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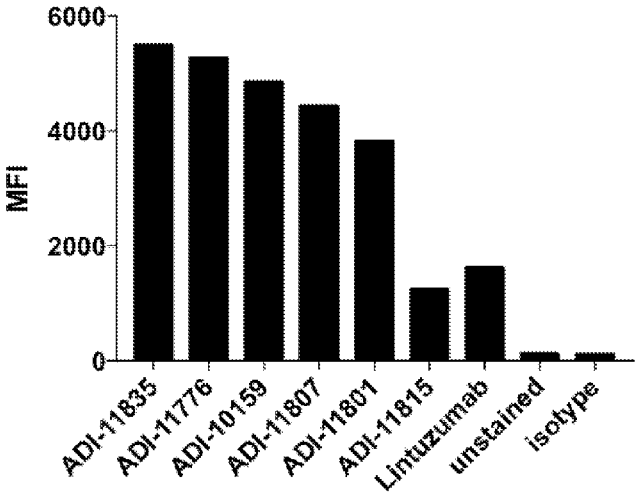
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(54) Title: ANTIBODY VARIABLE DOMAINS TARGETING CD33, AND USE THEREOF

FIG. 8



(57) Abstract: Disclosed are proteins with antibody heavy chain and light chain variable domains that can be paired to form an antigen binding site targeting CD33 (Siglec-3) on a cell, pharmaceutical compositions comprising such proteins, and therapeutic methods using such proteins and pharmaceutical compositions, including for the treatment of cancer.

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ANTIBODY VARIABLE DOMAINS TARGETING CD33, AND USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of and priority to U.S. Provisional Patent Application No. 62/632,756, filed February 20, 2018, 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 February 19, 2019, is named DFY_050WO_SL25.txt and is 571,095 bytes in size.

FIELD OF THE INVENTION

[0003] The invention provides proteins with antibody heavy chain and light chain variable domains that can be paired to form an antigen binding site targeting CD33 (Siglec-3) on a cell, pharmaceutical compositions comprising such proteins, and therapeutic methods using such proteins and pharmaceutical compositions, including for the treatment of cancer.

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 in adults include prostate cancer, breast cancer, and lung cancer. Hematological malignancies, though less frequent than solid cancers, have low survival rates. 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. T cells are major effectors of the adaptive immune system that attack foreign cells as well as host cells that present mutant or mis-expressed peptides. Cells targeted by T cells may be virally-infected, such that they express foreign proteins, or malignant, where they might express mutant

proteins. T cells recognize target cells via their T cell receptor (TCR) engaging intracellular peptides presented by major histocompatibility complex proteins on target cells. Individual T cells typically recognize target cells bearing specific MHC-peptide complexes, but novel agents have been developed that usurp and amplify this natural process for therapeutic benefit. Bi-specific T cell engagers link antigen binding site(s) of tumor-associated antigens to antigen binding site(s) of components of the TCR complex to redirect T cell activity towards desired target cells independent of native peptide-MHC recognition. For example, Blincyto is an FDA-approved T cell engager that targets CD19 on malignant B cells.

[0006] T cells can also be engineered to express chimeric antigen receptors (CAR) that endow it with target recognition capabilities of its CAR. CARs contain antigen binding site(s) to tumor associated antigens linked to T cell activation domains. These CAR-T cells can also be employed to target malignant cells, and some have been FDA-approved for use against B cell malignancies.

[0007] Antibodies that bind to certain tumor-associated antigens and to certain immune cells have been described in the literature. *See, e.g.*, WO 2016/134371 and WO 2015/095412. Antibody-drug conjugates or immunocytokines using antigen binding sites targeting tumor associated antigens to deliver toxic agents or immune-modulatory cytokines to specific target cells.

[0008] 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.

[0009] 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.

[0010] CD33 is a member of the sialic acid-binding immunoglobulin-like lectins. As a transmembrane receptor mainly expressed on cells of myeloid lineage, CD33 modulates inflammatory and immune responses through a dampening effect on tyrosine kinase-driven signaling pathways. For example, CD33 was shown to constitutively suppress the production of pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-8 by human monocytes.

[0011] CD33 is associated with hematopoietic cancers. It is broadly expressed in blasts of nearly all acute myeloid leukemia (AML). Furthermore, hematopoietic cancer stem and/or progenitor cells are found to be $CD33^+$, implying that CD33-directed therapy could potentially eradicate malignant stem and/or progenitor cells in such cases while sparing normal hematopoietic stem cells. In addition to its expression in AML, CD33 is found on other myeloid neoplasms (*e.g.*, myelodysplastic syndromes and myeloproliferative neoplasms) and on subsets of B-cell and T-cell acute lymphoblastic leukemias (ALL)/lymphoblastic lymphomas. This expression pattern has led to the use of CD33-directed therapeutics in patients with malignancies including AML, myelodysplastic syndromes, chronic myelomonocytic leukemia, myeloid blast crisis of chronic myeloid leukemia, and ALLs.

SUMMARY OF THE INVENTION

[0012] In one aspect, the invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and/or Cynomolgus/Rhesus (cyno) CD33. In one aspect, the present invention provides an antigen binding site that recognizes and binds one or more conformational epitopes on the extracellular domain of human CD33 and/or Cynomolgus/Rhesus (cyno) CD33. In one aspect, the present invention provides an antigen binding site that recognizes and binds one or more conformational epitopes on the extracellular domain of human CD33 but does not recognize and/or bind one or more conformational epitopes on the extracellular domain of cyno CD33. In one aspect, the present invention provides an antigen binding site that binds to the R69G allele of human CD33. In one aspect, the present invention provides an antigen binding site that binds to wild-type human CD33 (*e.g.*, having the amino acid sequence identified by NCBI Reference Sequence: NP_001763.3) but not the R69G allele of human CD33. In one aspect, the present invention provides an antigen binding site that binds to an epitope on human CD33 that includes R69. In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain that binds to the extracellular domain in human CD33 and/or cyno CD33, irrespective of the glycosylation profile of the targeted CD33.

[0013] In certain embodiments, the present invention provides an antigen binding site that binds to the extracellular domain of human CD33 and/or cyno CD33, such that the epitopes are unique compared to the epitopes targeted by one or more known anti-CD33 antibodies in the art. In certain embodiments, the present invention provides an antigen binding site that binds to the extracellular domain of human CD33 and/or cyno CD33, and shows human or cyno CD33 cross-reactivity and high affinity binding to the target CD33.

[0014] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYGMSWVRQAPGKGLEWVANIKQDGS EKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVY YGMDVWGQGTTVTVSS [SEQ ID NO:1]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:1. In some embodiments, the heavy chain variable domain includes amino acid sequences FTFSSYGMS [SEQ ID NO:21] as the first complementarity-determining region 1 ("CDR1"), NIKQDGSEKYYVDSVKG [SEQ ID NO:22] as the second CDR ("CDR2"), and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:23] as the third CDR ("CDR3") of SEQ ID NO:1. In some embodiments, the heavy chain variable domain includes amino acid sequences SYGMS [SEQ ID NO:434] as the first complementarity-determining region 1 ("CDR1"), NIKQDGSEKYYVDSVKG [SEQ ID NO:22] as the second CDR ("CDR2"), and EGGPYYDSSGYFVYYGMDV [SEQ ID NO:435] as the third CDR ("CDR3") of SEQ ID NO:1. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYESFPTFGGGTKVEIK [SEQ ID NO:2]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 can be paired with an antibody light chain variable domain at least

90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:2, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:24] as CDR1, DASSLES [SEQ ID NO:25] as CDR2, and QQYESFPT [SEQ ID NO:26] as CDR3 of SEQ ID NO:2.

[0015] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:1 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:2; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 21, 22, and 23, respectively, or SEQ ID NOs: 434, 22, and 435, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 24, 25, and 26, respectively.

[0016] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDG SEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ GTMVTVSS [SEQ ID NO:3]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:3. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:27] as CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:28] as CDR2, and ARPLNAGELDV [SEQ ID NO:29] as CDR3 of SEQ ID NO:3. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:28] as CDR2, and PLNAGELDV [SEQ ID NO:436] as CDR3 of SEQ ID NO:3. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV

PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQLESYPLTFGGGTKVEIK [SEQ ID NO:4]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:4, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:30] as CDR1, EASSLES [SEQ ID NO:31] as CDR2, and QQLESYPLT [SEQ ID NO:32] as CDR3 of SEQ ID NO:4.

[0017] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:3 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:4; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 27, 28, and 29, respectively, or SEQ ID NOs: 181, 28, and 436, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 30, 31, and 32, respectively.

[0018] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGKGLEWVSAIVGSGE STYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVY YGMDVWGQGTTVTVSS [SEQ ID NO:5]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:5. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSKYTMS [SEQ ID NO:33] as CDR1, AIVGSGESTYFADSVKG [SEQ ID NO:34] as CDR2, and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:35] as CDR3 of SEQ ID NO:5. In some embodiments, the heavy chain variable domain incorporates amino acid sequences KYTMS [SEQ ID NO:183] as CDR1, AIVGSGESTYFADSVKG [SEQ ID NO:34] as CDR2, and EGGPYYDSSGYFVYYGMDV [SEQ ID NO:184] as CDR3 of SEQ ID NO:5. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%,

96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFGGGTKVEIK [SEQ ID NO:6]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:36] as CDR1, KASSLES [SEQ ID NO:37] or KASSLE [SEQ ID NO:185] as CDR2, and QQYDDLPT [SEQ ID NO:38] as CDR3 of SEQ ID NO:6.

[0019] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:5 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:6; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 33, 34, and 35, respectively, or SEQ ID NOs: 183, 34, and 184, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 36, 37, and 38, respectively, or CDRs 1-3 having the sequences of SEQ ID NOs: 36, 185, and 38, respectively.

[0020] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQGLEWMGMINPS WGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAREAADGFVGERYF DLWGRGTLVTVSS [SEQ ID NO:7]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:7. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFSDYYMH [SEQ ID NO:39] as CDR1, MINPSWGSTSYAQKFQG [SEQ ID NO:40] as CDR2, and AREAADGFVGERYFDL [SEQ ID NO:41] as CDR3 of SEQ ID NO:7. In some embodiments, the heavy chain variable domain incorporates amino acid sequences DYYMH [SEQ ID NO:437] as CDR1, MINPSWGSTSYAQKFQG [SEQ ID NO:40] as CDR2, and EAADGFVGERYFDL [SEQ ID NO:438] as CDR3 of SEQ ID NO:7. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid

sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQSPQLLIYLGSN RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQDVALPITFGGGTKVEIK [SEQ ID NO:8]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8, which includes amino acid sequences RSSQSLLYSNGYNYLD [SEQ ID NO:42] as CDR1, LGSNRAS [SEQ ID NO:43] as CDR2, and MQDVALPIT [SEQ ID NO:44] as CDR3 of SEQ ID NO:8.

[0021] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:7 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:8; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 39, 40, and 41, respectively, or SEQ ID NOs: 437, 40, and 438, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 42, 43, and 44, respectively.

[0022] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPGKGLEWVATIKQDG SEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ GTMVTVSS [SEQ ID NO:9]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:9. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFGSYWMS [SEQ ID NO:45] as CDR1, TIKQDGSEKSYVDSVKG [SEQ ID NO:46] as CDR2, and ARPLNAGELDV [SEQ ID NO:47] as CDR3 of SEQ ID NO:9. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1,

TIKQDGSEKSYVDSVKG [SEQ ID NO:46] as CDR2, and RPLNAGELDV [SEQ ID NO:182] as CDR3 of SEQ ID NO:9. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIK [SEQ ID NO:10]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:10, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:48] as CDR1, EASSLES [SEQ ID NO:49] as CDR2, and QQSQSYPPIT [SEQ ID NO:50] as CDR3 of SEQ ID NO:10.

[0023] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:9 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:10; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 45, 46, and 47, respectively, or SEQ ID NOs: 181, 46, and 182, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 48, 49, and 50, respectively.

[0024] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFPSYWMSWVRQAPGKGLEWVATIKRDGS EKGYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQG TMVTVSS [SEQ ID NO:11]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:11. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFPSYWMS [SEQ ID NO:51] as

CDR1, TIKRDGSEKGYVDSVKG [SEQ ID NO:52] as CDR2, and ARPLNAGELDV [SEQ ID NO:53] as CDR3 of SEQ ID NO:11. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181]as CDR1, TIKRDGSEKGYVDSVKG [SEQ ID NO:52] as CDR2, and PLNAGELDV [SEQ ID NO:439] as CDR3 of SEQ ID NO:11. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIK [SEQ ID NO:12]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:12, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:54] as CDR1, EASSLES [SEQ ID NO:55] as CDR2, and QQSQSYPPIT [SEQ ID NO:56] as CDR3 of SEQ ID NO:12.

[0025] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:11 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:12; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 51, 52, and 53, respectively, or SEQ ID NOs: 181, 52, and 439, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 54, 55, and 56, respectively.

[0026] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQAPGQGLEWMGIINPSR GSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDV

WGKGTTVTVSS [SEQ ID NO:13]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:13. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFGTYYMH [SEQ ID NO:57] as CDR1, IINPSRGSTVYAQKFQG [SEQ ID NO:58] as CDR2, and ARGAGYDDEDMDV [SEQ ID NO:59] as CDR3 of SEQ ID NO:13. In some embodiments, the heavy chain variable domain incorporates amino acid sequences TYYMH [SEQ ID NO:440] as CDR1, IINPSRGSTVYAQKFQG [SEQ ID NO:58] as CDR2, and GAGYDDEDMDV [SEQ ID NO:441] as CDR3 of SEQ ID NO:13. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPLTFGGGTKVEIK [SEQ ID NO:14]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14, which includes amino acid sequences RASQGIDSWLA [SEQ ID NO:60] as CDR1, AASSLQS [SEQ ID NO:61] as CDR2, and QQAHSYPLT [SEQ ID NO:62] as CDR3 of SEQ ID NO:14.

[0027] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:13 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:14; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 57, 58, and 59, respectively, or SEQ ID NOs: 440, 58, and 441, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 60, 61, and 62, respectively.

[0028] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSISSSSEG IYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVYY GMDVWGQGTTVTVSS [SEQ ID NO:15]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:15. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYAMS [SEQ ID NO:63] as CDR1, SISSSSEGIYYADSVKG [SEQ ID NO:64] as CDR2, and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:65] as CDR3 of SEQ ID NO:15. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYAMS [SEQ ID NO:442] as CDR1, SISSSSEGIYYADSVKG [SEQ ID NO:64] as CDR2, and EGGPYYDSSGYFVYYGMDV [SEQ ID NO:443] as CDR3 of SEQ ID NO:15. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASNSISSWLAWYQQKPGKAPKLLIYEASSTKSGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFGGGTKVEIK [SEQ ID NO:16]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:16, which includes amino acid sequences RASNSISSWLA [SEQ ID NO:66] as CDR1, EASSTKS [SEQ ID NO:67] as CDR2, and QQYDDLPT [SEQ ID NO:68] as CDR3 of SEQ ID NO:16.

[0029] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:15 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:16; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 63, 64, and 65,

respectively, or SEQ ID NOs: 442, 64, and 443, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 66, 67, and 68, respectively.

[0030] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANINTDG SEVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDVGPGIAYQGHFD YWGQGTLVTVSS [SEQ ID NO:17]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:17. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:69] as CDR1, NINTDGSEVYYVDSVKG [SEQ ID NO:70] as CDR2, and ARDVGPGIAYQGHFDY [SEQ ID NO:71] as CDR3 of SEQ ID NO:17. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1, NINTDGSEVYYVDSVKG [SEQ ID NO:70] as CDR2, and DVGPGIAYQGHFDY [SEQ ID NO:444] as CDR3 of SEQ ID NO:17. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQVIYSYLNWYQQKPGKAPKLLIYAASSLKSGV PSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYDTPLTFGGGTKVEIK [SEQ ID NO:18]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:18, which includes amino acid sequences RASQVIYSYLN [SEQ ID NO:72] as CDR1, AASSLKS [SEQ ID NO:73] as CDR2, and QQVYDTPLT [SEQ ID NO:74] as CDR3 of SEQ ID NO:18.

[0031] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable

domain comprising the amino acid sequence of SEQ ID NO:17 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:18; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 69, 70, and 71, respectively, or SEQ ID NOs: 181, 70, and 444, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 72, 73, and 74, respectively.

[0032] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QLQLQESGPGLVKPSETLSLTCTVSGGSISSTDYYWGWIRQPPGKGLEWIGSIGYSGT YYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARETAHDVHGMDVWGQG TTVTVSS [SEQ ID NO:19]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:19. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GSISSTDYYWG [SEQ ID NO:75] as CDR1, SIGYSGTYYNPSLKS [SEQ ID NO:76] as CDR2, and ARETAHDVHGMDV [SEQ ID NO:77] as CDR3 of SEQ ID NO:19. In some embodiments, the heavy chain variable domain incorporates amino acid sequences STDYYWG [SEQ ID NO:445] as CDR1, SIGYSGTYYNPSLKS [SEQ ID NO:76] as CDR2, and ETAHDVHGMDV [SEQ ID NO:446] as CDR3 of SEQ ID NO:19. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence EIVLTQSPATLSLSPGERATLSCRASHSVYSYLAWYQQKPGQAPRLLIYDASNRATGI PARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLPTFGGGTKVEIK [SEQ ID NO:20]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:20, which includes amino acid

sequences RASHSVYSYLA [SEQ ID NO:78] as CDR1, DASNRAT [SEQ ID NO:79] as CDR2, and QQYDNLPT [SEQ ID NO:80] as CDR3 of SEQ ID NO:20.

[0033] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:19 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:20; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 75, 76, and 77, respectively, or SEQ ID NOs: 445, 76, and 446, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 78, 79, and 80, respectively.

[0034] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYAMS [SEQ ID NO:304] as CDR1, AISASGGSTYYADSVKG [SEQ ID NO:305] as CDR2, and PRAYYDSSGFKVNYGMDV [SEQ ID NO:306] as CDR3 of SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYAMS [SEQ ID NO:528] as CDR1, AISASGGSTYYADSVKG [SEQ ID NO:305] as CDR2, and ARPRAYYDSSGFKVNYGMDV [SEQ ID NO:529] as CDR3 of SEQ ID NO:266. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267, which includes amino acid sequences RASQSVSSSFLA [SEQ ID NO:307] as CDR1,

GASSRAT [SEQ ID NO:308] as CDR2, and QQASSSPPT [SEQ ID NO:309] as CDR3 of SEQ ID NO:267.

[0035] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:266 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:267; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 304, 305, and 306, respectively, or SEQ ID NOs: 528, 305, and 529, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 307, 308, and 309, respectively.

[0036] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYAMS [SEQ ID NO:310] as CDR1, GISGSGGSTYYADSVKG [SEQ ID NO:311] as CDR2, and EGHSSSYYDHAFDI [SEQ ID NO:312] as CDR3 of SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYAMS [SEQ ID NO:530] as CDR1, GISGSGGSTYYADSVKG [SEQ ID NO:311] as CDR2, and AREGHSSSYYDHAFDI [SEQ ID NO:531] as CDR3 of SEQ ID NO:268. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269, which includes amino acid sequences RASQSVSSDYLA

[SEQ ID NO:313] as CDR1, GASSRAT [SEQ ID NO:314] as CDR2, and QQHSSAPPT [SEQ ID NO:315] as CDR3 of SEQ ID NO:269.

