn His Gly Gly Tyr Val Thr Tyr Asn Pro Ser Leu Glu
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 Asp Tyr Gly Pro Gly Asn Tyr Asp Trp Tyr Phe Asp Leu Trp Gly

```
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
    210                 215                 220

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
            260                 265                 270

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
```

305 310 315 320

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
405 410 415

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<210> 455
<211> 216
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 455
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

```
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro
                85                  90                  95

Ala Leu Thr Phe Cys Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val
            100                 105                 110

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
        115                 120                 125

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
    130                 135                 140

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
145                 150                 155                 160

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
                165                 170                 175

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
            180                 185                 190

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
        195                 200                 205

Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 456
<211> 8
<212> PRT
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<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 456
Gly Gly Ser Phe Ser Gly Tyr Tyr
1 5

<210> 457
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 457
Asn His Gly Gly Tyr Val
1 5

<210> 458
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 458
Ala Arg Asp Tyr Gly Pro Gly Asn Tyr Asp Trp Tyr Phe Asp Leu
1 5 10 15

<210> 459
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 459
Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 460
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 460
Asp Ala Ser Asn Arg Ala Thr Gly Ile
1 5

<210> 461
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 461
Gln Gln Arg Ser Asn Trp Pro Pro Ala Leu Thr
1 5 10

<210> 462
<211> 442
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 462
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Ser Thr Tyr
20 25 30

Trp Ile Ser Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Lys Ile Tyr Pro Gly Asp Ser Tyr Thr Asn 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 Gly Tyr Gly Ile Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe
            180                 185                 190

Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro
225                 230                 235                 240

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
                245                 250                 255

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp
```

260 265 270

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
275 280 285

Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val
290 295 300

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
305 310 315 320

Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly
325 330 335

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
340 345 350

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
355 360 365

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
370 375 380

Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe
385 390 395 400

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
405 410 415

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
420 425 430

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> 463
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 463

```
Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1               5                  10                  15

Thr Ala Ser Ile Thr Cys Ser Gly Asp Asn Ile Gly Asp Gln Tyr Ala
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Val Leu Val Ile Tyr
        35                  40                  45

Gln Asp Lys Asn Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Tyr Thr Gly Phe Gly Ser Leu
                85                  90                  95

Ala Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys
            100                 105                 110

Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln
        115                 120                 125

Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly
    130                 135                 140

Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly
145                 150                 155                 160

Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala
                165                 170                 175

Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser
            180                 185                 190
```

Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val
195 200 205

Ala Pro Thr Glu Cys Ser
210

<210> 464
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 464
Gly Tyr Ser Phe Ser Thr Tyr Trp
1 5

<210> 465
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 465
Tyr Pro Gly Asp Ser Tyr Thr
1 5

<210> 466
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 466
Ala Arg Gly Tyr Gly Ile Phe Asp Tyr
1 5

<210> 467

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 467
Ser Gly Asp Asn Ile Gly Asp Gln Tyr Ala His
1 5 10

<210> 468
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 468
Gln Asp Lys Asn Arg Pro Ser
1 5

<210> 469
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 469
Ala Thr Tyr Thr Gly Phe Gly Ser Leu Ala Val
1 5 10

<210> 470
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 470
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 Tyr 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 Arg 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 Leu Gly Tyr Gly Arg Val Asp Glu Trp Gly Arg Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
```

```
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
```

420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 471
<211> 216
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 471
Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Leu Ser Asn Ile Gly Arg Asn
20 25 30

Pro Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Leu Asp Asn Leu Arg Leu Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Asp Ser His
85 90 95

Pro Gly Trp Thr Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
115 120 125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130 135 140

```
Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145                 150                 155                 160


Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
                165                 170                 175


Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
            180                 185                 190


Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
        195                 200                 205


Thr Val Ala Pro Thr Glu Cys Ser
    210                 215


<210> 472
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 472
Gly Phe Thr Phe Ser Ser Tyr Ala
1               5


<210> 473
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 473
Ser Gly Ser Gly Gly Arg Thr
1               5


<210> 474
<211> 10
<212> PRT
```

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 474
Ala Arg Leu Gly Tyr Gly Arg Val Asp Glu
1 5 10

<210> 475
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 475
Ser Gly Ser Leu Ser Asn Ile Gly Arg Asn Pro Val Asn
1 5 10

<210> 476
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 476
Leu Asp Asn Leu Arg Leu Ser
1 5

<210> 477
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 477
Ala Thr Trp Asp Asp Ser His Pro Gly Trp Thr
1 5 10

<210> 478
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 478
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 Asn 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 Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro 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 Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 479
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 479
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Leu
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 480
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 480
Asn Tyr Gly Met His
1   5

<210> 481
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 481
Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val Lys
1   5   10   15

<210> 482
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 482
Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile
1   5   10

<210> 483
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 483
Arg Ala Ser Gln Gly Val Ser Ser Tyr Leu Ala
1   5   10

<210> 484
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 484
Asp Ala Ser Asn Arg Ala Thr
1   5

<210> 485
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 485
Gln Gln Arg Ser Asn Trp His Leu Thr
1 5

<210> 486
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 486
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

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser 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 Gly Ile Ala Ala Ala Gly Pro Pro Tyr Tyr Tyr Tyr Tyr Tyr
100 105 110

Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 487

<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 487
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 Thr Ile Tyr Asn 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 Gly Gly
50 55 60

Arg Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Ser Tyr Thr Ser Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105

<210> 488
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 488
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 489

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 489
Ser Tyr Asp Gly Ser Asn
1 5

<210> 490
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 490
Gly Ile Ala Ala Ala Gly Pro Pro Tyr Tyr Tyr Tyr Tyr Tyr Tyr Met
1 5 10 15

Asp Val

<210> 491
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 491
Gln Thr Ile Tyr Asn Tyr Leu Asn
1 5

<210> 492
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 492
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 493
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 493
Gln Gln Ser Tyr Thr Ser Pro Leu Thr
1 5

<210> 494
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 494
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

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Ser Ser Gly Gly Thr Thr Tyr Tyr Pro 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 Val Gly Gly Tyr Tyr Asp Ser Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 495
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<220>
<221> MOD_RES
<222> (31)..(31)
<223> Any amino acid

<220>
<221> MOD_RES
<222> (57)..(57)
<223> Any amino acid

<400> 495
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Xaa Tyr
20 25 30

Gly Val Ser Phe Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
35 40 45

Arg Leu Leu Ile Tyr Ala Ala Ser Xaa Gln Gly Ser Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Lys
85 90 95

Glu Val Thr Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

<210> 496
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 496
Gly Phe Thr Phe Ser Ser Tyr Ala
1 5

<210> 497
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 497
Ser Ser Gly Gly Thr Thr
1 5

<210> 498
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 498
Ala Arg Val Gly Gly Tyr Tyr Asp Ser Met Asp Tyr
1 5 10

<210> 499
<211> 15

<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<220>
<221> MOD_RES
<222> (8)..(8)
<223> Any amino acid

<400> 499
Arg Ala Ser Glu Ser Val Asp Xaa Tyr Gly Val Ser Phe Met Asn
1 5 10 15

<210> 500
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<220>
<221> MOD_RES
<222> (4)..(4)
<223> Any amino acid

<400> 500
Ala Ala Ser Xaa Gln Gly Ser
1 5

<210> 501
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 501
Gln Gln Thr Lys Glu Val Thr Trp Thr
1 5

<210> 502
<211> 473
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 502

```
Met Asp Tyr Thr Leu Asp Leu Ser Val Thr Thr Val Thr Asp Tyr Tyr
1               5                  10                  15

Tyr Pro Asp Ile Phe Ser Ser Pro Cys Asp Ala Glu Leu Ile Gln Thr
            20                  25                  30

Asn Gly Lys Leu Leu Leu Ala Val Phe Tyr Cys Leu Leu Phe Val Phe
        35                  40                  45

Ser Leu Leu Gly Asn Ser Leu Val Ile Leu Val Leu Val Val Cys Lys
    50                  55                  60

Lys Leu Arg Ser Ile Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ser
65                  70                  75                  80

Asp Leu Leu Phe Val Phe Ser Phe Pro Phe Gln Thr Tyr Tyr Leu Leu
                85                  90                  95

Asp Gln Trp Val Phe Gly Thr Val Met Cys Lys Val Val Ser Gly Phe
            100                 105                 110

Tyr Tyr Ile Gly Phe Tyr Ser Ser Met Phe Phe Ile Thr Leu Met Ser
        115                 120                 125

Val Asp Arg Tyr Leu Ala Val Val His Ala Val Tyr Ala Leu Lys Val
    130                 135                 140

Arg Thr Ile Arg Met Gly Thr Thr Leu Cys Leu Ala Val Trp Leu Thr
145                 150                 155                 160

Ala Ile Met Ala Thr Ile Pro Leu Leu Val Phe Tyr Gln Val Ala Ser
                165                 170                 175
```

```
Glu Asp Gly Val Leu Gln Cys Tyr Ser Phe Tyr Asn Gln Gln Thr Leu
            180                 185                 190

Lys Trp Lys Ile Phe Thr Asn Phe Lys Met Asn Ile Leu Gly Leu Leu
        195                 200                 205

Ile Pro Phe Thr Ile Phe Met Phe Cys Tyr Ile Lys Ile Leu His Gln
    210                 215                 220

Leu Lys Arg Cys Gln Asn His Asn Lys Thr Lys Ala Ile Arg Leu Val
225                 230                 235                 240

Leu Ile Val Val Ile Ala Ser Leu Leu Phe Trp Val Pro Phe Asn Val
                245                 250                 255

Val Leu Phe Leu Thr Ser Leu His Ser Met His Ile Leu Asp Gly Cys
            260                 265                 270

Ser Ile Ser Gln Gln Leu Thr Tyr Ala Thr His Val Thr Glu Ile Ile
        275                 280                 285

Ser Phe Thr His Cys Cys Val Asn Pro Val Ile Tyr Ala Phe Val Gly
    290                 295                 300

Glu Lys Phe Lys Lys His Leu Ser Glu Ile Phe Gln Lys Ser Cys Ser
305                 310                 315                 320

Gln Ile Phe Asn Tyr Leu Gly Arg Gln Met Pro Arg Glu Ser Cys Glu
                325                 330                 335

Lys Ser Ser Ser Cys Gln Gln His Ser Ser Arg Ser Ser Ser Val Asp
            340                 345                 350

Tyr Ile Leu Leu Ile Leu Arg His Arg Arg Gln Gly Lys His Trp Thr
        355                 360                 365

Ser Thr Gln Arg Lys Ala Asp Phe Gln His Pro Ala Gly Ala Val Gly
    370                 375                 380
```

```
Pro Glu Pro Thr Asp Arg Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala
385                 390                 395                 400


Asp Ala Gln Glu Glu Asn Leu Tyr Ala Ala Val Lys Asp Thr Gln Pro
                405                 410                 415


Glu Asp Gly Val Glu Met Asp Thr Arg Ala Ala Ala Ser Glu Ala Pro
            420                 425                 430


Gln Asp Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Lys
        435                 440                 445


Ala Thr Glu Pro Pro Pro Ser Gln Glu Arg Glu Pro Pro Ala Glu Pro
    450                 455                 460


Ser Ile Tyr Ala Thr Leu Ala Ile His
465                 470


<210> 503
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 503
Met Ala Gly Pro Pro Arg Leu Leu Leu Leu Pro Leu Leu Leu Ala Leu
1               5                   10                  15


Ala Arg Gly Leu Pro Gly Ala Leu Ala Ala Gln Glu Val Gln Gln Ser
            20                  25                  30


Pro His Cys Thr Thr Val Pro Val Gly Ala Ser Val Asn Ile Thr Cys
        35                  40                  45


Ser Thr Ser Gly Gly Leu Arg Gly Ile Tyr Leu Arg Gln Leu Gly Pro
    50                  55                  60
```

```
Gln Pro Gln Asp Ile Ile Tyr Tyr Glu Asp Gly Val Val Pro Thr Thr
65                  70                  75                  80


Asp Arg Arg Phe Arg Gly Arg Ile Asp Phe Ser Gly Ser Gln Asp Asn
                85                  90                  95


Leu Thr Ile Thr Met His Arg Leu Gln Leu Ser Asp Thr Gly Thr Tyr
            100                 105                 110


Thr Cys Gln Ala Ile Thr Glu Val Asn Val Tyr Gly Ser Gly Thr Leu
        115                 120                 125


Val Leu Val Thr Glu Glu Gln Ser Gln Gly Trp His Arg Cys Ser Asp
    130                 135                 140


Ala Pro Pro Arg Ala Ser Ala Leu Pro Ala Pro Pro Thr Gly Ser Ala
145                 150                 155                 160


Leu Pro Asp Pro Gln Thr Ala Ser Ala Leu Pro Asp Pro Pro Ala Ala
                165                 170                 175


Ser Ala Leu Pro Ala Ala Leu Ala Val Ile Ser Phe Leu Leu Gly Leu
            180                 185                 190


Gly Leu Gly Val Ala Cys Val Leu Ala Arg Thr Gln Ile Lys Lys Leu
        195                 200                 205


Cys Ser Trp Arg Asp Lys Asn Ser Ala Ala Cys Val Val Tyr Glu Asp
    210                 215                 220


Met Ser His Ser Arg Cys Asn Thr Leu Ser Ser Pro Asn Gln Tyr Gln
225                 230                 235                 240