[0037] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:268 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:269; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 310, 311, and 312, respectively, or SEQ ID NOs: 530, 311, and 531, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 313, 314, and 315, respectively.

[0038] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYYWS [SEQ ID NO:316] as CDR1, SIYYSGSTNYNPSLKS [SEQ ID NO:317] as CDR2, and VGGVYSTIETYGMDV [SEQ ID NO:318] as CDR3 of SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GSISSYYWS [SEQ ID NO:532] as CDR1, SIYYSGSTNYNPSLKS [SEQ ID NO:317] as CDR2, and ARVGGVYSTIETYGMDV [SEQ ID NO:533] as CDR3 of SEQ ID NO:270. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271, which includes amino acid sequences RASQSVSSNLA [SEQ

ID NO:319] as CDR1, GASTRAT [SEQ ID NO:320] as CDR2, and QQYTVYPPT [SEQ ID NO:321] as CDR3 of SEQ ID NO:271.

[0039] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:270 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:271; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 316, 317, and 318, respectively, or SEQ ID NOs: 532, 317, and 533, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 319, 320, and 321, respectively.

[0040] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GYYWS [SEQ ID NO:322] as CDR1, EIDHSGSTNYNPSLKS [SEQ ID NO:323] as CDR2, and QGIHGLRYFDL [SEQ ID NO:324] as CDR3 of SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GSFSGYYWS [SEQ ID NO:534] as CDR1, EIDHSGSTNYNPSLKS [SEQ ID NO:323] as CDR2, and ARQGIHGLRYFDL [SEQ ID NO:535] as CDR3 of SEQ ID NO:272. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273, which includes amino acid sequences RASQSVSSYLA [SEQ

ID NO:325] as CDR1, DASNRAT [SEQ ID NO:326] as CDR2, and QQDHNFPYT [SEQ ID NO:327] as CDR3 of SEQ ID NO:273.

[0041] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:272 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:273; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 322, 323, and 324, respectively, or SEQ ID NOs: 534, 323, and 535, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 325, 326, and 327, respectively.

[0042] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:328] as CDR1, NINQDGSEKYYVDSVKG [SEQ ID NO:329] as CDR2, and EANYYGNVGDDY [SEQ ID NO:330] as CDR3 of SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:536] as CDR1, NINQDGSEKYYVDSVKG [SEQ ID NO:329] as CDR2, and AREANYYGNVGDDY [SEQ ID NO:537] as CDR3 of SEQ ID NO:274. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275, which includes amino acid sequences RASQSISSYLN [SEQ

ID NO:331] as CDR1, AASSLQS [SEQ ID NO:332] as CDR2, and QQQYVTPIT [SEQ ID NO:333] as CDR3 of SEQ ID NO:275.

[0043] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:274 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:275; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 328, 329, and 330, respectively, or SEQ ID NOs: 536, 329, and 537, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 331, 332, and 333, respectively.

[0044] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:334] as CDR1, NINQDGSEKYYVDSVKG [SEQ ID NO:335] as CDR2, and EGGDSWYHAFDI [SEQ ID NO:336] as CDR3 of SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:538] as CDR1, NINQDGSEKYYVDSVKG [SEQ ID NO:335] as CDR2, and AREGGDSWYHAFDI [SEQ ID NO:539] as CDR3 of SEQ ID NO:276. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277, which includes amino acid sequences RASQGISSWLA [SEQ

ID NO:337] as CDR1, AASNLQS [SEQ ID NO:338] as CDR2, and QQKLSLPLT [SEQ ID NO:339] as CDR3 of SEQ ID NO:277.

[0045] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:276 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:277; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 334, 335, and 336, respectively, or SEQ ID NOs: 538, 335, and 539, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 337, 338, and 339, respectively.

[0046] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SGGYYWS [SEQ ID NO:340] as CDR1, SIYYSGSTYYNPSLKS [SEQ ID NO:341] as CDR2, and DRLDYSYNYGMDV [SEQ ID NO:342] as CDR3 of SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GSISSGGYYWS [SEQ ID NO:540] as CDR1, SIYYSGSTYYNPSLKS [SEQ ID NO:341] as CDR2, and ARDRLDYSYNYGMDV [SEQ ID NO:541] as CDR3 of SEQ ID NO:278. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279, which includes amino acid sequences RASQSISSYLN [SEQ

ID NO:343] as CDR1, GASSLQS [SEQ ID NO:344] as CDR2, and QQVYSAPFT [SEQ ID NO:345] as CDR3 of SEQ ID NO:279.

[0047] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:278 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:279; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 340, 341, and 342, respectively, or SEQ ID NOs: 540, 341, and 541, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 343, 344, and 345, respectively.

[0048] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SGYYWG [SEQ ID NO:346] as CDR1, SIYHSGSTNYNPSLKS [SEQ ID NO:347] as CDR2, and LPPWFGFSYFDL [SEQ ID NO:348] as CDR3 of SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YSISSGYYWG [SEQ ID NO:542] as CDR1, SIYHSGSTNYNPSLKS [SEQ ID NO:347] as CDR2, and ARLPPWFGFSYFDL [SEQ ID NO:543] as CDR3 of SEQ ID NO:280. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281, which includes amino acid sequences RASQSVSSYLA [SEQ

ID NO:349] as CDR1, DASNRAT [SEQ ID NO:350] as CDR2, and QQVDNYPPT [SEQ ID NO:351] as CDR3 of SEQ ID NO:281.

[0049] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:280 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:281; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 346, 347, and 348, respectively, or SEQ ID NOs: 542, 347, and 543, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 349, 350, and 351, respectively.

[0050] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:352] as CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:353] as CDR2, and DVGPGIAYQGHFDY [SEQ ID NO:354] as CDR3 of SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:544] as CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:353] as CDR2, and ARDVGPGIAYQGHFDY [SEQ ID NO:545] as CDR3 of SEQ ID NO:282. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283, which includes amino acid sequences

RASQSISSYLN [SEQ ID NO:355] as CDR1, AASSLQS [SEQ ID NO:356] as CDR2, and QQVYDTPLT [SEQ ID NO:357] as CDR3 of SEQ ID NO:283.

[0051] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:282 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:283; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 352, 353, and 354, respectively, or SEQ ID NOs: 544, 353, and 545, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 355, 356, and 357, respectively.

[0052] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SSSYYWG [SEQ ID NO:358] as CDR1, SIYYSGSTYYNPSLKS [SEQ ID NO:359] as CDR2, and ETAHDVHGMDV [SEQ ID NO:360] as CDR3 of SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GSISSSSYYWG [SEQ ID NO:546] as CDR1, SIYYSGSTYYNPSLKS [SEQ ID NO:359] as CDR2, and ARETAHDVHGMDV [SEQ ID NO:547] as CDR3 of SEQ ID NO:284. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285, which includes amino acid sequences RASQSVSSYLA [SEQ

ID NO:361] as CDR1, DASNRAT [SEQ ID NO:362] as CDR2, and QQYDNLPT [SEQ ID NO:363] as CDR3 of SEQ ID NO:285.

[0053] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:284 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:285; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 358, 359, and 360, respectively, or SEQ ID NOs: 546, 359, and 547, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 361, 362, and 363, respectively.

[0054] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYAIS [SEQ ID NO:364] as CDR1, SIIPIFGTANYAQKFQG [SEQ ID NO:365] as CDR2, and EVGYGWYTKIAFDI [SEQ ID NO:366] as CDR3 of SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GTFSSYAIS [SEQ ID NO:548] as CDR1, SIIPIFGTANYAQKFQG [SEQ ID NO:365] as CDR2, and AREVGYGWYTKIAFDI [SEQ ID NO:549] as CDR3 of SEQ ID NO:286. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287, which includes amino acid sequences RASQSVSSYLA [SEQ

ID NO:367] as CDR1, DASKRAT [SEQ ID NO:368] as CDR2, and QQSSNHPST [SEQ ID NO:369] as CDR3 of SEQ ID NO:287.

[0055] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:286 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:287; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 364, 365, and 366, respectively, or SEQ ID NOs: 548, 365, and 549, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 367, 368, and 369, respectively.

[0056] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYYMH [SEQ ID NO:370] as CDR1, IINPSGGSTTYAQKFQG [SEQ ID NO:371] as CDR2, and EAADGFVGERYFDL [SEQ ID NO:372] as CDR3 of SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFTSYYMH [SEQ ID NO:550] as CDR1, IINPSGGSTTYAQKFQG [SEQ ID NO:371] as CDR2, and AREAADGFVGERYFDL [SEQ ID NO:551] as CDR3 of SEQ ID NO:288. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, which includes amino acid sequences

RSSQSLLHSNGYNYLD [SEQ ID NO:373] as CDR1, LGSNRAS [SEQ ID NO:374] as CDR2, and MQALGVPLT [SEQ ID NO:375] as CDR3 of SEQ ID NO:289.

[0057] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:288 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:289; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 370, 371, and 372, respectively, or SEQ ID NOs: 550, 371, and 551, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 373, 374, and 375, respectively.

[0058] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GYYMH [SEQ ID NO:376] as CDR1, MINPYGGSTRYAQKFQG [SEQ ID NO:377] as CDR2, and EAADGFVGERYFDL [SEQ ID NO:378] as CDR3 of SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFSGYYMH [SEQ ID NO:552] as CDR1, MINPYGGSTRYAQKFQG [SEQ ID NO:377] as CDR2, and AREAADGFVGERYFDL [SEQ ID NO:553] as CDR3 of SEQ ID NO:290. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291, which includes amino acid sequences

RSSQSLLYSNGYNYLD [SEQ ID NO:379] as CDR1, LGSNRAS [SEQ ID NO:380] as CDR2, and MQDVALPIT [SEQ ID NO:381] as CDR3 of SEQ ID NO:291.

[0059] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:290 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:291; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 376, 377, and 378, respectively, or SEQ ID NOs: 552, 377, and 553, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 379, 380, and 381, respectively.

[0060] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences IYYMH [SEQ ID NO:382] as CDR1, IINPSSGSTVYAQKFQG [SEQ ID NO:383] as CDR2, and GAGYDDEDMDV [SEQ ID NO:384] as CDR3 of SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFEIYYMH [SEQ ID NO:554] as CDR1, IINPSSGSTVYAQKFQG [SEQ ID NO:383] as CDR2, and ARGAGYDDEDMDV [SEQ ID NO:555] as CDR3 of SEQ ID NO:292. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293, which includes amino acid sequences RASQGIDSWLA [SEQ

ID NO:385] as CDR1, AASSLQS [SEQ ID NO:386] as CDR2, and QQAHSYPLT [SEQ ID NO:387] as CDR3 of SEQ ID NO:293.

[0061] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:292 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 382, 383, and 384, respectively, or SEQ ID NOs: 554, 383, and 555, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 385, 386, and 387, respectively.

[0062] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GYWMS [SEQ ID NO:388] as CDR1, NINQDGSEEYYVDSVKG [SEQ ID NO:389] as CDR2, and EANYYGNVGDDY [SEQ ID NO:390] as CDR3 of SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFGGYWMS [SEQ ID NO:556] as CDR1, NINQDGSEEYYVDSVKG [SEQ ID NO:389] as CDR2, and AREANYYGNVGDDY [SEQ ID NO:557] as CDR3 of SEQ ID NO:294. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295, which includes amino acid sequences RASQSIYNYLN [SEQ

ID NO:391] as CDR1, AASNLHS [SEQ ID NO:392] as CDR2, and QQAFHVPIT [SEQ ID NO:393] as CDR3 of SEQ ID NO:295.

[0063] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:295; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 388, 389, and 390, respectively, or SEQ ID NOs: 556, 389, and 557, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 391, 392, and 393, respectively.

[0064] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GYWMS [SEQ ID NO:394] as CDR1, NINQDGSEVYYVDSVKG [SEQ ID NO:395] as CDR2, and EANYYGNVGDDY [SEQ ID NO:396] as CDR3 of SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFPGYWMS [SEQ ID NO:558] as CDR1, NINQDGSEVYYVDSVKG [SEQ ID NO:395] as CDR2, and AREANYYGNVGDDY [SEQ ID NO:559] as CDR3 of SEQ ID NO:296. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297, which includes amino acid sequences RASQSIYNYLN [SEQ

ID NO:397] as CDR1, AASSTQS [SEQ ID NO:398] as CDR2, and QQAFHVPIT [SEQ ID NO:399] as CDR3 of SEQ ID NO:297.

[0065] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:296 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:297; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 394, 395, and 396, respectively, or SEQ ID NOs: 558, 395, and 559, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 397, 398, and 399, respectively.

[0066] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:400] as CDR1, NINQDGSEVYYVDSVKG [SEQ ID NO:401] as CDR2, and DVGPGIAYQGHFDY [SEQ ID NO:402] as CDR3 of SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:560] as CDR1, NINQDGSEVYYVDSVKG [SEQ ID NO:401] as CDR2, and ARDVGPGIAYQGHFDY [SEQ ID NO:561] as CDR3 of SEQ ID NO:298. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299, which includes amino acid sequences

RASQSIYYYLN [SEQ ID NO:403] as CDR1, AASSRQS [SEQ ID NO:404] as CDR2, and QQVYDTPLT [SEQ ID NO:405] as CDR3 of SEQ ID NO:299.

[0067] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:298 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:299; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 400, 401, and 402, respectively, or SEQ ID NOs: 560, 401, and 561, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 403, 404, and 405, respectively.

[0068] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences NYYMH [SEQ ID NO:406] as CDR1, WINPFSGGTRYAQKFQG [SEQ ID NO:407] as CDR2, and DVGSSAYYYMDV [SEQ ID NO:408] as CDR3 of SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFSNYYMH [SEQ ID NO:562] as CDR1, WINPFSGGTRYAQKFQG [SEQ ID NO:407] as CDR2, and ARDVGSSAYYYMDV [SEQ ID NO:563] as CDR3 of SEQ ID NO:300. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301, which includes amino acid sequences EASKGISSWLA [SEQ

ID NO:409] as CDR1, AASDLQS [SEQ ID NO:410] as CDR2, and QQAFLFPPT [SEQ ID NO:411] as CDR3 of SEQ ID NO:301.

[0069] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:300 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:301; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 406, 407, and 408, respectively, or SEQ ID NOs: 562, 407, and 563, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 409, 410, and 411, respectively.

[0070] In certain embodiments, the present invention provides an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWIG [SEQ ID NO:412] as CDR1, SIYPGDSDTRYSPSFQG [SEQ ID NO:413] as CDR2, and ELAYGDYKGGVDY [SEQ ID NO:414] as CDR3 of SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YSFTSYWIG [SEQ ID NO:564] as CDR1, SIYPGDSDTRYSPSFQG [SEQ ID NO:413] as CDR2, and ARELAYGDYKGGVDY [SEQ ID NO:565] as CDR3 of SEQ ID NO:302. In certain embodiments, the antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303, which includes amino acid sequences RASQSVSSSFLA [SEQ

ID NO:415] as CDR1, GASSRAT [SEQ ID NO:416] as CDR2, and QQLDSPPPT [SEQ ID NO:417] as CDR3 of SEQ ID NO:303.

[0071] In certain embodiments, the antigen-binding site is comprised within an antibody, *e.g.*, a monoclonal antibody, for example, an antibody that comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:302 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:303; or an antibody that comprises heavy chain CDRs 1-3 having the sequences of SEQ ID NOs: 412, 413, and 414, respectively, or SEQ ID NOs: 564, 413, and 565, respectively; and light chain CDRs 1-3 having the sequences of SEQ ID NOs: 415, 416, and 417, respectively.

[0072] An antibody heavy chain variable domain of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, and/or 302 can optionally be coupled to an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) 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% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an antibody constant region, such as a human antibody constant region, a human IgG1 constant region, a human IgG2 constant region, a human IgG3 constant region, or a human IgG4 constant region. In some other embodiments, the amino acid sequence of the constant region is at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) 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 a 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.

[0073] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:1 (**Ab1-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:2 (**Ab1-V_L**).

[0074] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:3 (**Ab2-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:4 (**Ab2-V_L**).

[0075] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:5 (**Ab3-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:6 (**Ab3-V_L**).

[0076] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:7 (**Ab4-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:8 (**Ab4-V_L**).

[0077] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:9 (**Ab5-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:10 (**Ab5-V_L**).

[0078] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:11 (**Ab6-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:12 (**Ab6-V_L**).

[0079] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:13 (**Ab7-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:14 (**Ab7-V_L**).

[0080] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:15 (**Ab8-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:16 (**Ab8-V_L**).

[0081] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:17 (**Ab9-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:18 (**Ab9-V_L**).

[0082] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:19 (**Ab10-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:20 (**Ab10-V_L**).

[0083] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:266 (**Ab11-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:267 (**Ab11-V_L**).

[0084] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:268 (**Ab12-V_H**), and the immunoglobulin

light chain variable region comprises the amino acid sequence of SEQ ID NO:269 (**Ab12-V_L**).

[0085] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:270 (**Ab13-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:271 (**Ab13-V_L**).

[0086] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:272 (**Ab14-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:273 (**Ab14-V_L**).

[0087] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:274 (**Ab15-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:275 (**Ab15-V_L**).

[0088] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:276 (**Ab16-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:277 (**Ab16-V_L**).

[0089] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:278 (**Ab17-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:279 (**Ab17-V_L**).

[0090] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:280 (**Ab18-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:281 (**Ab18-V_L**).

[0091] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:282 (**Ab19-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:283 (**Ab19-V_L**).

[0092] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:284 (**Ab20-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:285 (**Ab20-V_L**).

[0093] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:286 (**Ab21-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:287 (**Ab21-V_L**).

[0094] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:288 (**Ab22-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:289 (**Ab22-V_L**).

[0095] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:290 (**Ab23-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:291 (**Ab23-V_L**).

[0096] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:292 (**Ab24-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:293 (**Ab24-V_L**).

[0097] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:294 (**Ab25-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:295 (**Ab25-V_L**).

[0098] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:296 (**Ab26-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:297 (**Ab26-V_L**).

[0099] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:298 (**Ab27-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:299 (**Ab27-V_L**).

[0100] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:300 (**Ab28-V_H**), and the immunoglobulin light chain variable region comprises the amino acid sequence of SEQ ID NO:301 (**Ab28-V_L**).

[0101] In certain embodiments, the immunoglobulin heavy chain variable region comprises the amino acid sequence of SEQ ID NO:302 (**Ab29-V_H**), and the immunoglobulin

light chain variable region comprises the amino acid sequence of SEQ ID NO:303 (**Ab29-V_L**).

[0102] In certain embodiments, the present invention provides a protein that includes a human CD33 antigen-binding site including a heavy chain variable domain, which includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, or 302, and further comprises a second antigen binding site same or different from the antigen-binding site that binds to human CD33.

[0103] In certain embodiments, any of the foregoing isolated antibodies has a K_D of 1 nM or lower, 5 nM or lower, or 12 nM or lower for extracellular domain of human CD33, as measured by surface plasmon resonance (SPR) (*e.g.*, using the Biacore method described in Example 1 *infra*) or by bio-layer interferometry (BLI) (*e.g.*, using the Octet method described in Example 1 *infra*), and/or binds CD33 from a body fluid, tissue, and/or cell of a subject. In certain embodiments, any of the foregoing isolated antibodies has a K_d (*i.e.*, off-rate, also called K_{off}) equal to or lower than 1×10^{-5}, 1×10^{-4}, 1×10^{-3}, 5×10^{-3}, 0.01, 0.02, or 0.05 1/s, as measured by SPR (*e.g.*, using the Biacore method described in Example 1 *infra*) or by BLI (*e.g.*, using the Octet method described in Example 1 *infra*).