<210> 504
<211> 223
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide
```

<400> 504
Met Ala Cys Leu Gly Phe Gln Arg His Lys Ala Gln Leu Asn Leu Ala
1   5   10   15

Thr Arg Thr Trp Pro Cys Thr Leu Leu Phe Phe Leu Leu Phe Ile Pro
            20   25   30

Val Phe Cys Lys Ala Met His Val Ala Gln Pro Ala Val Val Leu Ala
        35   40   45

Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly
    50   55   60

Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln
65   70   75   80

Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr
                85   90   95

Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val
            100   105   110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile
        115   120   125

Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly
    130   135   140

Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser
145   150   155   160

Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe
                165   170   175

Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys
            180   185   190

Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu
        195   200   205

```
Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn
    210                 215                 220


<210> 505
<211> 387
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 505
Met Arg Glu Pro Leu Glu Ala Phe Lys Leu Ala Asp Leu Asp Phe Arg
1               5                   10                  15


Lys Ser Ser Leu Ala Ser Gly Trp Arg Met Ala Ser Gly Ala Phe Thr
            20                  25                  30


Met Asp Gln Phe Pro Glu Ser Val Thr Glu Asn Phe Glu Tyr Asp Asp
        35                  40                  45


Leu Ala Glu Ala Cys Tyr Ile Gly Asp Ile Val Val Phe Gly Thr Val
    50                  55                  60


Phe Leu Ser Ile Phe Tyr Ser Val Ile Phe Ala Ile Gly Leu Val Gly
65                  70                  75                  80


Asn Leu Leu Val Val Phe Ala Leu Thr Asn Ser Lys Lys Pro Lys Ser
                85                  90                  95


Val Thr Asp Ile Tyr Leu Leu Asn Leu Ala Leu Ser Asp Leu Leu Phe
            100                 105                 110


Val Ala Thr Leu Pro Phe Trp Thr His Tyr Leu Ile Asn Glu Lys Gly
        115                 120                 125


Leu His Asn Ala Met Cys Lys Phe Thr Thr Ala Phe Phe Phe Ile Gly
    130                 135                 140
```

```
Phe Phe Gly Ser Ile Phe Phe Ile Thr Val Ile Ser Ile Asp Arg Tyr
145                 150                 155                 160

Leu Ala Ile Val Leu Ala Ala Asn Ser Met Asn Asn Arg Thr Val Gln
                165                 170                 175

His Gly Val Thr Ile Ser Leu Gly Val Trp Ala Ala Ala Ile Leu Val
            180                 185                 190

Ala Ala Pro Gln Phe Met Phe Thr Lys Gln Lys Glu Asn Glu Cys Leu
        195                 200                 205

Gly Asp Tyr Pro Glu Val Leu Gln Glu Ile Trp Pro Val Leu Arg Asn
    210                 215                 220

Val Glu Thr Asn Phe Leu Gly Phe Leu Leu Pro Leu Leu Ile Met Ser
225                 230                 235                 240

Tyr Cys Tyr Phe Arg Ile Ile Gln Thr Leu Phe Ser Cys Lys Asn His
                245                 250                 255

Lys Lys Ala Lys Ala Ile Lys Leu Ile Leu Leu Val Val Ile Val Phe
            260                 265                 270

Phe Leu Phe Trp Thr Pro Tyr Asn Val Met Ile Phe Leu Glu Thr Leu
        275                 280                 285

Lys Leu Tyr Asp Phe Phe Pro Ser Cys Asp Met Arg Lys Asp Leu Arg
    290                 295                 300

Leu Ala Leu Ser Val Thr Glu Thr Val Ala Phe Ser His Cys Cys Leu
305                 310                 315                 320

Asn Pro Leu Ile Tyr Ala Phe Ala Gly Glu Lys Phe Arg Arg Tyr Leu
                325                 330                 335

Tyr His Leu Tyr Gly Lys Cys Leu Ala Val Leu Cys Gly Arg Ser Val
            340                 345                 350
```

His Val Asp Phe Ser Ser Ser Glu Ser Gln Arg Ser Arg His Gly Ser
        355   360   365

Val Leu Ser Ser Asn Phe Thr Tyr His Thr Ser Asp Gly Asp Ala Leu
    370   375   380

Leu Leu Leu
385

<210> 506
<211> 522
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 506
Met Gly Arg Glu Glu Leu Phe Leu Thr Phe Ser Phe Ser Ser Gly Phe
1   5   10   15

Gln Glu Ser Asn Val Lys Thr Phe Cys Ser Lys Asn Ile Leu Ala Ile
            20   25   30

Leu Gly Phe Ser Ser Ile Ile Ala Val Ile Ala Leu Leu Ala Val Gly
        35   40   45

Leu Thr Gln Asn Lys Ala Leu Pro Glu Asn Val Lys Tyr Gly Ile Val
    50   55   60

Leu Asp Ala Gly Ser Ser His Thr Ser Leu Tyr Ile Tyr Lys Trp Pro
65   70   75   80

Ala Glu Lys Glu Asn Asp Thr Gly Val Val His Gln Val Glu Glu Cys
                85   90   95

Arg Val Lys Gly Pro Gly Ile Ser Lys Phe Val Gln Lys Val Asn Glu
            100   105   110

Ile Gly Ile Tyr Leu Thr Asp Cys Met Glu Arg Ala Arg Glu Val Ile
        115   120   125

```
Pro Arg Ser Gln His Gln Glu Thr Pro Val Tyr Leu Gly Ala Thr Ala
    130                 135                 140

Gly Met Arg Leu Leu Arg Met Glu Ser Glu Glu Leu Ala Asp Arg Val
145                 150                 155                 160

Leu Asp Val Val Glu Arg Ser Leu Ser Asn Tyr Pro Phe Asp Phe Gln
                165                 170                 175

Gly Ala Arg Ile Ile Thr Gly Gln Glu Glu Gly Ala Tyr Gly Trp Ile
            180                 185                 190

Thr Ile Asn Tyr Leu Leu Gly Lys Phe Ser Gln Lys Thr Arg Trp Phe
        195                 200                 205

Ser Ile Val Pro Tyr Glu Thr Asn Asn Gln Glu Thr Phe Gly Ala Leu
    210                 215                 220

Asp Leu Gly Gly Ala Ser Thr Gln Val Thr Phe Val Pro Gln Asn Gln
225                 230                 235                 240

Thr Ile Glu Ser Pro Asp Asn Ala Leu Gln Phe Arg Leu Tyr Gly Lys
                245                 250                 255

Asp Tyr Asn Val Tyr Thr His Ser Phe Leu Cys Tyr Gly Lys Asp Gln
            260                 265                 270

Ala Leu Trp Gln Lys Leu Ala Lys Asp Ile Gln Val Ala Ser Asn Glu
        275                 280                 285

Ile Leu Arg Asp Pro Cys Phe His Pro Gly Tyr Lys Lys Val Val Asn
    290                 295                 300

Val Ser Asp Leu Tyr Lys Thr Pro Cys Thr Lys Arg Phe Glu Met Thr
305                 310                 315                 320

Leu Pro Phe Gln Gln Phe Glu Ile Gln Gly Ile Gly Asn Tyr Gln Gln
                325                 330                 335
```

```
Cys His Gln Ser Ile Leu Glu Leu Phe Asn Thr Ser Tyr Cys Pro Tyr
            340                 345                 350

Ser Gln Cys Ala Phe Asn Gly Ile Phe Leu Pro Pro Leu Gln Gly Asp
        355                 360                 365

Phe Gly Ala Phe Ser Ala Phe Tyr Phe Val Met Lys Phe Leu Asn Leu
    370                 375                 380

Thr Ser Glu Lys Val Ser Gln Glu Lys Val Thr Glu Met Met Lys Lys
385                 390                 395                 400

Phe Cys Ala Gln Pro Trp Glu Glu Ile Lys Thr Ser Tyr Ala Gly Val
                405                 410                 415

Lys Glu Lys Tyr Leu Ser Glu Tyr Cys Phe Ser Gly Thr Tyr Ile Leu
            420                 425                 430

Ser Leu Leu Leu Gln Gly Tyr His Phe Thr Ala Asp Ser Trp Glu His
        435                 440                 445

Ile His Phe Ile Gly Lys Ile Gln Gly Ser Asp Ala Gly Trp Thr Leu
    450                 455                 460

Gly Tyr Met Leu Asn Leu Thr Asn Met Ile Pro Ala Glu Gln Pro Leu
465                 470                 475                 480

Ser Thr Pro Leu Ser His Ser Thr Tyr Val Phe Leu Met Val Leu Phe
                485                 490                 495

Ser Leu Val Leu Phe Thr Val Ala Ile Ile Gly Leu Leu Ile Phe His
            500                 505                 510

Lys Pro Ser Tyr Phe Trp Lys Asp Met Val
        515                 520
```

<210> 507
<211> 301

<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 507

```
Met Phe Ser His Leu Pro Phe Asp Cys Val Leu Leu Leu Leu Leu Leu
1               5                  10                  15

Leu Leu Thr Arg Ser Ser Glu Val Glu Tyr Arg Ala Glu Val Gly Gln
            20                  25                  30

Asn Ala Tyr Leu Pro Cys Phe Tyr Thr Pro Ala Ala Pro Gly Asn Leu
        35                  40                  45

Val Pro Val Cys Trp Gly Lys Gly Ala Cys Pro Val Phe Glu Cys Gly
    50                  55                  60

Asn Val Val Leu Arg Thr Asp Glu Arg Asp Val Asn Tyr Trp Thr Ser
65                  70                  75                  80

Arg Tyr Trp Leu Asn Gly Asp Phe Arg Lys Gly Asp Val Ser Leu Thr
                85                  90                  95

Ile Glu Asn Val Thr Leu Ala Asp Ser Gly Ile Tyr Cys Cys Arg Ile
            100                 105                 110

Gln Ile Pro Gly Ile Met Asn Asp Glu Lys Phe Asn Leu Lys Leu Val
        115                 120                 125

Ile Lys Pro Ala Lys Val Thr Pro Ala Pro Thr Arg Gln Arg Asp Phe
    130                 135                 140

Thr Ala Ala Phe Pro Arg Met Leu Thr Thr Arg Gly His Gly Pro Ala
145                 150                 155                 160

Glu Thr Gln Thr Leu Gly Ser Leu Pro Asp Ile Asn Leu Thr Gln Ile
                165                 170                 175
```

```
Ser Thr Leu Ala Asn Glu Leu Arg Asp Ser Arg Leu Ala Asn Asp Leu
            180                 185                 190


Arg Asp Ser Gly Ala Thr Ile Arg Ile Gly Ile Tyr Ile Gly Ala Gly
        195                 200                 205


Ile Cys Ala Gly Leu Ala Leu Ala Leu Ile Phe Gly Ala Leu Ile Phe
    210                 215                 220


Lys Trp Tyr Ser His Ser Lys Glu Lys Ile Gln Asn Leu Ser Leu Ile
225                 230                 235                 240


Ser Leu Ala Asn Leu Pro Pro Ser Gly Leu Ala Asn Ala Val Ala Glu
                245                 250                 255


Gly Ile Arg Ser Glu Glu Asn Ile Tyr Thr Ile Glu Glu Asn Val Tyr
            260                 265                 270


Glu Val Glu Glu Pro Asn Glu Tyr Tyr Cys Tyr Val Ser Ser Arg Gln
        275                 280                 285


Gln Pro Ser Gln Pro Leu Gly Cys Arg Phe Ala Met Pro
    290                 295                 300


<210> 508
<211> 398
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 508
Met Leu Arg Leu Tyr Val Leu Val Met Gly Val Ser Ala Phe Thr Leu
1               5                   10                  15


Gln Pro Ala Ala His Thr Gly Ala Ala Arg Ser Cys Arg Phe Arg Gly
            20                  25                  30


Arg His Tyr Lys Arg Glu Phe Arg Leu Glu Gly Glu Pro Val Ala Leu
        35                  40                  45
```

```
Arg Cys Pro Gln Val Pro Tyr Trp Leu Trp Ala Ser Val Ser Pro Arg
    50                  55                  60

Ile Asn Leu Thr Trp His Lys Asn Asp Ser Ala Arg Thr Val Pro Gly
65                  70                  75                  80

Glu Glu Glu Thr Arg Met Trp Ala Gln Asp Gly Ala Leu Trp Leu Leu
                85                  90                  95

Pro Ala Leu Gln Glu Asp Ser Gly Thr Tyr Val Cys Thr Thr Arg Asn
            100                 105                 110

Ala Ser Tyr Cys Asp Lys Met Ser Ile Glu Leu Arg Val Phe Glu Asn
        115                 120                 125

Thr Asp Ala Phe Leu Pro Phe Ile Ser Tyr Pro Gln Ile Leu Thr Leu
    130                 135                 140

Ser Thr Ser Gly Val Leu Val Cys Pro Asp Leu Ser Glu Phe Thr Arg
145                 150                 155                 160

Asp Lys Thr Asp Val Lys Ile Gln Trp Tyr Lys Asp Ser Leu Leu Leu
                165                 170                 175

Asp Lys Asp Asn Glu Lys Phe Leu Ser Val Arg Gly Thr Thr His Leu
            180                 185                 190

Leu Val His Asp Val Ala Leu Glu Asp Ala Gly Tyr Tyr Arg Cys Val
        195                 200                 205

Leu Thr Phe Ala His Glu Gly Gln Gln Tyr Asn Ile Thr Arg Ser Ile
    210                 215                 220