[0104] In specific embodiments of any of the antibodies or binding fragments thereof, provided herein, the antibody is a monoclonal antibody, a chimeric antibody, a diabody, a Fab fragment, a Fab' fragment, or F(ab')2 fragment, an Fv, a bispecific antibody, a bispecific Fab2, a bispecific (mab)2, a humanized antibody, an artificially-generated human antibody, bispecific T-cell engager, bispecific NK cell engager, a single chain antibody (e.g., single-chain Fv fragment or scFv), triomab, knobs-into-holes (kih) IgG with common light chain, crossmab, ortho-Fab IgG, DVD-Ig, 2 in 1-IgG, IgG-scFv, sdFv2-Fc, bi-nanobody, tandAb, dual-affinity retargeting antibody (DART), DART-Fc, scFv-HSA-scFv (where HSA = human serum albumin), or dock-and-lock (DNL)-Fab3.

[0105] In another aspect, the invention provides one or more isolated nucleic acids comprising sequences encoding an immunoglobulin heavy chain and/or immunoglobulin light chain variable region of any one of the foregoing antibodies. The invention provides one or more expression vectors that express the immunoglobulin heavy chain and/or immunoglobulin light chain variable region of any one of the foregoing antibodies. Similarly the invention provides host cells comprising one or more of the foregoing expression vectors and/or isolated nucleic acids.

[0106] Formulations including any of the proteins that include a CD33-binding domain described herein and methods of enhancing tumor cell death using these proteins and/or formulations are also provided.

[0107] In another aspect, the invention provides a method of treating a cancer, for example, a CD33-associated cancer, in a subject. The method comprises administering to the subject an effective amount of a protein containing any CD33-binding domain described herein, for example, an anti-CD33 antibody, to treat the cancer in the subject.

[0108] In another aspect, the invention provides a method of inhibiting cancer growth, for example, the growth of a CD33-associated cancer, in a subject. The method comprises exposing the subject to an effective amount of a protein containing any CD33-binding domain described herein, for example, an anti-CD33 antibody, to inhibit cancer growth in the subject.

[0109] 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 a protein containing any CD33-binding domain described herein. Exemplary cancers for treatment using the protein include, for example, wherein the cancer is selected from the group consisting of AML, myelodysplastic syndromes, chronic myelomonocytic leukemia, myeloid blast crisis of chronic myeloid leukemia, and ALLs.

[0110] In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, SEQ ID NO:484, SEQ ID NO:485, SEQ ID NO:486, SEQ ID NO:487, and SEQ ID NO:488.

[0111] In certain embodiments, the present invention provides a protein disclosed herein comprising an scFv linked to an antibody Fc domain, wherein the scFv linked to the antibody

Fc domain is represented by a sequence selected from SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, and SEQ ID NO:243.

[0112] In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence selected from SEQ ID NO:189, SEQ ID NO:196, SEQ ID NO:244, and SEQ ID NO:245.

[0113] In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID

NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484.

[0114] In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an amino acid sequence selected from SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, and SEQ ID NO:243. In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, and SEQ ID NO:243. In certain embodiments, the present invention provides a protein disclosed herein comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID

NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, and SEQ ID NO:243.

[0115] Another aspect of the present invention provides a formulation comprising a protein as disclosed herein, and a pharmaceutically acceptable carrier.

[0116] Another aspect of the present invention provides a nucleic acid encoding a chimeric antigen receptor (CAR), wherein the nucleic acid comprises a nucleic acid sequence that encodes a CD33-binding scFv comprising a sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484; a nucleic acid sequence encoding a transmembrane domain; and a nucleic acid sequence encoding an intracellular signaling domain.

[0117] Another aspect of the present invention provides a CAR comprising a CD33-binding scFv comprising a sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID

NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484; a transmembrane domain; and an intracellular signaling domain.

[0118] In certain embodiments of the nucleic acid or the CAR, the CD33-binding scFv comprises a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the CD33-binding scFv comprises a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the CD33-binding scFv comprises an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID

NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484.

[0119] In certain embodiments, the transmembrane domain is selected from the transmembrane regions of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD152, and CD154. In certain embodiments, the CD33-binding scFv is connected to the transmembrane domain by a hinge region.

[0120] In certain embodiments, the intracellular signaling domain comprises a primary signaling domain comprising a functional signaling domain of CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12. In certain embodiments, the intracellular signaling domain further comprises a costimulatory signaling domain comprising a functional signaling domain of a costimulatory receptor. In certain embodiments, the costimulatory receptor is selected from the group consisting of OX40, CD27, CD28, CD30, CD40, PD-1, CD2, CD7, CD258, NKG2C, B7-H3, a ligand that binds to CD83, ICAM-1, LFA-1 (CD11a/CD18), ICOS and 4-1BB (CD137), or any combination thereof.

[0121] Another aspect of the present invention provides a vector comprising the nucleic acid. In certain embodiments, the vector is a viral vector (*e.g.*, AAV vector, lentiviral vector, or adenoviral vector).

[0122] Another aspect of the present invention provides an immune effector cell expressing the CAR as disclosed herein. In certain embodiments, the CAR is expressed on the plasma membrane of the cell. Another aspect of the present invention provides an immune effector cell comprising the nucleic acid encoding the CAR as disclosed herein. Also provided is an immune effector cell comprising the vector that comprises the nucleic acid. In certain embodiments, the immune effector cell is a T cell (*e.g.*, $CD8^+$ T cell, $CD4^+$ T cell, or NKT cell). In certain embodiments, the effector cell is an NK cell.

[0123] Another aspect of the present invention provides a CD33/CD3-directed bispecific T-cell engager comprising a protein comprising a sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides a CD33/CD3-directed bispecific T-cell engager comprising a protein comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides a CD33/CD3-directed bispecific T-cell engager comprising a protein comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID

NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides a CD33/CD3-directed bispecific T-cell engager comprising a protein comprising an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484.

[0124] Another aspect of the present invention provides an antibody-drug conjugate comprising a protein comprising a sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466,

SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides an antibody-drug conjugate comprising a protein comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides an antibody-drug conjugate comprising a protein comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the present invention provides an antibody-drug conjugate comprising a protein comprising an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,

SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the antibody-drug conjugate further comprises a drug moiety selected from auristatin, N-acetyl-γ calicheamicin, maytansinoid, pyrrolobenzodiazepine, and SN-38.

[0125] Another aspect of the present invention provides an immunocytokine comprising a sequence at least 90% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484 connected to a cytokine. In certain embodiments, the present invention provides an immunocytokine comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID

NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484 connected to a cytokine. In certain embodiments, the present invention provides an immunocytokine comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484 connected to a cytokine. In certain embodiments, the present invention provides an immunocytokine comprising an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484

connected to a cytokine. In certain embodiments, the cytokine is selected from IL-2, IL-4, IL-10, IL-12, IL-15, TNF, and IFNα.

[0126] Another aspect of the present invention provides a method of treating a CD33-expressing cancer, the method comprising administering a therapeutically effective amount of a protein or formulation thereof disclosed herein to a subject in need thereof. In certain embodiments, the method comprises administering a therapeutically effective amount of an antibody or formulation thereof to a subject in need thereof. In certain embodiments, the method comprises administering a therapeutically effective amount of a monoclonal antibody or formulation thereof to a subject in need thereof. In certain embodiments, the method comprises administering a therapeutically effective amount of an engager or formulation thereof to a subject in need thereof.

[0127] In certain embodiments, the cancer is selected from the group consisting of acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), acute lymphoblastic leukemia (ALL), myeloproliferative neoplasms (MPNs), lymphoma, non-Hodgkin lymphomas, and classical Hodgkin lymphoma. In certain embodiments, the AML is selected from undifferentiated acute myeloblastic leukemia, acute myeloblastic leukemia with minimal maturation, acute myeloblastic leukemia with maturation, acute promyelocytic leukemia (APL), acute myelomonocytic leukemia, acute myelomonocytic leukemia with eosinophilia, acute monocytic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia (AMKL), acute basophilic leukemia, acute panmyelosis with fibrosis, and blastic plasmacytoid dendritic cell neoplasm (BPDCN). In certain embodiments, the AML is characterized by expression of CLL-1 on the AML leukemia stem cells (LSCs). In certain embodiments, the LSCs further express a membrane marker selected from CD34, CD38, CD123, TIM3, CD25, CD32, and CD96.

[0128] In certain embodiments, the AML is a minimal residual disease (MRD). In certain embodiments, the MRD is characterized by the presence or absence of a mutation selected from FLT3-ITD ((Fms-like tyrosine kinase 3)-internal tandem duplications (ITD)), NPM1 (Nucleophosmin 1), DNMT3A (DNA methyltransferase gene DNMT3A), and IDH (Isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2)). In certain embodiments, the MDS is selected from MDS with multilineage dysplasia (MDS-MLD), MDS with single lineage dysplasia (MDS-SLD), MDS with ring sideroblasts (MDS-RS), MDS with excess blasts (MDS-EB), MDS with isolated del(5q), and MDS, unclassified (MDS-U). In certain embodiments, the MDS is a primary MDS or a secondary MDS.

[0129] In certain embodiments, the ALL is selected from B-cell acute lymphoblastic leukemia (B-ALL) and T-cell acute lymphoblastic leukemia (T-ALL). In certain embodiments, the MPN is selected from polycythaemia vera, essential thrombocythemia (ET), and myelofibrosis. In certain embodiments, the non-Hodgkin lymphoma is selected from B-cell lymphoma and T-cell lymphoma. In certain embodiments, the lymphoma is selected from chronic lymphocytic leukemia (CLL), lymphoblastic lymphoma (LPL), diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), primary mediastinal large B-cell lymphoma (PMBL), follicular lymphoma, mantle cell lymphoma, hairy cell leukemia, plasma cell myeloma (PCM) or multiple myeloma (MM), mature T/NK neoplasms, and histiocytic neoplasms.

[0130] These and other aspects and advantages of the invention are illustrated by the following figures, detailed description and claims.

DESCRIPTION OF THE DRAWINGS

[0131] The invention can be more completely understood with reference to the following drawings.

[0132] **FIG. 1** shows a structural representation of the extracellular domain of human CD33 extracellular domain (ECD). CD33 ECD contains two prominent domains: distal V domain and membrane proximal C domain. Ligand binding interface is located on the V domain. Function of the C domain is unknown. ECD of CD33 is heavily glycosylated, with 2 N-linked glycosylation sites located in the V domain and 3 N-linked glycosylation sites located in the C domain. ECD of human CD33 contains several SNPs, with most prominent mutation R69G that is found in 42% patients. SNP R69G is in the V domain.

[0133] **FIG. 2** shows an alignment of the primary sequences of full length human and cyno CD33 (SEQ ID NO:598 and SEQ ID NO:599, respectively). V domain is underlined in blue, C domain is underlined in green. Difference in sequences are framed in red.

[0134] **FIGs. 3A-3K** show SPR profiles of Fab fragments from CD33 monoclonal antibodies binding to human CD33 ECD measured by Biacore at 37 ^{o}C. Each Fab fragment includes a CD33-binding clone described herein. FIG. 3A is a Biacore profile of ADI-10159; FIG. 3B is a Biacore profile of ADI-10177; FIG. 3C is a Biacore profile of ADI-11776; FIG. 3D is a Biacore profile of ADI-11801; FIG. 3E is a Biacore profile of ADI-11807; FIG. 3F is a Biacore profile of ADI-11809; FIG. 3G is a Biacore profile of ADI-11815; FIG. 3H is a Biacore profile of ADI-11819; FIG. 3I is a Biacore profile of ADI-11830; FIG. 3J is a

Biacore profile of ADI-11835; and FIG. 3K is a Biacore profile of Fab fragment from Lintuzumab.

[0135] **FIGs. 4A-4H** show SPR profiles of Fab fragments from CD33 monoclonal antibodies binding to cyno CD33 ECD measured by Biacore at 37 °C. Each Fab fragment includes a CD33-binding clone described herein. FIG. 4A is a Biacore profile of ADI-10159; FIG. 4B is a Biacore profile of ADI-10177; FIG. 4C is a Biacore profile of ADI-11776; FIG. 4D is a Biacore profile of ADI-11807; FIG. 4E is a Biacore profile of ADI-11809; FIG. 4F is a Biacore profile of ADI-11819; FIG. 4G is a Biacore profile of ADI-11830; and FIG. 4H is a Biacore profile of ADI-11835.

[0136] **FIGs. 5A-5T** show SPR profiles of FABs from CD33 monoclonal antibodies binding to V domain and C domain of human CD33 measured at 37 °C. Each Fab fragment includes a CD33-binding clone described herein. FIGs. 5A-5J represent binding to the V-domain; panels K-T represent binding to the C domain. FIGs. 5A and 5K are Biacore profiles of ADI-10159; FIGs. 5B and 5L are Biacore profiles of ADI-10177; FIGs. 5C and 5M are Biacore profiles of ADI-11776; FIGs. 5D and 5N are Biacore profiles of ADI-11801; FIGs. 5E and 5O are Biacore profiles of ADI-11807; FIGs. 5F and 5P are Biacore profiles of ADI-11809; FIGs. 5G and 5Q are Biacore profiles of ADI-11815; FIGs. 5H and 5R are Biacore profiles of ADI-11819; FIGs. 5I and 5S are Biacore profiles of ADI-11830; and FIGs. 5J and 5T are Biacore profiles of ADI-11835.

[0137] **FIGs. 6A-6D** show SPR profiles of an Fab that comprises ADI-11815 binding to different domains of human CD33 and human CD33 having an R69G point mutation. **FIG. 6**A: Fab binding to human CD33 ECD; **FIG. 6**B: Fab binding to V domain; **FIG. 6**C: Fab binding to C domain: **FIG. 6D**: Fab binding to human CD33 having R69G.

[0138] **FIGs. 7A-7D** show SPR profiles of a Fab that comprises ADI-11801 binding to different domains of human CD33 and human CD33 having an R69G point mutation. FIG. 7A: human CD33 ECD; FIG. 7B: V domain; FIG. 7C: C domain: FIG. 7D: human CD33 having R69G.

[0139] **FIG. 8** are bar graphs showing binding of monoclonal antibodies comprising CD33-binding clones to CD33 expressed on Molm-13 human AML cells. CD33 antibody Lintuzumab was also tested, and mean fluorescence intensity (MFI) was plotted. Five of the six antibodies show higher binding signal to CD33 compared to Lintuzumab.

[0140] **FIG. 9** are bar graphs showing internalization of CD33 antibodies on Molm-13 cells after 24 hours. All the CD33 antibodies showed similar internalization after 24 hours. Lintuzumab showed slightly higher internalization compare to other anti-CD33 antibodies.

[0141] **FIGs. 10A-10B** show binding of CD33-targeting TriNKETs to human NKG2D expressed on EL4-hNKG2D and KHYG-1 cells. FIG. 10A shows binding of CD33-targeting TriNKETs to human NKG2D recombinantly expressed on EL4 cells. FIG. 10B shows binding of CD33-targeting TriNKETs to human NKG2D expressed on KHYG-1 cells. For each TriNKET, signal fold-over-background (FOB) was similar on both EL4-hNKG2D cells and KHYG-1 cells, and the rank of binding was also maintain on both cell lines.

[0142] **FIG. 11** shows binding of CD33-targeting TriNKETs to CD33 expressed on human AML Molm-13 cells. Four different CD33-binding clones were used with five NKG2D-binding clones to make a total of 20 different TriNKETs. NKG2D-binding domains TriNKET do not affect the binding of CD33-binding clones to CD33.

[0143] **FIG. 12** is a graph showing that rested human NK cells are activated by CD33-targeting TriNKETs in co-culture with CD33-expressing THP-1 AML cells.

[0144] **FIG. 13** is a bar graph showing that CD33 TriNKETs induce rested NK cell mediated killing of Molm-13 AML cells.

[0145] **FIG. 14** is a bar graph showing that CD33 TriNKETs induce activated NK cell mediated killing of THP-1 cells.

[0146] **FIG. 15A** are line graphs showing that TriNKETs mediate KHYG-1 killing of Molm-13 AML cells. **FIG. 15B** are line graphs showing that TriNKETs mediate rested human NK cell killing of Molm-13 human AML cells.

[0147] **FIG. 16** are line graphs showing that TriNKETs mediate KHYG-1 killing of EOL-1 AML cells.

[0148] **FIG. 17A** are line graphs showing that TriNKETs mediate KHYG-1 killing of THP-1 cells. **FIG. 17B** are line graphs showing that TriNKETs mediate rested human NK cell killing of THP-1 human AML cells.

[0149] **FIG. 18** is a representation of a multispecific binding protein that contains an NKG2D-binding domain (right arm), a CD33-binding domain (left arm), and an Fc domain or a portion thereof that binds to CD16.

[0150] **FIG. 19** is a representation of a multispecific binding protein that includes a NKG2D-binding domain or a CD33-binding domain, either one of which can be in a scFv format, and an Fc domain or a portion thereof that binds to CD16.

[0151] **FIG. 20** is a representation of a 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.

[0152] **FIG. 21** is a representation of a TriNKET in the KiH Common Light Chain (LC) form, which involves the knobs-into-holes (KIHs) technology. KiH is a heterodimer containing 2 Fabs binding to target 1 and 2, and an Fc stabilized by heterodimerization mutations. TriNKET in the KiH format may be an heterodimeric construct with 2 Fabs binding to target 1 and target 2, containing two different heavy chains and a common light chain that pairs with both heavy chains.

[0153] **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 variable domain of Fab targeting antigen 1 Construct contains normal Fc.

[0154] **FIG. 23** is a representation of a TriNKET in the Orthogonal Fab interface (Ortho-Fab) form, which is an heterodimeric construct that contains 2 Fabs binding to target1 and target 2 fused to Fc. LC-HC pairing is ensured by orthogonal interface. Heterodimerization is ensured by mutations in the Fc.

[0155] **FIG. 24** is a representation of a TrinKET in the 2-in-1 Ig format.

[0156] **FIG. 25** is a representation of a TriNKET in the ES form, which is an heterodimeric construct containing two different Fabs binding to target 1 and target 2 fused to the Fc. Heterodimerization is ensured by electrostatic steering mutations in the Fc.

[0157] **FIG. 26** is a representation of a TriNKET in the 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, resulting in bispecific antibodies. Fab Arm Exchange form (cFae) is a heterodimer containing 2 Fabs binding to target 1 and 2, and an Fc stabilized by heterodimerization mutations.

[0158] **FIG. 27** is a representation of a TriNKET in the SEED Body form, which is an heterodimer containing two Fabs binding to target 1 and 2, and an Fc stabilized by heterodimerization mutations.

[0159] **FIG. 28** is a representation of a TriNKET in the LuZ-Y form, in which leucine zipper is used to induce heterodimerization of two different HCs. LuZ-Y form is a heterodimer containing two different scFabs binding to target 1 and 2, fused to Fc.

[0160] **FIG. 29** is a representation of a TriNKET in the Cov-X-Body form.

[0161] **FIGs. 30A-30B** represent TriNKETs in the κλ-Body forms, which are an heterodimeric constructs with two different Fabs fused to Fc stabilized by heterodimerization

mutations: Fab1 targeting antigen 1 contains kappa LC, while second Fab 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.