Glu Leu Arg Ile Lys Lys Lys Lys Glu Glu Thr Ile Pro Val Ile Ile
225                 230                 235                 240

Ser Pro Leu Lys Thr Ile Ser Ala Ser Leu Gly Ser Arg Leu Thr Ile
                245                 250                 255
```

```
Pro Cys Lys Val Phe Leu Gly Thr Gly Thr Pro Leu Thr Thr Met Leu
            260                 265                 270

Trp Trp Thr Ala Asn Asp Thr His Ile Glu Ser Ala Tyr Pro Gly Gly
        275                 280                 285

Arg Val Thr Glu Gly Pro Arg Gln Glu Tyr Ser Glu Asn Asn Glu Asn
    290                 295                 300

Tyr Ile Glu Val Pro Leu Ile Phe Asp Pro Val Thr Arg Glu Asp Leu
305                 310                 315                 320

His Met Asp Phe Lys Cys Val Val His Asn Thr Leu Ser Phe Gln Thr
                325                 330                 335

Leu Arg Thr Thr Val Lys Glu Ala Ser Ser Thr Phe Ser Trp Gly Ile
            340                 345                 350

Val Leu Ala Pro Leu Ser Leu Ala Phe Leu Val Leu Gly Gly Ile Trp
        355                 360                 365

Met His Arg Arg Cys Lys His Arg Thr Gly Lys Ala Asp Gly Leu Thr
    370                 375                 380

Val Leu Trp Pro His His Gln Asp Phe Gln Ser Tyr Pro Lys
385                 390                 395


<210> 509
<211> 273
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 509
Met Ile Phe Leu Leu Leu Met Leu Ser Leu Glu Leu Gln Leu His Gln
1               5                   10                  15
```

```
Ile Ala Ala Leu Phe Thr Val Thr Val Pro Lys Glu Leu Tyr Ile Ile
            20                  25                  30

Glu His Gly Ser Asn Val Thr Leu Glu Cys Asn Phe Asp Thr Gly Ser
        35                  40                  45

His Val Asn Leu Gly Ala Ile Thr Ala Ser Leu Gln Lys Val Glu Asn
    50                  55                  60

Asp Thr Ser Pro His Arg Glu Arg Ala Thr Leu Leu Glu Glu Gln Leu
65                  70                  75                  80

Pro Leu Gly Lys Ala Ser Phe His Ile Pro Gln Val Gln Val Arg Asp
                85                  90                  95

Glu Gly Gln Tyr Gln Cys Ile Ile Ile Tyr Gly Val Ala Trp Asp Tyr
            100                 105                 110

Lys Tyr Leu Thr Leu Lys Val Lys Ala Ser Tyr Arg Lys Ile Asn Thr
        115                 120                 125

His Ile Leu Lys Val Pro Glu Thr Asp Glu Val Glu Leu Thr Cys Gln
    130                 135                 140

Ala Thr Gly Tyr Pro Leu Ala Glu Val Ser Trp Pro Asn Val Ser Val
145                 150                 155                 160

Pro Ala Asn Thr Ser His Ser Arg Thr Pro Glu Gly Leu Tyr Gln Val
                165                 170                 175

Thr Ser Val Leu Arg Leu Lys Pro Pro Pro Gly Arg Asn Phe Ser Cys
            180                 185                 190

Val Phe Trp Asn Thr His Val Arg Glu Leu Thr Leu Ala Ser Ile Asp
        195                 200                 205

Leu Gln Ser Gln Met Glu Pro Arg Thr His Pro Thr Trp Leu Leu His
    210                 215                 220
```

Ile Phe Ile Pro Phe Cys Ile Ile Ala Phe Ile Phe Ile Ala Thr Val
225 230 235 240

Ile Ala Leu Arg Lys Gln Leu Cys Gln Lys Leu Tyr Ser Ser Lys Asp
245 250 255

Thr Thr Lys Arg Pro Val Thr Thr Thr Lys Arg Glu Val Asn Ser Ala
260 265 270

Ile

<210> 510
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 510
Met Arg Trp Cys Leu Leu Leu Ile Trp Ala Gln Gly Leu Arg Gln Ala
1 5 10 15

Pro Leu Ala Ser Gly Met Met Thr Gly Thr Ile Glu Thr Thr Gly Asn
20 25 30

Ile Ser Ala Glu Lys Gly Gly Ser Ile Ile Leu Gln Cys His Leu Ser
35 40 45

Ser Thr Thr Ala Gln Val Thr Gln Val Asn Trp Glu Gln Gln Asp Gln
50 55 60

Leu Leu Ala Ile Cys Asn Ala Asp Leu Gly Trp His Ile Ser Pro Ser
65 70 75 80

Phe Lys Asp Arg Val Ala Pro Gly Pro Gly Leu Gly Leu Thr Leu Gln
85 90 95

Ser Leu Thr Val Asn Asp Thr Gly Glu Tyr Phe Cys Ile Tyr His Thr
100 105 110

```
Tyr Pro Asp Gly Thr Tyr Thr Gly Arg Ile Phe Leu Glu Val Leu Glu
        115                 120                 125


Ser Ser Val Ala Glu His Gly Ala Arg Phe Gln Ile Pro Leu Leu Gly
    130                 135                 140


Ala Met Ala Ala Thr Leu Val Val Ile Cys Thr Ala Val Ile Val Val
145                 150                 155                 160


Val Ala Leu Thr Arg Lys Lys Lys Ala Leu Arg Ile His Ser Val Glu
                165                 170                 175


Gly Asp Leu Arg Arg Lys Ser Ala Gly Gln Glu Glu Trp Ser Pro Ser
            180                 185                 190


Ala Pro Ser Pro Pro Gly Ser Cys Val Gln Ala Glu Ala Ala Pro Ala
        195                 200                 205


Gly Leu Cys Gly Glu Gln Arg Gly Glu Asp Cys Ala Glu Leu His Asp
    210                 215                 220


Tyr Phe Asn Val Leu Ser Tyr Arg Ser Leu Gly Asn Cys Ser Phe Phe
225                 230                 235                 240


Thr Glu Thr Gly



<210> 511
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 511
Met Cys Val Gly Ala Arg Arg Leu Gly Arg Gly Pro Cys Ala Ala Leu
1               5                   10                  15
```

```
Leu Leu Leu Gly Leu Gly Leu Ser Thr Val Thr Gly Leu His Cys Val
            20                  25                  30

Gly Asp Thr Tyr Pro Ser Asn Asp Arg Cys Cys His Glu Cys Arg Pro
        35                  40                  45

Gly Asn Gly Met Val Ser Arg Cys Ser Arg Ser Gln Asn Thr Val Cys
    50                  55                  60

Arg Pro Cys Gly Pro Gly Phe Tyr Asn Asp Val Val Ser Ser Lys Pro
65                  70                  75                  80

Cys Lys Pro Cys Thr Trp Cys Asn Leu Arg Ser Gly Ser Glu Arg Lys
                85                  90                  95

Gln Leu Cys Thr Ala Thr Gln Asp Thr Val Cys Arg Cys Arg Ala Gly
            100                 105                 110

Thr Gln Pro Leu Asp Ser Tyr Lys Pro Gly Val Asp Cys Ala Pro Cys
        115                 120                 125

Pro Pro Gly His Phe Ser Pro Gly Asp Asn Gln Ala Cys Lys Pro Trp
    130                 135                 140

Thr Asn Cys Thr Leu Ala Gly Lys His Thr Leu Gln Pro Ala Ser Asn
145                 150                 155                 160

Ser Ser Asp Ala Ile Cys Glu Asp Arg Asp Pro Pro Ala Thr Gln Pro
                165                 170                 175

Gln Glu Thr Gln Gly Pro Pro Ala Arg Pro Ile Thr Val Gln Pro Thr
            180                 185                 190

Glu Ala Trp Pro Arg Thr Ser Gln Gly Pro Ser Thr Arg Pro Val Glu
        195                 200                 205

Val Pro Gly Gly Arg Ala Val Ala Ala Ile Leu Gly Leu Gly Leu Val
    210                 215                 220
```

Leu Gly Leu Leu Gly Pro Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
225 230 235 240

Arg Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly
245 250 255

Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser
260 265 270

Thr Leu Ala Lys Ile
275

<210> 512
<211> 595
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 512
Met Arg Val Leu Leu Ala Ala Leu Gly Leu Leu Phe Leu Gly Ala Leu
1 5 10 15

Arg Ala Phe Pro Gln Asp Arg Pro Phe Glu Asp Thr Cys His Gly Asn
20 25 30

Pro Ser His Tyr Tyr Asp Lys Ala Val Arg Arg Cys Cys Tyr Arg Cys
35 40 45

Pro Met Gly Leu Phe Pro Thr Gln Gln Cys Pro Gln Arg Pro Thr Asp
50 55 60

Cys Arg Lys Gln Cys Glu Pro Asp Tyr Tyr Leu Asp Glu Ala Asp Arg
65 70 75 80

Cys Thr Ala Cys Val Thr Cys Ser Arg Asp Asp Leu Val Glu Lys Thr
85 90 95

Pro Cys Ala Trp Asn Ser Ser Arg Val Cys Glu Cys Arg Pro Gly Met
100 105 110

```
Phe Cys Ser Thr Ser Ala Val Asn Ser Cys Ala Arg Cys Phe Phe His
        115                 120                 125

Ser Val Cys Pro Ala Gly Met Ile Val Lys Phe Pro Gly Thr Ala Gln
    130                 135                 140

Lys Asn Thr Val Cys Glu Pro Ala Ser Pro Gly Val Ser Pro Ala Cys
145                 150                 155                 160

Ala Ser Pro Glu Asn Cys Lys Glu Pro Ser Ser Gly Thr Ile Pro Gln
                165                 170                 175

Ala Lys Pro Thr Pro Val Ser Pro Ala Thr Ser Ser Ala Ser Thr Met
            180                 185                 190

Pro Val Arg Gly Gly Thr Arg Leu Ala Gln Glu Ala Ala Ser Lys Leu
        195                 200                 205

Thr Arg Ala Pro Asp Ser Pro Ser Ser Val Gly Arg Pro Ser Ser Asp
    210                 215                 220

Pro Gly Leu Ser Pro Thr Gln Pro Cys Pro Glu Gly Ser Gly Asp Cys
225                 230                 235                 240

Arg Lys Gln Cys Glu Pro Asp Tyr Tyr Leu Asp Glu Ala Gly Arg Cys
                245                 250                 255

Thr Ala Cys Val Ser Cys Ser Arg Asp Asp Leu Val Glu Lys Thr Pro
            260                 265                 270

Cys Ala Trp Asn Ser Ser Arg Thr Cys Glu Cys Arg Pro Gly Met Ile
        275                 280                 285

Cys Ala Thr Ser Ala Thr Asn Ser Cys Ala Arg Cys Val Pro Tyr Pro
    290                 295                 300

Ile Cys Ala Ala Glu Thr Val Thr Lys Pro Gln Asp Met Ala Glu Lys
305                 310                 315                 320
```

```
Asp Thr Thr Phe Glu Ala Pro Pro Leu Gly Thr Gln Pro Asp Cys Asn
                325                 330                 335

Pro Thr Pro Glu Asn Gly Glu Ala Pro Ala Ser Thr Ser Pro Thr Gln
            340                 345                 350

Ser Leu Leu Val Asp Ser Gln Ala Ser Lys Thr Leu Pro Ile Pro Thr
        355                 360                 365

Ser Ala Pro Val Ala Leu Ser Ser Thr Gly Lys Pro Val Leu Asp Ala
    370                 375                 380

Gly Pro Val Leu Phe Trp Val Ile Leu Val Leu Val Val Val Val Gly
385                 390                 395                 400

Ser Ser Ala Phe Leu Leu Cys His Arg Arg Ala Cys Arg Lys Arg Ile
                405                 410                 415

Arg Gln Lys Leu His Leu Cys Tyr Pro Val Gln Thr Ser Gln Pro Lys
            420                 425                 430

Leu Glu Leu Val Asp Ser Arg Pro Arg Arg Ser Ser Thr Gln Leu Arg
        435                 440                 445

Ser Gly Ala Ser Val Thr Glu Pro Val Ala Glu Glu Arg Gly Leu Met
    450                 455                 460

Ser Gln Pro Leu Met Glu Thr Cys His Ser Val Gly Ala Ala Tyr Leu
465                 470                 475                 480

Glu Ser Leu Pro Leu Gln Asp Ala Ser Pro Ala Gly Gly Pro Ser Ser
                485                 490                 495

Pro Arg Asp Leu Pro Glu Pro Arg Val Ser Thr Glu His Thr Asn Asn
            500                 505                 510

Lys Ile Glu Lys Ile Tyr Ile Met Lys Ala Asp Thr Val Ile Val Gly
        515                 520                 525
```

```
Thr Val Lys Ala Glu Leu Pro Glu Gly Arg Gly Leu Ala Gly Pro Ala
    530                 535                 540

Glu Pro Glu Leu Glu Glu Glu Leu Glu Ala Asp His Thr Pro His Tyr
545                 550                 555                 560

Pro Glu Gln Glu Thr Glu Pro Pro Leu Gly Ser Cys Ser Asp Val Met
                565                 570                 575

Leu Ser Val Glu Glu Glu Gly Lys Glu Asp Pro Leu Pro Thr Ala Ala
            580                 585                 590

Ser Gly Lys
        595


<210> 513
<211> 255
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 513
Met Gly Asn Ser Cys Tyr Asn Ile Val Ala Thr Leu Leu Leu Val Leu
1               5                   10                  15