[0162] **FIG. 31** is an Oasc-Fab heterodimeric construct that includes Fab binding to target 1 and scFab binding to target 2 fused to Fc. Heterodimerization is ensured by mutations in the Fc.

[0163] **FIG. 32** is a DuetMab, which is an heterodimeric construct containing two different Fabs binding to antigens 1 and 2, and Fc stabilized by heterodimerization mutations. Fab 1 and 2 contain differential S-S bridges that ensure correct light chain (LC) and heavy chain (HC) pairing.

[0164] **FIG. 33** is a CrossmAb, which is an heterodimeric construct with two different Fabs 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] **FIG. 34** is a Fit-Ig, which is a homodimeric constructs where Fab binding to antigen 2 is fused to the N terminus of HC of Fab that binds to antigen 1. The construct contains wild-type Fc.

[0166] **FIG. 35** is a graph showing binding of A49-F3'-TriNKET-I07 and I07-F405L mAb to cell surface human NKG2D expressed on EL4 cells.

[0167] **FIGs. 36A-36B** are graphs showing binding of A49-F3'-TriNKET-I07 and I07-F405L mAb to $CD33^+$ human AML cell lines Mv4-11 (FIG. 36A) and Molm-13 (FIG. 36B).

[0168] **FIGs. 37A-37B** are graphs showing internalization of A49-F3'-TriNKET-I07 and I07-F405L mAb after incubation with EOL-1 cells (FIG. 37A) and Molm-13 cells (FIG. 37B).

[0169] **FIGs. 38A-38D** are graphs showing specific lysis of Molm-13 (FIG. 38A), EOL-1 (FIG. 38B), and THP-1 (FIGs. 38C and 38D) human AML cells by rested human NK cells in the presence of A49-F3'-TriNKET-I07 and anti-CD33 monoclonal antibodies.

[0170] **FIG. 39** is a series of flow cytograms showing the expression level of CD3, CD8, NKG2D, and CD16 on isolated primary $CD8^+$ T cells.

[0171] **FIGs. 40A-40B** are graphs showing specific lysis of Molm-13 cells by isolated primary $CD8^+$ T cells in the presence of A49-F3'-TriNKET-I07, A49-F3'-TriNKET-H76, a non-target TriNKET, or I07-F405L mAb (denoted as I07 in the figures). The primary $CD8^+$ T cells in FIG. 40A were isolated from PBMCs of donor 1, and the primary $CD8^+$ T cells in

FIG. 40B were isolated from PBMCs of donor 2. The dotted lines indicate specific lysis of Molm-13 cells by $CD8^+$ T cells in the absence of TriNKET or antibody.

[0172] **FIGs. 41A-41E** are histograms showing the binding of A49-F3'-TriNKET-I07 to NK cells (FIG. 41A), $CD8^+$ T cells (FIG. 41B), $CD4^+$ T cells (FIG. 41C), B cells (FIG. 41D), and monocytes (FIG. 41E) in human whole blood. The dotted lines without fill represent binding of A49-F3'-TriNKET-I07 to the cells; the solid lines with fill represent binding of human IgG1 isotype control to the cells.

[0173] **FIGs. 42A-42B** are graphs showing CD33 expression on monocytes. FIG. 42A shows CD33 expression on monocytes from four healthy donors (dark gray) and Molm-13 (light grey). The bottom five rows are signals from the cell samples stained with an anti-CD33 antibody; the top five rows are signals from the same samples stained with an isotype antibody. FIG. 42B shows CD33 expression on monocytes from the same donor before (light grey) and after (dark grey) negative selection for monocytes.

[0174] **FIGs. 43A-43B** are graphs showing long-term cytotoxicity of NK cells against Molm-13 AML cells and human primary monocytes in the presence of A49-F3'-TriNKET-I07. Proliferation of the target cells are plotted against the time of co-culture with NK cells in the presence of A49-F3'-TriNKET-I07 or PMA + ionomycin. FIG. 43A represents the results from an experiment using NK cells from one donor, and FIG. 43B represents the results from another experiment using NK cells from a different donor.

[0175] **FIG. 44** illustrates a trispecific antibody (TriNKET) that contains a CD33-binding scFv, a NKG2D-targeting Fab, and a heterodimerized antibody constant domain that binds CD16. The antibody format is referred to herein as F3'-TriNKET.

DETAILED DESCRIPTION

[0176] In one aspect, the invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and/or Cynomolgus/Rhesus (cyno) CD33. In one aspect, the present invention provides an antigen binding site that recognizes and binds one or more conformational epitopes on the extracellular domain of human CD33 and/or Cynomolgus/Rhesus (cyno) CD33. In one aspect, the present invention provides an antigen binding site that recognizes and binds one or more conformational epitopes on the extracellular domain of human CD33 but does not recognize and/or bind one or more conformational epitopes on the extracellular domain of cyno CD33. In one aspect, the present invention provides an antigen binding site that binds to the R69G allele of human CD33. In

one aspect, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the R69G allele of human CD33. In one aspect, the present invention provides an antigen binding site that binds to an epitope on human CD33 that includes R69. In one aspect, the present invention provides an antigen binding site that binds to the S128N allele of human CD33. In one aspect, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33. In one aspect, the present invention provides an antigen binding site that binds to an epitope on human CD33 that includes S128. In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain, which binds to the extracellular domain in human CD33 and/or cyno CD33, irrespective of the glycosylation profile of the targeted CD33.

[0177] In certain embodiments the present invention provides an antigen binding site, which binds to the extracellular domain in human CD33 and/or cyno CD33, such that the epitopes are unique compared to the epitopes targeted by one or more known anti-CD33 antibodies in the art. In certain embodiments, the present invention provides an antigen binding site, which binds to the extracellular domain in human CD33 and/or cyno CD33, and shows human or Cynomolgus/Rhesus (cyno) CD33 cross reactivity and high affinity binding to the target CD33.

[0178] The invention provides antigen-binding proteins that bind CD33 on a cancer cell and pharmaceutical compositions comprising such proteins, and therapeutic methods using such proteins and pharmaceutical compositions, including for the treatment of cancer. Various aspects of the invention are set forth in the sections below; however, aspects of the invention described in one particular section are not to be limited to any particular section.

[0179] To facilitate an understanding of the present invention, a number of terms and phrases are defined below.

[0180] The terms “a” and “an” as used herein mean “one or more” and include the plural unless the context is inappropriate.

[0181] 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. All the amino acid positions in heavy or light chain variable regions disclosed herein are numbered according to Kabat numbering.

[0182] The CDRs of an antigen-binding site can be determined by the methods described in Kabat et al., J. Biol. Chem. 252, 6609-6616 (1977) and Kabat et al., Sequences of protein of immunological interest. (1991), Chothia et al., J. Mol. Biol. 196:901-917 (1987), and MacCallum et al., J. Mol. Biol. 262:732-745 (1996). The CDRs determined under these definitions typically include overlapping or subsets of amino acid residues when compared against each other. In certain embodiments, the term "CDR" is a CDR as defined by MacCallum et al., J. Mol. Biol. 262:732-745 (1996) and Martin A., Protein Sequence and Structure Analysis of Antibody Variable Domains, in Antibody Engineering, Kontermann and Dubel, eds., Chapter 31, pp. 422-439, Springer-Verlag, Berlin (2001). In certain embodiments, the term "CDR" is a CDR as defined by Kabat et al., J. Biol. Chem. 252, 6609-6616 (1977) and Kabat et al., Sequences of protein of immunological interest. (1991). In certain embodiments, heavy chain CDRs and light chain CDRs of an antibody are defined using different conventions. For example, in certain embodiments, the heavy chain CDRs are defined according to MacCallum (*supra*), and the light CDRs are defined according to Kabat (*supra*). CDRH1, CDRH2 and CDRH3 denote the heavy chain CDRs, and CDRL1, CDRL2 and CDRL3 denote the light chain CDRs.

[0183] 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.

[0184] 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.

[0185] 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*.

[0186] 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].

[0187] 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.

[0188] 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.

[0189] 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.

[0190] 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.

[0191] 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.

[0192] 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.

[0193] Various features and aspects of the invention are discussed in more detail below.

I. Antigen-Binding Site

[0194] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:2. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:21, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:22, and a CDR3 sequence

represented by the amino acid sequence of SEQ ID NO:23. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:434, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:22, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:435. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:2, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:24, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:25, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:26.

[0195] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:4. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:27, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:28, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:29. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:181, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:28, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:436. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:4, includes a CDR1 sequence represented by the

amino acid sequence of SEQ ID NO:30, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:31, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:32.

[0196] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:6. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:33, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:34, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:35. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:183, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:34, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:184. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:36, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:37, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:38. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:36, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:185, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:38. In certain embodiments, the antigen-binding site comprises an amino acid sequence at least 90% (*e.g.*, at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ

ID NO:188. In certain embodiments, the antigen-binding site comprises an amino acid sequence at least 95% identical to SEQ ID NO:188. In certain embodiments, the antigen-binding site comprises an amino acid sequence at least 99% identical to SEQ ID NO:188. In certain embodiments, the antigen-binding site comprises the amino acid sequence of SEQ ID NO:188.

[0197] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:8. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:39, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:40, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:41. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:437, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:40, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:438. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:42, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:43, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:44.

[0198] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:10. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:45, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:46, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:47. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:181, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:46, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:182. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:10, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:48, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:49, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:50. In certain embodiments, the antigen-binding site comprises an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:198. In certain embodiments, the antigen-binding site comprises an amino acid sequence at least 95% identical to SEQ ID NO:198. In certain embodiments, the antigen-binding site comprises an amino acid sequence at least 99% identical to SEQ ID NO:198. In certain embodiments, the antigen-binding site comprises the amino acid sequence of SEQ ID NO:198.

[0199] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:12. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11, includes a

CDR1 sequence represented by the amino acid sequence of SEQ ID NO:51, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:52, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:53. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:181, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:52, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:439. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:12, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:54, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:55, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:56.

[0200] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:14. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:57, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:58, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:59. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:440, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:58, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:441. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least

90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:60, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:61, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:62.

[0201] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:16. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:63, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:64, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:65. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:442, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:64, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:443. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:16, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:66, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:67, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:68.

[0202] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:18. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:69, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:70, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:71. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:181, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:70, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:444. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:18, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:72, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:73, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:74.

[0203] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:20. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:75, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:76, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:77. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19, includes a CDR1 sequence

represented by the amino acid sequence of SEQ ID NO:445, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:76, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:446. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:20, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:78, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:79, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:80.

[0204] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:267. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:304, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:305, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:306. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:528, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:305, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:529. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:307, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:308, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:309.

[0205] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:269. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:310, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:311, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:312. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:530, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:311, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:531. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:313, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:314, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:315.

[0206] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:271. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:316, a CDR2

sequence represented by the amino acid sequence of SEQ ID NO:317, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:318. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:532, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:317, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:533. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:319, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:320, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:321.

[0207] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:273. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:322, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:323, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:324. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:534, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:323, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:535. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100%) identical to the amino acid sequence of SEQ ID NO:273, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:325, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:326, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:327.

[0208] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:275. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:328, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:329, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:330. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:536, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:329, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:537. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:331, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:332, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:333.

[0209] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:277. In certain

embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:334, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:335, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:336. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:538, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:335, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:539. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:337, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:338, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:339.

[0210] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:279. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:340, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:341, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:342. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:540, a CDR2 sequence

represented by the amino acid sequence of SEQ ID NO:341, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:541. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:343, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:344, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:345.

[0211] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:281. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:346, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:347, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:348. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:542, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:347, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:543. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:349, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:350, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:351.

[0212] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence

at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:283. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:352, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:353, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:354. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:544, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:353, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:545. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:355, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:356, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:357.

[0213] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:285. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:358, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:359, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:360. In certain embodiments, an

antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:546, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:359, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:547. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:361, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:362, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:363.

[0214] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:287. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:364, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:365, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:366. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:548, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:365, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:549. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:367, a CDR2 sequence represented

by the amino acid sequence of SEQ ID NO:368, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:369.

[0215] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:289. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:370, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:371, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:372. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:550, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:371, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:551. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:373, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:374, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:375.

[0216] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:291. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%,

97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:376, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:377, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:378. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:552, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:377, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:553. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:379, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:380, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:381.

[0217] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:293. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:382, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:383, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:384. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:554, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:383, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:555. In certain embodiments, an

antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:385, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:386, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:387.

[0218] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:295. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:388, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:389, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:390. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:556, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:389, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:557. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:391, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:392, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:393.

[0219] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296, and an antibody light chain variable

domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:297. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:394, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:395, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:396. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:558, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:395, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:559. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:397, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:398, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:399.

[0220] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:299. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:400, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:401, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:402. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%,

or 100%) identical to the amino acid sequence of SEQ ID NO:298, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:560, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:401, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:561. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:403, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:404, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:405.

[0221] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:301. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:406, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:407, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:408. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:562, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:407, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:563. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:409, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:410, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:411.

[0222] In certain embodiments, the present invention provides an antigen-binding site that includes an antibody heavy chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302, and an antibody light chain variable domain that includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to SEQ ID NO:303. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:412, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:413, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:414. In certain embodiments, an antigen-binding site that includes an antibody heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:564, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:413, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:565. In certain embodiments, an antigen-binding site that includes an antibody light chain variable domain with an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303, includes a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:415, a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:416, and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:417.

[0223] In each of the foregoing embodiments, it is contemplated herein that immunoglobulin heavy chain variable region sequences and/or light chain variable region sequences that together bind CD33 may contain amino acid alterations (*e.g.*, at least 1, 2, 3, 4, 5, or 10 amino acid substitutions, deletions, or additions) in the framework regions of the heavy and/or light chain variable regions without affecting their ability to bind to CD33 significantly.

[0224] Table 1 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination (either as a Fab fragment or a single-chain variable fragment (scFv)), can bind to CD33. Unless indicated otherwise, the CDR sequences provided in Table 1 are determined under Kabat. The CD33-binding domains can vary in

their binding affinity to CD33. Table 1 also lists scFv forms of the CD33-binding heavy and light chain variable domains. The exemplary nucleic acid sequences listed in Table 1 are predicted possible nucleic acid sequences that the listed corresponding peptide sequences originated from, and were generated using EMBL-EBI's Protein Sequence Back-translation program.

Table 1	VH	VL
ADI-10159 [Ab1] (G59)	EVQLVESGGGLVQPGGSLRLSC AASGFTFSSYGMSWVRQAPGK GLEWVANIKQDGSEKYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCAREGGPYYDSS GYFVYYGMDVWGQGTTVTVSS [SEQ ID NO:1] CDR1: FTFSSYGMS [SEQ ID NO:21] (non-Kabat) or SYGMS [SEQ ID NO:434] CDR2: NIKQDGSEKYYVDSVKG [SEQ ID NO:22] CDR3: AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:23] (non-Kabat) or EGGPYYDSSGYFVYYGMDV [SEQ ID NO:435]	DIQMTQSPSTLSASVGDRVTITCR ASQSISSWLAWYQQKPGKAPKL LIYDASSLESGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYESF PTFGGGTKVEIK [SEQ ID NO:2] CDR1: RASQSISSWLA [SEQ ID NO:24] CDR2: DASSLES [SEQ ID NO:25] CDR3: QQYESFPT [SEQ ID NO:26]
scFv of Ab1	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLI YDASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYESFPTF G*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQPG GSLRLSCAASGFTFSSYGMSWVRQAPGK*C*LEWVANIKQDGSEKYYV DSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSS GYFVYYGMDVWGQGTTVTVSS [SEQ ID NO:206] EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYGMSWVRQAPGK*C*LE WVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCAREGGPYYDSSGYFVYYGMDVWGQGTTVTVSS**GGGGSGGG GSGGGGSGGGGS**DIQMTQSPSTLSASVGDRVTITCRASQSISSWLA WYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTEFTLTISSLQPDD FATYYCQQYESFPTFG*C*GTKVEIK [SEQ ID NO:207]	
Exemplary nucleotide sequence of Ab1	GACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGACGCCAGCAGCCTGGAGAGCGGCGTGCC CAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGA	

Table 1	VH	VL
scFv	CCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTGCC AGCAGTACGAGAGCTTCCCCACCTTCGGCTGCGGCACCAAGGTGG AGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGC GGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGAGAG CGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCT GCGCCGCCAGCGGCTTCACCTTCAGCAGCTACGGCATGAGCTGGG TGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAACATC AAGCAGGACGGCAGCGAGAAGTACTACGTGGACAGCGTGAAGGG CAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGTACC TGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTAC TGCGCCAGGGAGGGCGGCCCCTACTACGACAGCAGCGGCTACTTC GTGTACTACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGAC CGTGAGCAGC [SEQ ID NO:246] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACGGCATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAAGCAGGACGGCAGCGAGAAGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGGCGGCCCCTACT ACGACAGCAGCGGCTACTTCGTGTACTACGGCATGGACGTGTGGG GCCAGGGCACCACCGTGACCGTGAGCAGCGGCGGCGGCGGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCA GCGACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCAT CAGCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCC CCAAGCTGCTGATCTACGACGCCAGCAGCCTGGAGAGCGGCGTG CCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCT GACCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTG CCAGCAGTACGAGAGCTTCCCCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAG [SEQ ID NO:247]	
ADI-10177 [Ab2]	EVQLVESGGGLVQPGGSLRLSC AASGFTFSSYWMSWVRQAPGK GLEWVANIKQDGSEKYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCARPLNAGELDV WGQGTMVTVSS [SEQ ID NO:3] CDR1: FTFSSYWMS [SEQ ID NO:27] (non-Kabat) or SYWMS [SEQ ID NO:181] CDR2: NIKQDGSEKYYVDSVKG [SEQ ID NO:28] CDR3: ARPLNAGELDV [SEQ ID NO:29] (non-Kabat) or	DIQMTQSPSTLSASVGDRVTITCR ASQSISSWLAWYQQKPGKAPKL LIYEASSLESGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQLESY PLTFGGGTKVEIK [SEQ ID NO:4] CDR1: RASQSISSWLA [SEQ ID NO:30] CDR2: EASSLES [SEQ ID NO:31] CDR3: QQLESYPLT [SEQ ID NO:32]

Table 1	VH	VL
	PLNAGELDV [SEQ ID NO:436]	
scFv of Ab2	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLI YEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQLESYPLT FG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQP GGSLRLSCAASGFTFSSYWMSWVRQAPGK***C***LEWVANIKQDGSEKY YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGEL DVWGQGTMVTVSS [SEQ ID NO:208] EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK***C***LE WVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCARPLNAGELDVWGQGTMVTVSS**GGGGSGGGGSGGGGSGG GGS**DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAP KLLIYEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQLES YPLTFG***C***GTKVEIK [SEQ ID NO:209]
Exemplary nucleotide sequence of Ab2 scFv	GACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGAGGCCAGCAGCCTGGAGAGCGGCGTGCC CAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGA CCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTGCC AGCAGCTGGAGAGCTACCCCCTGACCTTCGGCTGCGGCACCAAGG TGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGA GAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGA GCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACTGGATGAGCT GGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAAC ATCAAGCAGGACGGCAGCGAGAAGTACTACGTGGACAGCGTGAA GGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGT ACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGGCCCCTGAACGCCGGCGAGCTGGACGTGTGGGG CCAGGGCACCATGGTGACCGTGAGCAGC [SEQ ID NO:248] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAAGCAGGACGGCAGCGAGAAGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGCCCCTGAACGCCGGCG AGCTGGACGTGTGGGGCCAGGGCACCATGGTGACCGTGAGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCA GCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGAGCCCCAGC ACCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAG GGCCAGCCAGAGCATCAGCAGCTGGCTGGCCTGGTACCAGCAGA AGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGAGGCCAGCAGC CTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGG

Table 1	VH	VL
	CACCGAGTTCACCCTGACCATCAGCAGCCTGCAGCCCGACGACTT CGCCACCTACTACTGCCAGCAGCTGGAGAGCTACCCCCTGACCTT CGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:249]	
ADI-11776 [Ab3] (H76)	EVQLLESGGGLVQPGGSLRLSC AASGFTFSKYTMSWVRQAPGK GLEWVSAIVGSGESTYFADSVK GRFTISRDNSKNTLYLQMNSLR AEDTAVYYCAREGGPYYDSSG YFVYYGMDVWGQGTTVTVSS [SEQ ID NO:5] CDR1: FTFSKYTMS [SEQ ID NO:33] (non-Kabat) or KYTMS [SEQ ID NO:183] CDR2: AIVGSGESTYFADSVKG [SEQ ID NO:34] CDR3: AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:35] (non-Kabat) or EGGPYYDSSGYFVYYGMDV [SEQ ID NO:184]	DIQMTQSPSTLSASVGDRVTITCR ASQSISSWLAWYQQKPGKAPKL LIYKASSLESGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYDD LPTFGGGTKVEIK [SEQ ID NO:6] CDR1: RASQSISSWLA [SEQ ID NO:36] CDR2: KASSLES [SEQ ID NO:37] or KASSLE [SEQ ID NO:185] (non-Kabat) CDR3: QQYDDLPT [SEQ ID NO:38]
scFv of Ab3	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLI YKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPT FG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLLESGGGLVQP GGSLRLSCAASGFTFSKYTMSWVRQAPGK*C*LEWVSAIVGSGESTYF ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREGGPYYDS SGYFVYYGMDVWGQGTTVTVSS [SEQ ID NO:198] EVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGK*C*LE WVSAIVGSGESTYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAV YYCAREGGPYYDSSGYFVYYGMDVWGQGTTVTVSS**GGGGSGGGG SGGGGSGGGGS**DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAW YQQKPGKAPKLLIYKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFA TYYCQQYDDLPTFG*C*GTKVEIK [SEQ ID NO:210]	
Exemplary nucleotide sequence of Ab3 scFv	GACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACAAGGCCAGCAGCCTGGAGAGCGGCGTGCC CAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGA CCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTGCC AGCAGTACGACGACCTGCCCACCTTCGGCTGCGGCACCAAGGTGG AGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGC	

Table 1	VH	VL
	GGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGCTGGAGAG CGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCT GCGCCGCCAGCGGCTTCACCTTCAGCAAGTACACCATGAGCTGGG TGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGAGCGCCATC GTGGGCAGCGGCGAGAGCACCTACTTCGCCGACAGCGTGAAGGG CAGGTTCACCATCAGCAGGGACAACAGCAAGAACACCCTGTACC TGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTAC TGCGCCAGGGAGGGCGGCCCCTACTACGACAGCAGCGGCTACTTC GTGTACTACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGAC CGTGAGCAGC [SEQ ID NO:250] GAGGTGCAGCTGCTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAAGTACACCATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGAGCGCCATCGTGGGCAGCGGCGAGAGCACCTAC TTCGCCGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CAGCAAGAACACCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGGCGGCCCCTACT ACGACAGCAGCGGCTACTTCGTGTACTACGGCATGGACGTGTGGG GCCAGGGCACCACCGTGACCGTGAGCAGCGGCGGCGGCGGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCA GCGACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCAT CAGCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCC CCAAGCTGCTGATCTACAAGGCCAGCAGCCTGGAGAGCGGCGTG CCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCT GACCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTG CCAGCAGTACGACGACCTGCCCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAG [SEQ ID NO:251]	
ADI-11801 [Ab4]	QVQLVQSGAEVKKPGASVKVS CKASGYTFSDYYMHWVRQAPG QGLEWMGMINPSWGSTSYAQK FQGRVTMTRDTSTSTVYMELSS LRSEDTAVYYCAREAADGFVGE RYFDLWGRGTLVTVSS [SEQ ID NO:7] CDR1: YTFSDYYMH [SEQ ID NO:39] (non-Kabat) or DYYMH [SEQ ID NO:437] CDR2: MINPSWGSTSYAQKFQG [SEQ ID NO:40] CDR3: AREAADGFVGERYFDL [SEQ ID NO:41] (non-Kabat) or EAADGFVGERYFDL [SEQ ID NO:438]	DIVMTQSPLSLPVTPGEPASISCR SSQSLLYSNGYNYLDWYLQKPG QSPQLLIYLGSNRASGVPDRFSGS GSGTDFTLKISRVEAEDVGVYYC MQDVALPITFGGGTKVEIK [SEQ ID NO:8] CDR1: RSSQSLLYSNGYNYLD [SEQ ID NO:42] CDR2: LGSNRAS [SEQ ID NO:43] CDR3: MQDVALPIT [SEQ ID NO:44]

Table 1	VH	VL
scFv of Ab4	DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQS PQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQ DVALPITFG<u>C</u>GTKVEIK<u>**GGGGSGGGGSGGGGSGGGGS**</u>QVQLVQSG AEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQ<u>C</u>LEWMGMIN PSWGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAR EAADGFVGERYFDLWGRGTLVTVSS [SEQ ID NO:211] QVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQ<u>C</u>L EWMGMINPSWGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDT AVYYCAREAADGFVGERYFDLWGRGTLVTVSS<u>**GGGGSGGGGSGG GGSGGGGS**</u>DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLD WYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAED VGVYYCMQDVALPITFG<u>C</u>GTKVEIK [SEQ ID NO:212]	
Exemplary nucleotide sequence of Ab4 scFv	GACATCGTGATGACCCAGAGCCCCCTGAGCCTGCCCGTGACCCCC GGCGAGCCCGCCAGCATCAGCTGCAGGAGCAGCCAGAGCCTGCT GTACAGCAACGGCTACAACTACCTGGACTGGTACCTGCAGAAGCC CGGCCAGAGCCCCCAGCTGCTGATCTACCTGGGCAGCAACAGGG CCAGCGGCGTGCCCGACAGGTTCAGCGGCAGCGGCAGCGGCACC GACTTCACCCTGAAGATCAGCAGGGTGGAGGCCGAGGACGTGGG CGTGTACTACTGCATGCAGGACGTGGCCCTGCCCATCACCTTCGG CTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCG GCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCAG GTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGGCGC CAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCAGCG ACTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCCTGG AGTGGATGGGCATGATCAACCCCAGCTGGGGCAGCACCAGCTAC GCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACACCAG CACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCGAGG ACACCGCCGTGTACTACTGCGCCAGGGAGGCCGCCGACGGCTTCG TGGGCGAGAGGTACTTCGACCTGTGGGGCAGGGGCACCCTGGTG ACCGTGAGCAGC [SEQ ID NO:252] CAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGG CGCCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCA GCGACTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCC TGGAGTGGATGGGCATGATCAACCCCAGCTGGGGCAGCACCAGC TACGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACAC CAGCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGCCGCCGACGGC TTCGTGGGCGAGAGGTACTTCGACCTGTGGGGCAGGGGCACCCTG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCGTGATGA CCCAGAGCCCCCTGAGCCTGCCCGTGACCCCCGGCGAGCCCGCCA GCATCAGCTGCAGGAGCAGCCAGAGCCTGCTGTACAGCAACGGC TACAACTACCTGGACTGGTACCTGCAGAAGCCCGGCCAGAGCCCC CAGCTGCTGATCTACCTGGGCAGCAACAGGGCCAGCGGCGTGCCC GACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAA	

Table 1	VH	VL
	GATCAGCAGGGTGGAGGCCGAGGACGTGGGCGTGTACTACTGCA TGCAGGACGTGGCCCTGCCCATCACCTTCGGCTGCGGCACCAAGG TGGAGATCAAG [SEQ ID NO:253]	
ADI-11807 [Ab5] (I07)	EVQLVESGGGLVQPGGSLRLSC AASGFTFGSYWMSWVRQAPGK GLEWVATIKQDGSEKSYVDSVK GRFTISRDNAKNSLYLQMNSLR AEDTAVYYCARPLNAGELDVW GQGTMVTVSS [SEQ ID NO:9] CDR1: FTFGSYWMS [SEQ ID NO:45] (non-Kabat) or SYWMS [SEQ ID NO:181] CDR2: TIKQDGSEKSYVDSVKG [SEQ ID NO:46] CDR3: ARPLNAGELDV [SEQ ID NO:47] (non-Kabat) or RPLNAGELDV [SEQ ID NO:182]	DIQMTQSPSTLSASVGDRVTITCR ASQSISSWLAWYQQKPGKAPKL LIYEASSLESGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQSQSY PPITFGGGTKVEIK [SEQ ID NO:10] CDR1: RASQSISSWLA [SEQ ID NO:48] CDR2: EASSLES [SEQ ID NO:49] CDR3: QQSQSYPPIT [SEQ ID NO:50]
scFv of Ab5	***I07 scFv*** DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLI YEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPI TFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQ PGGSLRLSCAASGFTFGSYWMSWVRQAPGK***C***LEWVATIKQDGSEKS YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGEL DVWGQGTMVTVSS [SEQ ID NO:188] EVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPGK***C***LE WVATIKQDGSEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCARPLNAGELDVWGQGTMVTVSS**GGGGSGGGGSGGGGSGG GGS**DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAP KLLIYEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQS YPPITFG***C***GTKVEIK [SEQ ID NO:213]	
Exemplary nucleotide sequence of Ab5 scFv	GACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGAGGCCAGCAGCCTGGAGAGCGGCGTGCC CAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGA CCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTGCC AGCAGAGCCAGAGCTACCCCCCCATCACCTTCGGCTGCGGCACCA AGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGT GGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGC TGAGCTGCGCCGCCAGCGGCTTCACCTTCGGCAGCTACTGGATGA	

Table 1	VH	VL
	GCTGGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCC ACCATCAAGCAGGACGGCAGCGAGAAGAGCTACGTGGACAGCGT GAAGGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCC TGTACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTG TACTACTGCGCCAGGCCCCTGAACGCCGGCGAGCTGGACGTGTGG GGCCAGGGCACCATGGTGACCGTGAGCAGC [SEQ ID NO:254] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCGG CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCACCATCAAGCAGGACGGCAGCGAGAAGAGC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGCCCCTGAACGCCGGCG AGCTGGACGTGTGGGGCCAGGGCACCATGGTGACCGTGAGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCA GCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGAGCCCCAGC ACCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAG GGCCAGCCAGAGCATCAGCAGCTGGCTGGCCTGGTACCAGCAGA AGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGAGGCCAGCAGC CTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGG CACCGAGTTCACCCTGACCATCAGCAGCCTGCAGCCCGACGACTT CGCCACCTACTACTGCCAGCAGAGCCAGAGCTACCCCCCCATCAC CTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:255]
ADI-11809 [Ab6]	EVQLVESGGGLVQPGGSLRLSC AASGFTFPSYWMSWVRQAPGK GLEWVATIKRDGSEKGYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCARPLNAGELDV WGQGTMVTVSS [SEQ ID NO:11] CDR1: FTFPSYWMS [SEQ ID NO:51] (non-Kabat) or SYWMS [SEQ ID NO:181] CDR2: TIKRDGSEKGYVDSVKG [SEQ ID NO:52] CDR3: ARPLNAGELDV [SEQ ID NO:53] (non-Kabat) or PLNAGELDV [SEQ ID NO:439]	DIQMTQSPSTLSASVGDRVTITCR ASQSISSWLAWYQQKPGKAPKL LIYEASSLESGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQSQSY PPITFGGGTKVEIK [SEQ ID NO:12] CDR1: RASQSISSWLA [SEQ ID NO:54] CDR2: EASSLES [SEQ ID NO:55] CDR3: QQSQSYPPIT [SEQ ID NO:56]
scFv of Ab6	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLI YEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPI TFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQ PGGSLRLSCAASGFTFPSYWMSWVRQAPGK***C***LEWVATIKRDGSEKG YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGEL	

Table 1	VH	VL
	DVWGQGTMVTVSS [SEQ ID NO:214] EVQLVESGGGLVQPGGSLRLSCAASGFTFPSYWMSWVRQAPGK***C***LE WVATIKRDGSEKGYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCARPLNAGELDVWGQGTMVTVSS**GGGGSGGGGSGGGGSGG GGS**DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAP KLLIYEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQS YPPITFG***C***GTKVEIK [SEQ ID NO:215]	
Exemplary nucleotide sequence of Ab6 scFv	GACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGAGGCCAGCAGCCTGGAGAGCGGCGTGCC CAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGA CCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTGCC AGCAGAGCCAGAGCTACCCCCCCATCACCTTCGGCTGCGGCACCA AGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGT GGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGC TGAGCTGCGCCGCCAGCGGCTTCACCTTCCCCAGCTACTGGATGA GCTGGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCC ACCATCAAGAGGGACGGCAGCGAGAAGGGCTACGTGGACAGCGT GAAGGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCC TGTACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTG TACTACTGCGCCAGGCCCCTGAACGCCGGCGAGCTGGACGTGTGG GGCCAGGGCACCATGGTGACCGTGAGCAGC [SEQ ID NO:256] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCCC CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCACCATCAAGAGGGACGGCAGCGAGAAGGGC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGCCCCTGAACGCCGGCG AGCTGGACGTGTGGGGCCAGGGCACCATGGTGACCGTGAGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCA GCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGAGCCCCAGC ACCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAG GGCCAGCCAGAGCATCAGCAGCTGGCTGGCCTGGTACCAGCAGA AGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGAGGCCAGCAGC CTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGG CACCGAGTTCACCCTGACCATCAGCAGCCTGCAGCCCGACGACTT CGCCACCTACTACTGCCAGCAGAGCCAGAGCTACCCCCCCATCAC CTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:257]		
ADI-11815 [Ab7]	QVQLVQSGAEVKKPGASVKVS CKASGYTFGTYYMHWVRQAPG QGLEWMGIINPSRGSTVYAQKF QGRVTMTRDTSTSTVYMELSSL	DIQMTQSPSSVSASVGDRVTITC RASQGIDSWLAWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQAHS

Table 1	VH	VL
	RSEDTAVYYCARGAGYDDEDM DVWGKGTTVTVSS [SEQ ID NO:13] CDR1: YTFGTYYMH [SEQ ID NO:57] (non-Kabat) or TYYMH [SEQ ID NO:440] CDR2: IINPSRGSTVYAQKFQG [SEQ ID NO:58] CDR3: ARGAGYDDEDMDV [SEQ ID NO:59] (non-Kabat) or GAGYDDEDMDV [SEQ ID NO:441]	YPLTFGGGTKVEIK [SEQ ID NO:14] CDR1: RASQGIDSWLA [SEQ ID NO:60] CDR2: AASSLQS [SEQ ID NO:61] CDR3: QQAHSYPLT [SEQ ID NO:62]
scFv of Ab7	DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLL IYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPL TFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQSGAEVKK PGASVKVSCKASGYTFGTYYMHWVRQAPGQ***C***LEWMGIINPSRGSTV YAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDD EDMDVWGKGTTVTVSS [SEQ ID NO:216] QVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQAPGQ***C*** LEWMGIINPSRGSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDT AVYYCARGAGYDDEDMDVWGKGTTVTVSS**GGGGSGGGGSGGGG SGGGGS**DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKP GKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ QAHSYPLTFG***C***GTKVEIK [SEQ ID NO:217]
Exemplary nucleotide sequence of Ab7 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCGTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGGGCATCG ACAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCAGCCTGCAGAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGGCCCACAGCTACCCCCTGACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGGTGCA GAGCGGCGCCGAGGTGAAGAAGCCCGGCGCCAGCGTGAAGGTGA GCTGCAAGGCCAGCGGCTACACCTTCGGCACCTACTACATGCACT GGGTGAGGCAGGCCCCCGGCCAGTGCCTGGAGTGGATGGGCATC ATCAACCCCAGCAGGGGCAGCACCGTGTACGCCCAGAAGTTCCA GGGCAGGGTGACCATGACCAGGGACACCAGCACCAGCACCGTGT ACATGGAGCTGAGCAGCCTGAGGAGCGAGGACACCGCCGTGTAC TACTGCGCCAGGGGCGCCGGCTACGACGACGAGGACATGGACGT GTGGGGCAAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:258]	

Table 1	VH	VL
	CAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGG CGCCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCG GCACCTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCC TGGAGTGGATGGGCATCATCAACCCCAGCAGGGGCAGCACCGTG TACGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACAC CAGCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCG AGGACACCGCCGTGTACTACTGCGCCAGGGGCGCCGGCTACGAC GACGAGGACATGGACGTGTGGGGCAAGGGCACCACCGTGACCGT GAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGC GGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGAG CCCCAGCAGCGTGAGCGCCAGCGTGGGCGACAGGGTGACCATCA CCTGCAGGGCCAGCCAGGGCATCGACAGCTGGCTGGCCTGGTACC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGCC AGCAGCCTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGG CAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGA GGACTTCGCCACCTACTACTGCCAGCAGGCCCACAGCTACCCCCT GACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO: 259]	
ADI-11819 [Ab8]	EVQLVESGGGLVKPGGSLRLSC AASGFTFSSYAMSWVRQAPGK GLEWVSSISSSSEGIYYADSVKG RFTISRDNAKNSLYLQMNSLRA EDTAVYYCAREGGPYYDSSGYF VYYGMDVWGQGTTVTVSS [SEQ ID NO:15] CDR1: FTFSSYAMS [SEQ ID NO:63] (non-Kabat) or SYAMS [SEQ ID NO:442] CDR2: SISSSSEGIYYADSVKG [SEQ ID NO:64] CDR3: AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:65] (non-Kabat) or EGGPYYDSSGYFVYYGMDV [SEQ ID NO:443]	DIQMTQSPSTLSASVGDRVTITCR ASNSISSWLAWYQQKPGKAPKL LIYEASSTKSGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYDD LPTFGGGTKVEIK [SEQ ID NO:16] CDR1: RASNSISSWLA [SEQ ID NO:66] CDR2: EASSTKS [SEQ ID NO:67] CDR3: QQYDDLPT [SEQ ID NO:68]
scFv of Ab8	DIQMTQSPSTLSASVGDRVTITCRASNSISSWLAWYQQKPGKAPKLLI YEASSTKSGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPT FG**C**GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVKP GGSLRLSCAASGFTFSSYAMSWVRQAPGK**C**LEWVSSISSSSEGIYYA DSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSS GYFVYYGMDVWGQGTTVTVSS [SEQ ID NO:218] EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYAMSWVRQAPGK**C**LE WVSSISSSSEGIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAV YYCAREGGPYYDSSGYFVYYGMDVWGQGTTVTVSS**GGGGSGGGG**	