Asn Phe Glu Arg Thr Arg Ser Leu Gln Asp Pro Cys Ser Asn Cys Pro
            20                  25                  30

Ala Gly Thr Phe Cys Asp Asn Asn Arg Asn Gln Ile Cys Ser Pro Cys
        35                  40                  45

Pro Pro Asn Ser Phe Ser Ser Ala Gly Gly Gln Arg Thr Cys Asp Ile
    50                  55                  60

Cys Arg Gln Cys Lys Gly Val Phe Arg Thr Arg Lys Glu Cys Ser Ser
65                  70                  75                  80
```

```
Thr Ser Asn Ala Glu Cys Asp Cys Thr Pro Gly Phe His Cys Leu Gly
                85                  90                  95

Ala Gly Cys Ser Met Cys Glu Gln Asp Cys Lys Gln Gly Gln Glu Leu
            100                 105                 110

Thr Lys Lys Gly Cys Lys Asp Cys Cys Phe Gly Thr Phe Asn Asp Gln
        115                 120                 125

Lys Arg Gly Ile Cys Arg Pro Trp Thr Asn Cys Ser Leu Asp Gly Lys
    130                 135                 140

Ser Val Leu Val Asn Gly Thr Lys Glu Arg Asp Val Val Cys Gly Pro
145                 150                 155                 160

Ser Pro Ala Asp Leu Ser Pro Gly Ala Ser Ser Val Thr Pro Pro Ala
                165                 170                 175

Pro Ala Arg Glu Pro Gly His Ser Pro Gln Ile Ile Ser Phe Phe Leu
            180                 185                 190

Ala Leu Thr Ser Thr Ala Leu Leu Phe Leu Leu Phe Phe Leu Thr Leu
        195                 200                 205

Arg Phe Ser Val Val Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
    210                 215                 220

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
225                 230                 235                 240

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
                245                 250                 255
```

<210> 514
<211> 296
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 514
Met Thr Leu Asn Asn Val Thr Met Arg Gln Gly Thr Val Gly Met Gln
1   5   10   15

Pro Gln Gln Gln Arg Trp Ser Ile Pro Ala Asp Gly Arg His Leu Met
            20   25   30

Val Gln Lys Glu Pro His Gln Tyr Ser His Arg Asn Arg His Ser Ala
        35   40   45

Thr Pro Glu Asp His Cys Arg Arg Ser Trp Ser Ser Asp Ser Thr Asp
    50   55   60

Ser Val Ile Ser Ser Glu Ser Gly Asn Thr Tyr Tyr Arg Val Val Leu
65   70   75   80

Ile Gly Glu Gln Gly Val Gly Lys Ser Thr Leu Ala Asn Ile Phe Ala
                85   90   95

Gly Val His Asp Ser Met Asp Ser Asp Cys Glu Val Leu Gly Glu Asp
            100   105   110

Thr Tyr Glu Arg Thr Leu Met Val Asp Gly Glu Ser Ala Thr Ile Ile
        115   120   125

Leu Leu Asp Met Trp Glu Asn Lys Gly Glu Asn Glu Trp Leu His Asp
    130   135   140

His Cys Met Gln Val Gly Asp Ala Tyr Leu Ile Val Tyr Ser Ile Thr
145   150   155   160

Asp Arg Ala Ser Phe Glu Lys Ala Ser Glu Leu Arg Ile Gln Leu Arg
                165   170   175

Arg Ala Arg Gln Thr Glu Asp Ile Pro Ile Ile Leu Val Gly Asn Lys
            180   185   190

Ser Asp Leu Val Arg Cys Arg Glu Val Ser Val Ser Glu Gly Arg Ala
        195   200   205

```
Cys Ala Val Val Phe Asp Cys Lys Phe Ile Glu Thr Ser Ala Ala Val
    210                 215                 220


Gln His Asn Val Lys Glu Leu Phe Glu Gly Ile Val Arg Gln Val Arg
225                 230                 235                 240


Leu Arg Arg Asp Ser Lys Glu Lys Asn Glu Arg Arg Leu Ala Tyr Gln
                245                 250                 255


Lys Arg Lys Glu Ser Met Pro Arg Lys Ala Arg Arg Phe Trp Gly Lys
            260                 265                 270


Ile Val Ala Lys Asn Asn Lys Asn Met Ala Phe Lys Leu Lys Ser Lys
        275                 280                 285


Ser Cys His Asp Leu Ser Val Leu
    290                 295


<210> 515
<211> 574
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 515
Met Cys Pro Arg Ala Ala Arg Ala Pro Ala Thr Leu Leu Leu Ala Leu
1               5                   10                  15


Gly Ala Val Leu Trp Pro Ala Ala Gly Ala Trp Glu Leu Thr Ile Leu
            20                  25                  30


His Thr Asn Asp Val His Ser Arg Leu Glu Gln Thr Ser Glu Asp Ser
        35                  40                  45


Ser Lys Cys Val Asn Ala Ser Arg Cys Met Gly Gly Val Ala Arg Leu
    50                  55                  60
```

```
Phe Thr Lys Val Gln Gln Ile Arg Arg Ala Glu Pro Asn Val Leu Leu
65                  70                  75                  80

Leu Asp Ala Gly Asp Gln Tyr Gln Gly Thr Ile Trp Phe Thr Val Tyr
                85                  90                  95

Lys Gly Ala Glu Val Ala His Phe Met Asn Ala Leu Arg Tyr Asp Ala
            100                 105                 110

Met Ala Leu Gly Asn His Glu Phe Asp Asn Gly Val Glu Gly Leu Ile
        115                 120                 125

Glu Pro Leu Leu Lys Glu Ala Lys Phe Pro Ile Leu Ser Ala Asn Ile
    130                 135                 140

Lys Ala Lys Gly Pro Leu Ala Ser Gln Ile Ser Gly Leu Tyr Leu Pro
145                 150                 155                 160

Tyr Lys Val Leu Pro Val Gly Asp Glu Val Val Gly Ile Val Gly Tyr
                165                 170                 175

Thr Ser Lys Glu Thr Pro Phe Leu Ser Asn Pro Gly Thr Asn Leu Val
            180                 185                 190

Phe Glu Asp Glu Ile Thr Ala Leu Gln Pro Glu Val Asp Lys Leu Lys
        195                 200                 205

Thr Leu Asn Val Asn Lys Ile Ile Ala Leu Gly His Ser Gly Phe Glu
    210                 215                 220

Met Asp Lys Leu Ile Ala Gln Lys Val Arg Gly Val Asp Val Val Val
225                 230                 235                 240

Gly Gly His Ser Asn Thr Phe Leu Tyr Thr Gly Asn Pro Pro Ser Lys
                245                 250                 255