Table 1	VH	VL
	SGGGGSGGGGSDIQMTQSPSTLSASVGDRVTITCRASNSISSWLAW YQQKPGKAPKLLIYEASSTKSGVPSRFSGSGSGTEFTLTISSLQPDDFA TYYCQQYDDLPTFG**C**GTKVEIK [SEQ ID NO:219]	
Exemplary nucleotide sequence of Ab8 scFv	GACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCAACAGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGAGGCCAGCAGCACCAAGAGCGGCGTGCC CAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGA CCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTGCC AGCAGTACGACGACCTGCCCACCTTCGGCTGCGGCACCAAGGTGG AGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGC GGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGAGAG CGGCGGCGGCCTGGTGAAGCCCGGCGGCAGCCTGAGGCTGAGCT GCGCCGCCAGCGGCTTCACCTTCAGCAGCTACGCCATGAGCTGGG TGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGAGCAGCATC AGCAGCAGCAGCGAGGGCATCTACTACGCCGACAGCGTGAAGGG CAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGTACC TGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTAC TGCGCCAGGGAGGGCGGCCCCTACTACGACAGCAGCGGCTACTTC GTGTACTACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGAC CGTGAGCAGC [SEQ ID NO:260] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGAAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACGCCATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGAGCAGCATCAGCAGCAGCAGCGAGGGCATCTAC TACGCCGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGGCGGCCCCTACT ACGACAGCAGCGGCTACTTCGTGTACTACGGCATGGACGTGTGGG GCCAGGGCACCACCGTGACCGTGAGCAGCGGCGGCGGCGGCAGC GGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCA GCGACATCCAGATGACCCAGAGCCCCAGCACCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCAACAGCAT CAGCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCC CCAAGCTGCTGATCTACGAGGCCAGCAGCACCAAGAGCGGCGTG CCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCT GACCATCAGCAGCCTGCAGCCCGACGACTTCGCCACCTACTACTG CCAGCAGTACGACGACCTGCCCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAG [SEQ ID NO:261]	
ADI-11830 [Ab9]	EVQLVESGGGLVQPGGSLRLSC AASGFTFSSYWMSWVRQAPGK GLEWVANINTDGSEVYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCARDVGPGIAYQ GHFDYWGQGTLVTVSS [SEQ ID	DIQMTQSPSSLSASVGDRVTITCR ASQVIYSYLNWYQQKPGKAPKL LIYAASSLKSGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQVYD TPLTFGGGTKVEIK [SEQ ID NO:18]

Table 1	VH	VL
	NO:17] CDR1: FTFSSYWMS [SEQ ID NO:69] (non-Kabat) or SYWMS [SEQ ID NO:181] CDR2: NINTDGSEVYYVDSVKG [SEQ ID NO:70] CDR3: ARDVGPGIAYQGHFDY [SEQ ID NO:71] (non-Kabat) or DVGPGIAYQGHFDY [SEQ ID NO:444]	CDR1: RASQVIYSYLN [SEQ ID NO:72] CDR2: AASSLKS [SEQ ID NO:73] CDR3: QQVYDTPLT [SEQ ID NO:74]
scFv of Ab9	DIQMTQSPSSLSASVGDRVTITCRASQVIYSYLNWYQQKPGKAPKLLI YAASSLKSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYDTPL TFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYWMSWVRQAPGK***C***LEWVANINTDGSEVY YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDVGPGIA YQGHFDYWGQGTLVTVSS [SEQ ID NO:220] EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK***C***LE WVANINTDGSEVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCARDVGPGIAYQGHFDYWGQGTLVTVSS**GGGGSGGGGSGGG GSGGGGS**DIQMTQSPSSLSASVGDRVTITCRASQVIYSYLNWYQQKP GKAPKLLIYAASSLKSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ QVYDTPLTFG***C***GTKVEIK [SEQ ID NO:221]
Exemplary nucleotide sequence of Ab9 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGGTGATCT ACAGCTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCAGCCTGAAGAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGGTGTACGACACCCCCCTGACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGA GAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGA GCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACTGGATGAGCT GGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAAC ATCAACACCGACGGCAGCGAGGTGTACTACGTGGACAGCGTGAA GGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGT ACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGGGACGTGGGCCCCGGCATCGCCTACCAGGGCCAC TTCGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:262] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG	

Table 1	VH	VL
	CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAACACCGACGGCAGCGAGGTGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGACGTGGGCCCCGGC ATCGCCTACCAGGGCCACTTCGACTACTGGGGCCAGGGCACCCTG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGA CCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTG ACCATCACCTGCAGGGCCAGCCAGGTGATCTACAGCTACCTGAAC TGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC GCCGCCAGCAGCCTGAAGAGCGGCGTGCCCAGCAGGTTCAGCGG CAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCA GCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGTGTACGACAC CCCCCTGACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:263]	
ADI-11835 [Ab10] (I35)	QLQLQESGPGLVKPSETLSLTCT VSGGSISSTDYYWGWIRQPPGK GLEWIGSIGYSGTYYNPSLKSRV TISVDTSKNQFSLKLSSVTAADT AVYYCARETAHDVHGMDVWG QGTTVTVSS [SEQ ID NO:19] CDR1: GSISSTDYYWG [SEQ ID NO:75] (non-Kabat) or STDYYWG [SEQ ID NO:445] CDR2: SIGYSGTYYNPSLKS [SEQ ID NO:76] CDR3: ARETAHDVHGMDV [SEQ ID NO:77] (non-Kabat) or ETAHDVHGMDV [SEQ ID NO:446]	EIVLTQSPATLSLSPGERATLSCR ASHSVYSYLAWYQQKPGQAPRL LIYDASNRATGIPARFSGSGSGTD FTLTISSLEPEDFAVYYCQQYDN LPTFGGGTKVEIK [SEQ ID NO:20] CDR1: RASHSVYSYLA [SEQ ID NO:78] CDR2: DASNRAT [SEQ ID NO:79] CDR3: QQYDNLPT [SEQ ID NO:80]
scFv of Ab10	EIVLTQSPATLSLSPGERATLSCRASHSVYSYLAWYQQKPGQAPRLLI YDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLPT FG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QLQLQESGPGLVKPS ETLSLTCTVSGGSISSTDYYWGWIRQPPGK***C***LEWIGSIGYSGTYYNPS LKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARETAHDVHGMDV WGQGTTVTVSS [SEQ ID NO:222] QLQLQESGPGLVKPSETLSLTCTVSGGSISSTDYYWGWIRQPPGK***C***LE WIGSIGYSGTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYC ARETAHDVHGMDVWGQGTTVTVSS**GGGGSGGGGSGGGGSGGGG S**EIVLTQSPATLSLSPGERATLSCRASHSVYSYLAWYQQKPGQAPRLL IYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLPT FG***C***GTKVEIK [SEQ ID NO:223]	

Table 1	VH	VL
Exemplary nucleotide sequence of Ab10 scFv	GAGATCGTGCTGACCCAGAGCCCCGCCACCCTGAGCCTGAGCCCC GGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCACAGCGTGTA CAGCTACCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCA GGCTGCTGATCTACGACGCCAGCAACAGGGCCACCGGCATCCCCG CCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCA TCAGCAGCCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGC AGTACGACAACCTGCCCACCTTCGGCTGCGGCACCAAGGTGGAG ATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGG CGGCAGCGGCGGCGGCGGCAGCCAGCTGCAGCTGCAGGAGAGCG GCCCCGGCCTGGTGAAGCCCAGCGAGACCCTGAGCCTGACCTGCA CCGTGAGCGGCGGCAGCATCAGCAGCACCGACTACTACTGGGGC TGGATCAGGCAGCCCCCCGGCAAGTGCCTGGAGTGGATCGGCAG CATCGGCTACAGCGGCACCTACTACAACCCCAGCCTGAAGAGCA GGGTGACCATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCTG AAGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACTGC GCCAGGGAGACCGCCCACGACGTGCACGGCATGGACGTGTGGGG CCAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:264] CAGCTGCAGCTGCAGGAGAGCGGCCCCGGCCTGGTGAAGCCCAG CGAGACCCTGAGCCTGACCTGCACCGTGAGCGGCGGCAGCATCA GCAGCACCGACTACTACTGGGGCTGGATCAGGCAGCCCCCCGGC AAGTGCCTGGAGTGGATCGGCAGCATCGGCTACAGCGGCACCTA CTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGGACA CCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCC GCCGACACCGCCGTGTACTACTGCGCCAGGGAGACCGCCCACGA CGTGCACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGACCG TGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGC GGCGGCAGCGGCGGCGGCGGCAGCGAGATCGTGCTGACCCAGAG CCCCGCCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCTGA GCTGCAGGGCCAGCCACAGCGTGTACAGCTACCTGGCCTGGTACC AGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGACGCC AGCAACAGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAGCGG CAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGGAGCCCGA GGACTTCGCCGTGTACTACTGCCAGCAGTACGACAACCTGCCCAC CTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:265]	
ADI-10154 [Ab11]	EVQLLESGGGLVQPGGSLRLSC AASGFTFSSYAMSWVRQAPGK GLEWVSAISASGGSTYYADSVK GRFTISRDNSKNTLYLQMNSLR AEDTAVYYCARPRAYYDSSGFK VNYGMDVWGQGTTVTVSS [SEQ ID NO:266] CDR1: SYAMS [SEQ ID NO:304] or FTFSSYAMS [SEQ ID NO:528] (non-Kabat) CDR2: AISASGGSTYYADSVKG	EIVLTQSPGTLSLSPGERATLSCR ASQSVSSSFLAWYQQKPGQAPR LLIYGASSRATGIPDRFSGSGSGT DFTLTISRLEPEDFAVYYCQQASS SPPTFGGGTKVEIK [SEQ ID NO:267] CDR1: RASQSVSSSFLA [SEQ ID NO:307] CDR2: GASSRAT [SEQ ID NO:308] CDR3: QQASSSPPT [SEQ ID

Table 1	VH	VL
	[SEQ ID NO:305] CDR3: PRAYYDSSGFKVNYGMDV [SEQ ID NO:306] or ARPRAYYDSSGFKVNYGMDV [SEQ ID NO:529] (non-Kabat)	NO:309]
scFv of Ab11	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQASSSPPTFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK***C***LEWVSAISASGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARPRAYYDSSGFKVNYGMDVWGQGTTVTVSS [SEQ ID NO:447] EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK***C***LEWVSAISASGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARPRAYYDSSGFKVNYGMDVWGQGTTVTVSS**GGGGSGGGGSGGGGSGGGGS**EIVLTQSPGTLSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQASSSPPTFG***C***GTKVEIK [SEQ ID NO:448]
Exemplary nucleotide sequence of Ab11 scFv	GAGATCGTGCTGACCCAGAGCCCCGGCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCAGCTTCCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGGCGCCAGCAGCAGGGCCACCGGCATCCCCGACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGGCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGCAGGCCAGCAGCAGCCCCCCCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGCTGGAGAGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACGCCATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGAGCGCCATCAGCGCCAGCGGCGGCAGCACCTACTACGCCGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGCCCAGGGCCTACTACGACAGCAGCGGCTTCAAGGTGAACTACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:489] GAGGTGCAGCTGCTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACGCCATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGAGCGCCATCAGCGCCAGCGGCGGCAGCACCTACTACGCCGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAACAGCAAGAACACCCTGTACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGCCCAGGGCCTACTACGACAGCAGCGGCTTCAAGGTGAACTACGGCATGGACGTGTGGGGC

Table 1	VH	VL
	CAGGGCACCACCGTGACCGTGAGCAGCGGCGGCGGCGGCAGCGG CGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCG AGATCGTGCTGACCCAGAGCCCCGGCACCCTGAGCCTGAGCCCCG GCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGC AGCAGCTTCCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCC AGGCTGCTGATCTACGGCGCCAGCAGCAGGGCCACCGGCATCCCC GACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGGCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCA GCAGGCCAGCAGCAGCCCCCCCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAG [SEQ ID NO:490]	
ADI-10155 [Ab12]	EVQLLESGGGLVQPGGSLRLSC AASGFTFSSYAMSWVRQAPGK GLEWVSGISGSGGSTYYADSVK GRFTISRDNSKNTLYLQMNSLR AEDTAVYYCAREGHSSSYYDH AFDIWGQGTMVTVSS [SEQ ID NO:268] CDR1: SYAMS [SEQ ID NO:310] or FTFSSYAMS [SEQ ID NO:530] (non-Kabat) CDR2: GISGSGGSTYYADSVKG [SEQ ID NO:311] CDR3: EGHSSSYYDHAFDI [SEQ ID NO:312] or AREGHSSSYYDHAFDI [SEQ ID NO:531] (non-Kabat)	EIVLTQSPGTLSLSPGERATLSCR ASQSVSSDYLAWYQQKPGQAPR LLIYGASSRATGIPDRFSGSGSGT DFTLTISRLEPEDFAVYYCQQHSS APPTFGGGTKVEIK [SEQ ID NO:269] CDR1: RASQSVSSDYLA [SEQ ID NO:313] CDR2: GASSRAT [SEQ ID NO:314] CDR3: QQHSSAPPT [SEQ ID NO:315]
scFv of Ab12	EIVLTQSPGTLSLSPGERATLSCRASQSVSSDYLAWYQQKPGQAPRLL IYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQHSSAPP TFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLLESGGGLVQP GGSLRLSCAASGFTFSSYAMSWVRQAPGK***C***LEWVSGISGSGGSTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREGHSSSYY DHAFDIWGQGTMVTVSS [SEQ ID NO:449] EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK***C***LE WVSGISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTA VYYCAREGHSSSYYDHAFDIWGQGTMVTVSS**GGGGSGGGGSGGG GSGGGGS**EIVLTQSPGTLSLSPGERATLSCRASQSVSSDYLAWYQQK PGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC QQHSSAPPTFG***C***GTKVEIK [SEQ ID NO:450]	
Exemplary nucleotide sequence of Ab12	GAGATCGTGCTGACCCAGAGCCCCGGCACCCTGAGCCTGAGCCCC GGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAG CAGCGACTACCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCC CCAGGCTGCTGATCTACGGCGCCAGCAGCAGGGCCACCGGCATCC CCGACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTG	

Table 1	VH	VL
scFv	ACCATCAGCAGGCTGGAGCCCGAGGACTTCGCCGTGTACTACTGC CAGCAGCACAGCAGCGCCCCCCCCACCTTCGGCTGCGGCACCAAG GTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGG CGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGCTGG AGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTG AGCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACGCCATGAGC TGGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGAGCGG CATCAGCGGCAGCGGCGGCAGCACCTACTACGCCGACAGCGTGA AGGGCAGGTTCACCATCAGCAGGGACAACAGCAAGAACACCCTG TACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTA CTACTGCGCCAGGGAGGGCCACAGCAGCAGCTACTACGACCACG CCTTCGACATCTGGGGCCAGGGCACCATGGTGACCGTGAGCAGC [SEQ ID NO:491] GAGGTGCAGCTGCTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACGCCATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGAGCGGCATCAGCGGCAGCGGCGGCAGCACCTAC TACGCCGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CAGCAAGAACACCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGGCCACAGCAGC AGCTACTACGACCACGCCTTCGACATCTGGGGCCAGGGCACCATG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGATCGTGCTGA CCCAGAGCCCCGGCACCCTGAGCCTGAGCCCCGGCGAGAGGGCC ACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCGACTACCT GGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGA TCTACGGCGCCAGCAGCAGGGCCACCGGCATCCCCGACAGGTTCA GCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGG CTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGCAGCACAGC AGCGCCCCCCCCCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:492]	
ADI-10157 [Ab13]	QVQLQESGPGLVKPSETLSLTCT VSGGSISSYYWSWIRQPPGKGLE WIGSIYYSGSTNYNPSLKSRVTIS VDTSKNQFSLKLSSVTAADTAV YYCARVGGVYSTIETYGMDVW GQGTTVTVSS [SEQ ID NO:270] CDR1: SYYWS [SEQ ID NO:316] or GSISSYYWS [SEQ ID NO:532] (non-Kabat) CDR2: SIYYSGSTNYNPSLKS [SEQ ID NO:317] CDR3: VGGVYSTIETYGMDV [SEQ ID NO:318] or	EIVMTQSPATLSVSPGERATLSCR ASQSVSSNLAWYQQKPGQAPRL LIYGASTRATGIPARFSGSGSGTE FTLTISSLQSEDFAVYYCQQYTV YPPTFGGGTKVEIK [SEQ ID NO:271] CDR1: RASQSVSSNLA [SEQ ID NO:319] CDR2: GASTRAT [SEQ ID NO:320] CDR3: QQYTVYPPT [SEQ ID NO:321]

Table 1	VH	VL
	ARVGGVYSTIETYGMDV [SEQ ID NO:533] (non-Kabat)	
scFv of Ab13	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYTVYPPTFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGK***C***LEWIGSIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARVGGVYSTIETYGMDVWGQGTTVTVSS [SEQ ID NO:451] QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGK***C***LEWIGSIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARVGGVYSTIETYGMDVWGQGTTVTVSS**GGGGSGGGGSGGGGSGGGGS**EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYTVYPPTFG***C***GTKVEIK [SEQ ID NO:452]
Exemplary nucleotide sequence of Ab13 scFv	GAGATCGTGATGACCCAGAGCCCCGCCACCCTGAGCGTGAGCCCCGGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCAACCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGGCGCCAGCACCAGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGACCATCAGCAGCCTGCAGAGCGAGGACTTCGCCGTGTACTACTGCCAGCAGTACACCGTGTACCCCCCCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGCAGGAGAGCGGCCCCGGCCTGGTGAAGCCCAGCGAGACCCTGAGCCTGACCTGCACCGTGAGCGGCGGCAGCATCAGCAGCTACTACTGGAGCTGGATCAGGCAGCCCCCCGGCAAGTGCCTGGAGTGGATCGGCAGCATCTACTACAGCGGCAGCACCAACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACTGCGCCAGGGTGGGCGGCGTGTACAGCACCATCGAGACCTACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:493] CAGGTGCAGCTGCAGGAGAGCGGCCCCGGCCTGGTGAAGCCCAGCGAGACCCTGAGCCTGACCTGCACCGTGAGCGGCGGCAGCATCAGCAGCTACTACTGGAGCTGGATCAGGCAGCCCCCCGGCAAGTGCCTGGAGTGGATCGGCAGCATCTACTACAGCGGCAGCACCAACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACTGCGCCAGGGTGGGCGGCGTGTACAGCACCATCGAGACCTACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGATCGTGATGACCCAGAGCCCCGCCACCCTGAGCGTGAGCCCCGGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCAACCTGGC

Table 1	VH	VL
	CTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGGCGCCAGCACCAGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAGCGGCAGCGGCACCGAGTTCACCCTGACCATCAGCAGCCTGCAGAGCGAGGACTTCGCCGTGTACTACTGCCAGCAGTACACCGTGTACCCCCCCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:494]	
ADI-10158 [Ab14]	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWIGEIDHSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARQGIHGLRYFDLWGRGTLVTVSS [SEQ ID NO:272] CDR1: GYYWS [SEQ ID NO:322] or GSFSGYYWS [SEQ ID NO:534] (non-Kabat) CDR2: EIDHSGSTNYNPSLKS [SEQ ID NO:323] CDR3: QGIHGLRYFDL [SEQ ID NO:324] or ARQGIHGLRYFDL [SEQ ID NO:535] (non-Kabat)	EIVMTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQDHNFPYTFGGGTKVEIK [SEQ ID NO:273] CDR1: RASQSVSSYLA [SEQ ID NO:325] CDR2: DASNRAT [SEQ ID NO:326] CDR3: QQDHNFPYT [SEQ ID NO:327]
scFv of Ab14	EIVMTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQDHNFPYTFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGK*C*LEWIGEIDHSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARQGIHGLRYFDLWGRGTLVTVSS [SEQ ID NO:453] QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGK*C*LEWIGEIDHSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARQGIHGLRYFDLWGRGTLVTVSS**GGGGSGGGGSGGGGSGGGGS**EIVMTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQDHNFPYTFG*C*GTKVEIK [SEQ ID NO:454]	
Exemplary nucleotide sequence of Ab14 scFv	GAGATCGTGATGACCCAGAGCCCCGCCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCTACCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGACGCCAGCAACAGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGCAGGACCACAACTTCCCCTACACCTTCGGCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGCAGCAGTGGGGCGCCGGCCTGCTGAAGCCCAGCGAGACCCTGAGCCTGACCTGCGCCGTGTACGGCGGCAGCTTCAGCGGCTACTACTGGAGCTGGA	