Glu Val Pro Ala Gly Lys Tyr Pro Phe Ile Val Thr Ser Asp Asp Gly
            260                 265                 270
```

```
Arg Lys Val Pro Val Val Gln Ala Tyr Ala Phe Gly Lys Tyr Leu Gly
        275                 280                 285

Tyr Leu Lys Ile Glu Phe Asp Glu Arg Gly Asn Val Ile Ser Ser His
    290                 295                 300

Gly Asn Pro Ile Leu Leu Asn Ser Ser Ile Pro Glu Asp Pro Ser Ile
305                 310                 315                 320

Lys Ala Asp Ile Asn Lys Trp Arg Ile Lys Leu Asp Asn Tyr Ser Thr
                325                 330                 335

Gln Glu Leu Gly Lys Thr Ile Val Tyr Leu Asp Gly Ser Ser Gln Ser
            340                 345                 350

Cys Arg Phe Arg Glu Cys Asn Met Gly Asn Leu Ile Cys Asp Ala Met
        355                 360                 365

Ile Asn Asn Asn Leu Arg His Thr Asp Glu Met Phe Trp Asn His Val
    370                 375                 380

Ser Met Cys Ile Leu Asn Gly Gly Gly Ile Arg Ser Pro Ile Asp Glu
385                 390                 395                 400

Arg Asn Asn Gly Thr Ile Thr Trp Glu Asn Leu Ala Ala Val Leu Pro
                405                 410                 415

Phe Gly Gly Thr Phe Asp Leu Val Gln Leu Lys Gly Ser Thr Leu Lys
            420                 425                 430

Lys Ala Phe Glu His Ser Val His Arg Tyr Gly Gln Ser Thr Gly Glu
        435                 440                 445

Phe Leu Gln Val Gly Gly Ile His Val Val Tyr Asp Leu Ser Arg Lys
    450                 455                 460

Pro Gly Asp Arg Val Val Lys Leu Asp Val Leu Cys Thr Lys Cys Arg
465                 470                 475                 480
```

Val Pro Ser Tyr Asp Pro Leu Lys Met Asp Glu Val Tyr Lys Val Ile
485 490 495

Leu Pro Asn Phe Leu Ala Asn Gly Gly Asp Gly Phe Gln Met Ile Lys
500 505 510

Asp Glu Leu Leu Arg His Asp Ser Gly Asp Gln Asp Ile Asn Val Val
515 520 525

Ser Thr Tyr Ile Ser Lys Met Lys Val Ile Tyr Pro Ala Val Glu Gly
530 535 540

Arg Ile Lys Phe Ser Thr Gly Ser His Cys His Gly Ser Phe Ser Leu
545 550 555 560

Ile Phe Leu Ser Leu Trp Ala Val Ile Phe Val Leu Tyr Gln
565 570

<210> 516
<211> 255
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 516
Met Ala Gln His Gly Ala Met Gly Ala Phe Arg Ala Leu Cys Gly Leu
1 5 10 15

Ala Leu Leu Cys Ala Leu Ser Leu Gly Gln Arg Pro Thr Gly Gly Pro
20 25 30

Gly Cys Gly Pro Gly Arg Leu Leu Leu Gly Thr Gly Thr Asp Ala Arg
35 40 45

Cys Cys Arg Val His Thr Thr Arg Cys Cys Arg Asp Tyr Pro Gly Glu
50 55 60

Glu Cys Cys Ser Glu Trp Asp Cys Met Cys Val Gln Pro Glu Phe His
65 70 75 80

```
Cys Gly Asp Pro Cys Cys Thr Thr Cys Arg His His Pro Cys Pro Pro
                85                  90                  95

Gly Gln Gly Val Gln Ser Gln Gly Lys Phe Ser Phe Gly Phe Gln Cys
            100                 105                 110

Ile Asp Cys Ala Ser Gly Thr Phe Ser Gly Gly His Glu Gly His Cys
        115                 120                 125

Lys Pro Trp Thr Asp Cys Cys Trp Arg Cys Arg Arg Arg Pro Lys Thr
    130                 135                 140

Pro Glu Ala Ala Ser Ser Pro Arg Lys Ser Gly Ala Ser Asp Arg Gln
145                 150                 155                 160

Arg Arg Arg Gly Gly Trp Glu Thr Cys Gly Cys Glu Pro Gly Arg Pro
                165                 170                 175

Pro Gly Pro Pro Thr Ala Ala Ser Pro Ser Pro Gly Ala Pro Gln Ala
            180                 185                 190

Ala Gly Ala Leu Arg Ser Ala Leu Gly Arg Ala Leu Leu Pro Trp Gln
        195                 200                 205

Gln Lys Trp Val Gln Glu Gly Gly Ser Asp Gln Arg Pro Gly Pro Cys
    210                 215                 220

Ser Ser Ala Ala Ala Ala Gly Pro Cys Arg Arg Glu Arg Glu Thr Gln
225                 230                 235                 240

Ser Trp Pro Pro Ser Ser Leu Ala Gly Pro Asp Gly Val Gly Ser
                245                 250                 255


<210> 517
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
```

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 517
Gly Thr Phe Ser Ser Tyr Ala Ile Ser
1 5

<210> 518
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 518
Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 519
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 519
Ala Arg Arg Gly Arg Lys Ala Ser Gly Ser Phe Tyr Tyr Tyr Tyr Gly
1 5 10 15

Met Asp Val

<210> 520
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 520
Glu Ser Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
1 5 10 15

Thr

<210> 521
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 521
Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 522
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 522
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Thr Asp Asn
20 25 30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Phe Ile Arg Asn Lys Ala Asn Gly Tyr Thr Thr Glu Tyr Ala Ala
50 55 60

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

Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Ala Arg Asp Val Gly Ser Asn Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 523
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 523
Phe Thr Phe Thr Asp Asn Tyr Met Ser
1 5

<210> 524
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 524
Phe Ile Arg Asn Lys Ala Asn Gly Tyr Thr Thr Glu Tyr Ala Ala Ser
1 5 10 15

Val

<210> 525
<211> 11
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 525
Ala Arg Asp Val Gly Ser Asn Tyr Phe Asp Tyr
1 5 10

<210> 526
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 526
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Phe Asn Ser
20 25 30

Arg Thr Arg Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Ala Arg Asp Ser Gly Val
50 55 60

Pro Ala Arg Phe Thr Gly Ser Gly Ser Glu Thr Tyr Phe Thr Leu Thr
65 70 75 80

Ile Ser Arg Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Met Gln
85 90 95

Ser Phe Asn Leu Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 527
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 527
Lys Ser Ser Gln Ser Leu Phe Asn Ser Arg Thr Arg Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 528
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 528
Trp Ala Ser Ala Arg Asp Ser
1 5

<210> 529
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 529
Met Gln Ser Phe Asn Leu Arg Thr
1 5