Table 1	VH	VL
	TCAGGCAGCCCCCCGGCAAGTGCCTGGAGTGGATCGGCGAGATC GACCACAGCGGCAGCACCAACTACAACCCCAGCCTGAAGAGCAG GGTGACCATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCTGA AGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACTGCG CCAGGCAGGGCATCCACGGCCTGAGGTACTTCGACCTGTGGGGCA GGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:495] CAGGTGCAGCTGCAGCAGTGGGGCGCCGGCCTGCTGAAGCCCAG CGAGACCCTGAGCCTGACCTGCGCCGTGTACGGCGGCAGCTTCAG CGGCTACTACTGGAGCTGGATCAGGCAGCCCCCCGGCAAGTGCCT GGAGTGGATCGGCGAGATCGACCACAGCGGCAGCACCAACTACA ACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGGACACCAGC AAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCCGCCGA CACCGCCGTGTACTACTGCGCCAGGCAGGGCATCCACGGCCTGAG GTACTTCGACCTGTGGGGCAGGGGCACCCTGGTGACCGTGAGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCA GCGGCGGCGGCGGCAGCGAGATCGTGATGACCCAGAGCCCCGCC ACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCTGAGCTGCAG GGCCAGCCAGAGCGTGAGCAGCTACCTGGCCTGGTACCAGCAGA AGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGACGCCAGCAAC AGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAGCGGCAGCGG CACCGACTTCACCCTGACCATCAGCAGCCTGGAGCCCGAGGACTT CGCCGTGTACTACTGCCAGCAGGACCACAACTTCCCCTACACCTT CGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:496]	
ADI-10160 [Ab15]	EVQLVESGGGLVQPGGSLRLSC AASGFTFSSYWMSWVRQAPGK GLEWVANINQDGSEKYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCAREANYYGNVG DDYWGQGTLVTVSS [SEQ ID NO:274] CDR1: SYWMS [SEQ ID NO:328] or FTFSSYWMS [SEQ ID NO:536] (non-Kabat) CDR2: NINQDGSEKYYVDSVKG [SEQ ID NO:329] CDR3: EANYYGNVGDDY [SEQ ID NO:330] or AREANYYGNVGDDY [SEQ ID NO:537] (non-Kabat)	DIQMTQSPSSLSASVGDRVTITCR ASQSISSYLNWYQQKPGKAPKLL IYAASSLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQQYVT PITFGGGTKVEIK [SEQ ID NO:275] CDR1: RASQSISSYLN [SEQ ID NO:331] CDR2: AASSLQS [SEQ ID NO:332] CDR3: QQQYVTPIT [SEQ ID NO:333]
scFv of Ab15	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQQYVTPIT FG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQP GGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LEWVANINQDGSEKY YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREANYYG	

Table 1	VH	VL
	NVGDDYWGQGTLVTVSS [SEQ ID NO:455] EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LE WVANINQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCAREANYYGNVGDDYWGQGTLVTVSS**GGGGSGGGGSGGGG SGGGGS**DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPG KAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ QYVTPITFG*C*GTKVEIK [SEQ ID NO:456]	
Exemplary nucleotide sequence of Ab15 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCAGCCTGCAGAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGCAGTACGTGACCCCCATCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGA GAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGA GCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACTGGATGAGCT GGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAAC ATCAACCAGGACGGCAGCGAGAAGTACTACGTGGACAGCGTGAA GGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGT ACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGGGAGGCCAACTACTACGGCAACGTGGGCGACGA CTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:497] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAACCAGGACGGCAGCGAGAAGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGCCAACTACTAC GGCAACGTGGGCGACGACTACTGGGGCCAGGGCACCCTGGTGAC CGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCG GCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGACCCAG AGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCAT CACCTGCAGGGCCAGCCAGAGCATCAGCAGCTACCTGAACTGGT ACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCC GCCAGCAGCCTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAG CGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCC CGAGGACTTCGCCACCTACTACTGCCAGCAGCAGTACGTGACCCC CATCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:498]	
ADI-10161	EVQLVESGGGLVQPGGSLRLSC AASGFTFSSYWMSWVRQAPGK	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK

Table 1	VH	VL
[Ab16]	GLEWVANINQDGSEKYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCAREGGDSWYHA FDIWGQGTMVTVSS [SEQ ID NO:276] CDR1: SYWMS [SEQ ID NO:334] or FTFSSYWMS [SEQ ID NO:538] (non-Kabat) CDR2: NINQDGSEKYYVDSVKG [SEQ ID NO:335] CDR3: EGGDSWYHAFDI [SEQ ID NO:336] or AREGGDSWYHAFDI [SEQ ID NO:539] (non-Kabat)	LLIYAASNLQSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQKLS LPLTFGGGTKVEIK [SEQ ID NO:277] CDR1: RASQGISSWLA [SEQ ID NO:337] CDR2: AASNLQS [SEQ ID NO:338] CDR3: QQKLSLPLT [SEQ ID NO:339]
scFv of Ab16	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLL IYAASNLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQKLSLPL TFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LEWVANINQDGSEKY YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGDSW YHAFDIWGQGTMVTVSS [SEQ ID NO:457] EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LE WVANINQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCAREGGDSWYHAFDIWGQGTMVTVSS**GGGGSGGGGSGGGG SGGGGS**DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKP GKAPKLLIYAASNLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQKLSLPLTFG*C*GTKVEIK [SEQ ID NO:458]
Exemplary nucleotide sequence of Ab16 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCGTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGGGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCAACCTGCAGAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGAAGCTGAGCCTGCCCCTGACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGA GAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGA GCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACTGGATGAGCT GGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAAC ATCAACCAGGACGGCAGCGAGAAGTACTACGTGGACAGCGTGAA GGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGT ACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGGGAGGGCGGCGACAGCTGGTACCACGCCTTCGA CATCTGGGGCCAGGGCACCATGGTGACCGTGAGCAGC [SEQ ID	

Table 1	VH	VL
	NO:499] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAACCAGGACGGCAGCGAGAAGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGGCGGCGACAGC TGGTACCACGCCTTCGACATCTGGGGCCAGGGCACCATGGTGACC GTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGG CGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGA GCCCCAGCAGCGTGAGCGCCAGCGTGGGCGACAGGGTGACCATC ACCTGCAGGGCCAGCCAGGGCATCAGCAGCTGGCTGGCCTGGTA CCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCG CCAGCAACCTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCC GAGGACTTCGCCACCTACTACTGCCAGCAGAAGCTGAGCCTGCCC CTGACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:500]	
ADI-10163 [Ab17]	QVQLQESGPGLVKPSQTLSLTCT VSGGSISSGGYYWSWIRQHPGK GLEWIGSIYYSGSTYYNPSLKSR VTISVDTSKNQFSLKLSSVTAAD TAVYYCARDRLDYSYNYGMDV WGQGTTVTVSS [SEQ ID NO:278] CDR1: SGGYYWS [SEQ ID NO:340] or GSISSGGYYWS [SEQ ID NO:540] (non-Kabat) CDR2: SIYYSGSTYYNPSLKS [SEQ ID NO:341] CDR3: DRLDYSYNYGMDV [SEQ ID NO:342] or ARDRLDYSYNYGMDV [SEQ ID NO:541] (non-Kabat)	DIQMTQSPSSLSASVGDRVTITCR ASQSISSYLNWYQQKPGKAPKLL IYGASSLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQVYSAP FTFGGGTKVEIK [SEQ ID NO:279] CDR1: RASQSISSYLN [SEQ ID NO:343] CDR2: GASSLQS [SEQ ID NO:344] CDR3: QQVYSAPFT [SEQ ID NO:345]
scFv of Ab17	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLI YGASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYSAPF TFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLQESGPGLVKP SQTLSLTCTVSGGSISSGGYYWSWIRQHPGK*C*LEWIGSIYYSGSTYYN PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDRLDYSYNYG MDVWGQGTTVTVSS [SEQ ID NO:459] QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGK*C*L EWIGSIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVY	

Table 1	VH	VL
	YCARDRLDYSYNYGMDVWGQGTTVTVSS**GGGGSGGGGSGGGGS GGGGS**DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGK APKLLIYGASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQV YSAPFTFG**C**GTKVEIK [SEQ ID NO:460]	
Exemplary nucleotide sequence of Ab17 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGGCGCCAGCAGCCTGCAGAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGGTGTACAGCGCCCCCTTCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGCAGGA GAGCGGCCCCGGCCTGGTGAAGCCCAGCCAGACCCTGAGCCTGA CCTGCACCGTGAGCGGCGGCAGCATCAGCAGCGGCGGCTACTACT GGAGCTGGATCAGGCAGCACCCCGGCAAGTGCCTGGAGTGGATC GGCAGCATCTACTACAGCGGCAGCACCTACTACAACCCCAGCCTG AAGAGCAGGGTGACCATCAGCGTGGACACCAGCAAGAACCAGTT CAGCCTGAAGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGT ACTACTGCGCCAGGGACAGGCTGGACTACAGCTACAACTACGGC ATGGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:501] CAGGTGCAGCTGCAGGAGAGCGGCCCCGGCCTGGTGAAGCCCAG CCAGACCCTGAGCCTGACCTGCACCGTGAGCGGCGGCAGCATCA GCAGCGGCGGCTACTACTGGAGCTGGATCAGGCAGCACCCCGGC AAGTGCCTGGAGTGGATCGGCAGCATCTACTACAGCGGCAGCAC CTACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGG ACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACC GCCGCCGACACCGCCGTGTACTACTGCGCCAGGGACAGGCTGGA CTACAGCTACAACTACGGCATGGACGTGTGGGGCCAGGGCACCA CCGTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGC AGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGAT GACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGG TGACCATCACCTGCAGGGCCAGCCAGAGCATCAGCAGCTACCTGA ACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCT ACGGCGCCAGCAGCCTGCAGAGCGGCGTGCCCAGCAGGTTCAGC GGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTG CAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGTGTACAGC GCCCCCTTCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:502]	
ADI-10164 [Ab18]	QVQLQESGPGLVKPSETLSLTCA VSGYSISSGYYWGWIRQPPGKG LEWIGSIYHSGSTNYNPSLKSRV TISVDTSKNQFSLKLSSVTAADT AVYYCARLPPWFGFSYFDLWG	EIVLTQSPATLSLSPGERATLSCR ASQSVSSYLAWYQQKPGQAPRL LIYDASNRATGIPARFSGSGSGTD FTLTISSLEPEDFAVYYCQQVDN YPPTFGGGTKVEIK [SEQ ID

Table 1	VH	VL
	RGTLVTVSS [SEQ ID NO:280] CDR1: SGYYWG [SEQ ID NO:346] or YSISSGYYWG [SEQ ID NO:542] (non-Kabat) CDR2: SIYHSGSTNYNPSLKS [SEQ ID NO:347] CDR3: LPPWFGFSYFDL [SEQ ID NO:348] or ARLPPWFGFSYFDL [SEQ ID NO:543] (non-Kabat)	NO:281] CDR1: RASQSVSSYLA [SEQ ID NO:349] CDR2: DASNRAT [SEQ ID NO:350] CDR3: QQVDNYPPT [SEQ ID NO:351]
scFv of Ab18	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQVDNYPPTFG***C***GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLQESGPGLVKPSETLSLTCAVSGYSISSGYYWGWIRQPPGK***C***LEWIGSIYHSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARLPPWFGFSYFDLWGRGTLVTVSS [SEQ ID NO:461] QVQLQESGPGLVKPSETLSLTCAVSGYSISSGYYWGWIRQPPGK***C***LEWIGSIYHSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARLPPWFGFSYFDLWGRGTLVTVSS**GGGGSGGGGSGGGGSGGGGS**EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQVDNYPPTFG***C***GTKVEIK [SEQ ID NO:462]
Exemplary nucleotide sequence of Ab18 scFv	GAGATCGTGCTGACCCAGAGCCCCGCCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCTACCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGACGCCAGCAACAGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGCAGGTGGACAACTACCCCCCCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGCAGGAGAGCGGCCCCGGCCTGGTGAAGCCCAGCGAGACCCTGAGCCTGACCTGCGCCGTGAGCGGCTACAGCATCAGCAGCGGCTACTACTGGGGCTGGATCAGGCAGCCCCCCGGCAAGTGCCTGGAGTGGATCGGCAGCATCTACCACAGCGGCAGCACCAACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACTGCGCCAGGCTGCCCCCCTGGTTCGGCTTCAGCTACTTCGACCTGTGGGGCAGGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:503] CAGGTGCAGCTGCAGGAGAGCGGCCCCGGCCTGGTGAAGCCCAGCGAGACCCTGAGCCTGACCTGCGCCGTGAGCGGCTACAGCATCAGCAGCGGCTACTACTGGGGCTGGATCAGGCAGCCCCCCGGCAAGTGCCTGGAGTGGATCGGCAGCATCTACCACAGCGGCAGCACCAAC

Table 1	VH	VL
	TACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGGACAC CAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCCG CCGACACCGCCGTGTACTACTGCGCCAGGCTGCCCCCCTGGTTCG GCTTCAGCTACTTCGACCTGTGGGGCAGGGGCACCCTGGTGACCG TGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGC GGCGGCAGCGGCGGCGGCGGCAGCGAGATCGTGCTGACCCAGAG CCCCGCCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCTGA GCTGCAGGGCCAGCCAGAGCGTGAGCAGCTACCTGGCCTGGTAC CAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGACGC CAGCAACAGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAGCG GCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGGAGCCCG AGGACTTCGCCGTGTACTACTGCCAGCAGGTGGACAACTACCCCC CCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:504]	
ADI-10165 [Ab19]	EVQLVESGGGLVQPGGSLRLSC AASGFTFSSYWMSWVRQAPGK GLEWVANIKQDGSEKYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCARDVGPGIAYQ GHFDYWGQGTLVTVSS [SEQ ID NO:282] CDR1: SYWMS [SEQ ID NO:352] or FTFSSYWMS [SEQ ID NO:544] (non-Kabat) CDR2: NIKQDGSEKYYVDSVKG [SEQ ID NO:353] CDR3: DVGPGIAYQGHFDY [SEQ ID NO:354] or ARDVGPGIAYQGHFDY [SEQ ID NO:545] (non-Kabat)	DIQMTQSPSSLSASVGDRVTITCR ASQSISSYLNWYQQKPGKAPKLL IYAASSLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQVYDT PLTFGGGTKVEIK [SEQ ID NO:283] CDR1: RASQSISSYLN [SEQ ID NO:355] CDR2: AASSLQS [SEQ ID NO:356] CDR3: QQVYDTPLT [SEQ ID NO:357]
scFv of Ab19	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYDTPL TFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LEWVANIKQDGSEKY YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDVGPGIA YQGHFDYWGQGTLVTVSS [SEQ ID NO:463] EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LE WVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCARDVGPGIAYQGHFDYWGQGTLVTVSS**GGGGSGGGGSGGG GSGGGGS**DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKP GKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ QVYDTPLTFG*C*GTKVEIK [SEQ ID NO:464]	
Exemplary	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGT	

Table 1	VH	VL
nucleotide sequence of Ab19 scFv	GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCA GCAGCTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCAGCCTGCAGAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGGTGTACGACACCCCCCTGACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGA GAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGA GCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACTGGATGAGCT GGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAAC ATCAAGCAGGACGGCAGCGAGAAGTACTACGTGGACAGCGTGAA GGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGT ACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGGGACGTGGGCCCCGGCATCGCCTACCAGGGCCAC TTCGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:505] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAAGCAGGACGGCAGCGAGAAGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGACGTGGGCCCCGGC ATCGCCTACCAGGGCCACTTCGACTACTGGGGCCAGGGCACCCTG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGA CCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTG ACCATCACCTGCAGGGCCAGCCAGAGCATCAGCAGCTACCTGAA CTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTA CGCCGCCAGCAGCCTGCAGAGCGGCGTGCCCAGCAGGTTCAGCG GCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGC AGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGTGTACGACA CCCCCCTGACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:506]	
ADI-10167 [Ab20]	QLQLQESGPGLVKPSETLSLTCT VSGGSISSSSYYWGWIRQPPGK GLEWIGSIYYSGSTYYNPSLKSR VTISVDTSKNQFSLKLSSVTAAD TAVYYCARETAHDVHGMDVW GQGTTVTVSS [SEQ ID NO:284] CDR1: SSSYYWG [SEQ ID NO:358] or GSISSSSYYWG [SEQ ID NO:546] (non-Kabat) CDR2: SIYYSGSTYYNPSLKS	EIVLTQSPATLSLSPGERATLSCR ASQSVSSYLAWYQQKPGQAPRL LIYDASNRATGIPARFSGSGSGTD FTLTISSLEPEDFAVYYCQQYDN LPTFGGGTKVEIK [SEQ ID NO:285] CDR1: RASQSVSSYLA [SEQ ID NO:361] CDR2: DASNRAT [SEQ ID

Table 1	VH	VL
	[SEQ ID NO:359] CDR3: ETAHDVHGMDV [SEQ ID NO:360] or ARETAHDVHGMDV [SEQ ID NO:547] (non-Kabat)	NO:362] CDR3: QQYDNLPT [SEQ ID NO:363]
scFv of Ab20	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI YDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLPT FG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QLQLQESGPGLVKPS ETLSLTCTVSGGSISSSSYYWGWIRQPPGK*C*LEWIGSIYYSGSTYYNP SLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARETAHDVHGMD VWGQGTTVTVSS [SEQ ID NO:465] QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGK*C*LE WIGSIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYY CARETAHDVHGMDVWGQGTTVTVSS**GGGGSGGGGSGGGGSGGG GS**EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRL LIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLP TFG*C*GTKVEIK [SEQ ID NO:466]
Exemplary nucleotide sequence of Ab20 scFv	GAGATCGTGCTGACCCAGAGCCCCGCCACCCTGAGCCTGAGCCCC GGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAG CAGCTACCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCA GGCTGCTGATCTACGACGCCAGCAACAGGGCCACCGGCATCCCCG CCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCA TCAGCAGCCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGC AGTACGACAACCTGCCCACCTTCGGCTGCGGCACCAAGGTGGAG ATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGG CGGCAGCGGCGGCGGCGGCAGCCAGCTGCAGCTGCAGGAGAGCG GCCCCGGCCTGGTGAAGCCCAGCGAGACCCTGAGCCTGACCTGCA CCGTGAGCGGCGGCAGCATCAGCAGCAGCAGCTACTACTGGGGC TGGATCAGGCAGCCCCCCGGCAAGTGCCTGGAGTGGATCGGCAG CATCTACTACAGCGGCAGCACCTACTACAACCCCAGCCTGAAGAG CAGGGTGACCATCAGCGTGGACACCAGCAAGAACCAGTTCAGCC TGAAGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACT GCGCCAGGGAGACCGCCCACGACGTGCACGGCATGGACGTGTGG GGCCAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:507] CAGCTGCAGCTGCAGGAGAGCGGCCCCGGCCTGGTGAAGCCCAG CGAGACCCTGAGCCTGACCTGCACCGTGAGCGGCGGCAGCATCA GCAGCAGCAGCTACTACTGGGGCTGGATCAGGCAGCCCCCCGGC AAGTGCCTGGAGTGGATCGGCAGCATCTACTACAGCGGCAGCAC CTACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCGTGG ACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACC GCCGCCGACACCGCCGTGTACTACTGCGCCAGGGAGACCGCCCAC GACGTGCACGGCATGGACGTGTGGGGCCAGGGCACCACCGTGAC CGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCG GCGGCGGCAGCGGCGGCGGCGGCAGCGAGATCGTGCTGACCCAG AGCCCCGCCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCT

Table 1	VH	VL
	GAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCTACCTGGCCTGGT ACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGAC GCCAGCAACAGGGCCACCGGCATCCCCGCCAGGTTCAGCGGCAG CGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGGAGCC CGAGGACTTCGCCGTGTACTACTGCCAGCAGTACGACAACCTGCC CACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:508]	
ADI-10168 [Ab21]	QVQLVQSGAEVKKPGSSVKVSC KASGGTFSSYAISWVRQAPGQG LEWMGSIIPIFGTANYAQKFQGR VTITADESTSTAYMELSSLRSED TAVYYCAREVGYGWYTKIAFDI WGQGTMVTVSS [SEQ ID NO:286] CDR1: SYAIS [SEQ ID NO:364] or GTFSSYAIS [SEQ ID NO:548] (non-Kabat) CDR2: SIIPIFGTANYAQKFQG [SEQ ID NO:365] CDR3: EVGYGWYTKIAFDI [SEQ ID NO:366] or AREVGYGWYTKIAFDI [SEQ ID NO:549] (non-Kabat)	EIVLTQSPATLSLSPGERATLSCR ASQSVSSYLAWYQQKPGQAPRL LIYDASKRATGIPARFSGSGSGTD FTLTISSLEPEDFAVYYCQQSSNH PSTFGGGTKVEIK [SEQ ID NO:287] CDR1: RASQSVSSYLA [SEQ ID NO:367] CDR2: DASKRAT [SEQ ID NO:368] CDR3: QQSSNHPST [SEQ ID NO:369]
scFv of Ab21	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI YDASKRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQSSNHPST FG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQSGAEVKKP GSSVKVSCKASGGTFSSYAISWVRQAPGQ*C*LEWMGSIIPIFGTANYA QKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCAREVGYGWYTK IAFDIWGQGTMVTVSS [SEQ ID NO:467] QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQ*C*LE WMGSIIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVY YCAREVGYGWYTKIAFDIWGQGTMVTVSS**GGGGSGGGGSGGGGS GGGGS**EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQ APRLLIYDASKRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQS SNHPSTFG*C*GTKVEIK [SEQ ID NO:468]	
Exemplary nucleotide sequence of Ab21 scFv	GAGATCGTGCTGACCCAGAGCCCCGCCACCCTGAGCCTGAGCCCC GGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAG CAGCTACCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCA GGCTGCTGATCTACGACGCCAGCAAGAGGGCCACCGGCATCCCC GCCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACC ATCAGCAGCCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAG CAGAGCAGCAACCACCCCAGCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC	

Table 1	VH	VL
	GGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGGTGCA GAGCGGCGCCGAGGTGAAGAAGCCCGGCAGCAGCGTGAAGGTGA GCTGCAAGGCCAGCGGCGGCACCTTCAGCAGCTACGCCATCAGCT GGGTGAGGCAGGCCCCCGGCCAGTGCCTGGAGTGGATGGGCAGC ATCATCCCCATCTTCGGCACCGCCAACTACGCCCAGAAGTTCCAG GGCAGGGTGACCATCACCGCCGACGAGAGCACCAGCACCGCCTA CATGGAGCTGAGCAGCCTGAGGAGCGAGGACACCGCCGTGTACT ACTGCGCCAGGGAGGTGGGCTACGGCTGGTACACCAAGATCGCC TTCGACATCTGGGGCCAGGGCACCATGGTGACCGTGAGCAGC [SEQ ID NO:509] CAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGG CAGCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCGGCACCTTCA GCAGCTACGCCATCAGCTGGGTGAGGCAGGCCCCCGGCCAGTGC CTGGAGTGGATGGGCAGCATCATCCCCATCTTCGGCACCGCCAAC TACGCCCAGAAGTTCCAGGGCAGGGTGACCATCACCGCCGACGA GAGCACCAGCACCGCCTACATGGAGCTGAGCAGCCTGAGGAGCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGTGGGCTACGGC TGGTACACCAAGATCGCCTTCGACATCTGGGGCCAGGGCACCATG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGATCGTGCTGA CCCAGAGCCCCGCCACCCTGAGCCTGAGCCCCGGCGAGAGGGCC ACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCTACCTGGC CTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTA CGACGCCAGCAAGAGGGCCACCGGCATCCCCGCCAGGTTCAGCG GCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGG AGCCCGAGGACTTCGCCGTGTACTACTGCCAGCAGAGCAGCAACC ACCCCAGCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:510]	
ADI-10173 [Ab22]	QVQLVQSGAEVKKPGASVKVS CKASGYTFTSYYMHWVRQAPG QGLEWMGIINPSGGSTTYAQKF QGRVTMTRDTSTSTVYMELSSL RSEDTAVYYCAREAADGFVGE RYFDLWGRGTLVTVSS [SEQ ID NO:288] CDR1: SYYMH [SEQ ID NO:370] or YTFTSYYMH [SEQ ID NO:550] (non-Kabat) CDR2: IINPSGGSTTYAQKFQG [SEQ ID NO:371] CDR3: EAADGFVGERYFDL [SEQ ID NO:372] or AREAADGFVGERYFDL [SEQ ID NO:551] (non-Kabat)	DIVMTQSPLSLPVTPGEPASISCR SSQSLLHSNGYNYLDWYLQKPG QSPQLLIYLGSNRASGVPDRFSGS GSGTDFTLKISRVEAEDVGVYYC MQALGVPLTFGGGTKVEIK [SEQ ID NO:289] CDR1: RSSQSLLHSNGYNYLD [SEQ ID NO:373] CDR2: LGSNRAS [SEQ ID NO:374] CDR3: MQALGVPLT [SEQ ID NO:375]

Table 1	VH	VL
scFv of Ab22	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQS PQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQ ALGVPLTFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQS GAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQ*C*LEWMGIIN PSGGSTTYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAR EAADGFVGERYFDLWGRGTLVTVSS [SEQ ID NO:469] QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQ*C*L EWMGIINPSGGSTTYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCAREAADGFVGERYFDLWGRGTLVTVSS**GGGGSGGGGSGGG GSGGGGS**DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDW YLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDV GVYYCMQALGVPLTFG*C*GTKVEIK [SEQ ID NO:470]	
Exemplary nucleotide sequence of Ab22 scFv	GACATCGTGATGACCCAGAGCCCCCTGAGCCTGCCCGTGACCCCC GGCGAGCCCGCCAGCATCAGCTGCAGGAGCAGCCAGAGCCTGCT GCACAGCAACGGCTACAACTACCTGGACTGGTACCTGCAGAAGC CCGGCCAGAGCCCCCAGCTGCTGATCTACCTGGGCAGCAACAGG GCCAGCGGCGTGCCCGACAGGTTCAGCGGCAGCGGCAGCGGCAC CGACTTCACCCTGAAGATCAGCAGGGTGGAGGCCGAGGACGTGG GCGTGTACTACTGCATGCAGGCCCTGGGCGTGCCCCTGACCTTCG GCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCA GGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGGCG CCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCACC AGCTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCCTG GAGTGGATGGGCATCATCAACCCCAGCGGCGGCAGCACCACCTA CGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACACCA GCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCGAG GACACCGCCGTGTACTACTGCGCCAGGGAGGCCGCCGACGGCTTC GTGGGCGAGAGGTACTTCGACCTGTGGGGCAGGGGCACCCTGGT GACCGTGAGCAGC [SEQ ID NO:511] CAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGG CGCCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCA CCAGCTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCC TGGAGTGGATGGGCATCATCAACCCCAGCGGCGGCAGCACCACC TACGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACAC CAGCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGCCGCCGACGGC TTCGTGGGCGAGAGGTACTTCGACCTGTGGGGCAGGGGCACCCTG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCGTGATGA CCCAGAGCCCCCTGAGCCTGCCCGTGACCCCCGGCGAGCCCGCCA GCATCAGCTGCAGGAGCAGCCAGAGCCTGCTGCACAGCAACGGC TACAACTACCTGGACTGGTACCTGCAGAAGCCCGGCCAGAGCCCC CAGCTGCTGATCTACCTGGGCAGCAACAGGGCCAGCGGCGTGCCC GACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAA	

Table 1	VH	VL
	GATCAGCAGGGTGGAGGCCGAGGACGTGGGCGTGTACTACTGCA TGCAGGCCCTGGGCGTGCCCCTGACCTTCGGCTGCGGCACCAAGG TGGAGATCAAG [SEQ ID NO:512]	
ADI-11802 [Ab23]	QVQLVQSGAEVKKPGASVKVS CKASGYTFSGYYMHWVRQAPG QGLEWMGMINPYGGSTRYAQK FQGRVTMTRDTSTSTVYMELSS LRSEDTAVYYCAREAADGFVGE RYFDLWGRGTLVTVSS [SEQ ID NO:290] CDR1: GYYMH [SEQ ID NO:376] or YTFSGYYMH [SEQ ID NO:552] (non-Kabat) CDR2: MINPYGGSTRYAQKFQG [SEQ ID NO:377] CDR3: EAADGFVGERYFDL [SEQ ID NO:378] or AREAADGFVGERYFDL [SEQ ID NO:553] (non-Kabat)	DIVMTQSPLSLPVTPGEPASISCR SSQSLLYSNGYNYLDWYLQKPG QSPQLLIYLGSNRASGVPDRFSGS GSGTDFTLKISRVEAEDVGVYYC MQDVALPITFGGGTKVEIK [SEQ ID NO:291] CDR1: RSSQSLLYSNGYNYLD [SEQ ID NO:379] CDR2: LGSNRAS [SEQ ID NO:380] CDR3: MQDVALPIT [SEQ ID NO:381]
scFv of Ab23	DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQS PQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQ DVALPITFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQSG AEVKKPGASVKVSCKASGYTFSGYYMHWVRQAPGQ*C*LEWMGMIN PYGGSTRYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAR EAADGFVGERYFDLWGRGTLVTVSS [SEQ ID NO:471] QVQLVQSGAEVKKPGASVKVSCKASGYTFSGYYMHWVRQAPGQ*C*L EWMGMINPYGGSTRYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDT AVYYCAREAADGFVGERYFDLWGRGTLVTVSS**GGGGSGGGGSGG GGSGGGGS**DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLD WYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAED VGVYYCMQDVALPITFG*C*GTKVEIK [SEQ ID NO:472]
Exemplary nucleotide sequence of Ab23 scFv	GACATCGTGATGACCCAGAGCCCCCTGAGCCTGCCCGTGACCCCC GGCGAGCCCGCCAGCATCAGCTGCAGGAGCAGCCAGAGCCTGCT GTACAGCAACGGCTACAACTACCTGGACTGGTACCTGCAGAAGCC CGGCCAGAGCCCCCAGCTGCTGATCTACCTGGGCAGCAACAGGG CCAGCGGCGTGCCCGACAGGTTCAGCGGCAGCGGCAGCGGCACC GACTTCACCCTGAAGATCAGCAGGGTGGAGGCCGAGGACGTGGG CGTGTACTACTGCATGCAGGACGTGGCCCTGCCCATCACCTTCGG CTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCG GCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCAG GTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGGCGC CAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCAGCG GCTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCCTGG	

Table 1	VH	VL
	AGTGGATGGGCATGATCAACCCCTACGGCGGCAGCACCAGGTAC GCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACACCAG CACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCGAGG ACACCGCCGTGTACTACTGCGCCAGGGAGGCCGCCGACGGCTTCG TGGGCGAGAGGTACTTCGACCTGTGGGGCAGGGGCACCCTGGTG ACCGTGAGCAGC [SEQ ID NO:513] CAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGG CGCCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCA GCGGCTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCC TGGAGTGGATGGGCATGATCAACCCCTACGGCGGCAGCACCAGG TACGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACAC CAGCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGCCGCCGACGGC TTCGTGGGCGAGAGGTACTTCGACCTGTGGGGCAGGGGCACCCTG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCGTGATGA CCCAGAGCCCCCTGAGCCTGCCCGTGACCCCCGGCGAGCCCGCCA GCATCAGCTGCAGGAGCAGCCAGAGCCTGCTGTACAGCAACGGC TACAACTACCTGGACTGGTACCTGCAGAAGCCCGGCCAGAGCCCC CAGCTGCTGATCTACCTGGGCAGCAACAGGGCCAGCGGCGTGCCC GACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAA GATCAGCAGGGTGGAGGCCGAGGACGTGGGCGTGTACTACTGCA TGCAGGACGTGGCCCTGCCCATCACCTTCGGCTGCGGCACCAAGG TGGAGATCAAG [SEQ ID NO:514]	
ADI-11812 [Ab24]	QVQLVQSGAEVKKPGASVKVS CKASGYTFEIYYMHWVRQAPG QGLEWMGIINPSSGSTVYAQKF QGRVTMTRDTSTSTVYMELSSL RSEDTAVYYCARGAGYDDEDM DVWGKGTTVTVSS [SEQ ID NO:292] CDR1: IYYMH [SEQ ID NO:382] or YTFEIYYMH [SEQ ID NO:554] (non-Kabat) CDR2: IINPSSGSTVYAQKFQG [SEQ ID NO:383] CDR3: GAGYDDEDMDV [SEQ ID NO:384] or ARGAGYDDEDMDV [SEQ ID NO:555] (non-Kabat)	DIQMTQSPSSVSASVGDRVTITC RASQGIDSWLAWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQAHS YPLTFGGGTKVEIK [SEQ ID NO:293] CDR1: RASQGIDSWLA [SEQ ID NO:385] CDR2: AASSLQS [SEQ ID NO:386] CDR3: QQAHSYPLT [SEQ ID NO:387]
scFv of Ab24	DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLL IYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPL TFG**C**GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQSGAEVKK PGASVKVSCKASGYTFEIYYMHWVRQAPGQ**C**LEWMGIINPSSGSTV	

Table 1	VH	VL
	YAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDVWGKGTTVTVSS [SEQ ID NO:473] QVQLVQSGAEVKKPGASVKVSCKASGYTFEIYYMHWVRQAPGQCLEWMGIINPSSGSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDVWGKGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPLTFGCGTKVEIK [SEQ ID NO:474]
Exemplary nucleotide sequence of Ab24 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCGTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGGGCATCGACAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGCCAGCAGCCTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGCCCACAGCTACCCCCTGACCTTCGGCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGGCGCCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCGAGATCTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCCTGGAGTGGATGGGCATCATCAACCCCAGCAGCGGCAGCACCGTGTACGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACACCAGCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCGAGGACACCGCCGTGTACTACTGCGCCAGGGGCGCCGGCTACGACGACGAGGACATGGACGTGTGGGGCAAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:515] CAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGGCGCCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCGAGATCTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCCTGGAGTGGATGGGCATCATCAACCCCAGCAGCGGCAGCACCGTGTACGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACACCAGCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCGAGGACACCGCCGTGTACTACTGCGCCAGGGGCGCCGGCTACGACGACGAGGACATGGACGTGTGGGGCAAGGGCACCACCGTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGAGCCCCAGCAGCGTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGGGCATCGACAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGCCAGCAGCCTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGCCCACAGCTACCCCCTGACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:516]

Table 1	VH	VL
ADI-11825 [Ab25]	EVQLVESGGGLVQPGGSLRLSC AASGFTFGGYWMSWVRQAPGK GLEWVANINQDGSEEYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCAREANYYGNVG DDYWGQGTLVTVSS [SEQ ID NO:294] CDR1: GYWMS [SEQ ID NO:388] or FTFGGYWMS [SEQ ID NO:556] (non-Kabat) CDR2: NINQDGSEEYYVDSVKG [SEQ ID NO:389] CDR3: EANYYGNVGDDY [SEQ ID NO:390] or AREANYYGNVGDDY [SEQ ID NO:557] (non-Kabat)	DIQMTQSPSSLSASVGDRVTITCR ASQSIYNYLNWYQQKPGKAPKL LIYAASNLHSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQAFH VPITFGGGTKVEIK [SEQ ID NO:295] CDR1: RASQSIYNYLN [SEQ ID NO:391] CDR2: AASNLHS [SEQ ID NO:392] CDR3: QQAFHVPIT [SEQ ID NO:393]
scFv of Ab25	DIQMTQSPSSLSASVGDRVTITCRASQSIYNYLNWYQQKPGKAPKLLI YAASNLHSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAFHVPI TFG**C**GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQ PGGSLRLSCAASGFTFGGYWMSWVRQAPGK**C**LEWVANINQDGSEE YYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREANYY GNVGDDYWGQGTLVTVSS [SEQ ID NO:475] EVQLVESGGGLVQPGGSLRLSCAASGFTFGGYWMSWVRQAPGK**C**L EWVANINQDGSEEYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDT AVYYCAREANYYGNVGDDYWGQGTLVTVSS**GGGGSGGGGSGGG GSGGGGS**DIQMTQSPSSLSASVGDRVTITCRASQSIYNYLNWYQQKP GKAPKLLIYAASNLHSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQAFHVPITFG**C**GTKVEIK [SEQ ID NO:476]
Exemplary nucleotide sequence of Ab25 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCT ACAACTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCAACCTGCACAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGGCCTTCCACGTGCCCATCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGA GAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGA GCTGCGCCGCCAGCGGCTTCACCTTCGGCGGCTACTGGATGAGCT GGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAAC ATCAACCAGGACGGCAGCGAGGAGTACTACGTGGACAGCGTGAA GGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGT ACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTAC	

Table 1	VH	VL
	TACTGCGCCAGGGAGGCCAACTACTACGGCAACGTGGGCGACGA CTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:517] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCGG CGGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAACCAGGACGGCAGCGAGGAGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGAGGCCAACTACTAC GGCAACGTGGGCGACGACTACTGGGGCCAGGGCACCCTGGTGAC CGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCG GCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGACCCAG AGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCAT CACCTGCAGGGCCAGCCAGAGCATCTACAACTACCTGAACTGGTA CCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCG CCAGCAACCTGCACAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCC GAGGACTTCGCCACCTACTACTGCCAGCAGGCCTTCCACGTGCCC ATCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:518]	
ADI-11826 [Ab26]	EVQLVESGGGLVQPGGSLRLSC AASGFTFPGYWMSWVRQAPGK GLEWVANINQDGSEVYYVDSV KGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCAREANYYGNVG DDYWGQGTLVTVSS [SEQ ID NO:296] CDR1: GYWMS [SEQ ID NO:394] or FTFPGYWMS [SEQ ID NO:558] (non-Kabat) CDR2: NINQDGSEVYYVDSVKG [SEQ ID NO:395] CDR3: EANYYGNVGDDY [SEQ ID NO:396] or AREANYYGNVGDDY [SEQ ID NO:559] (non-Kabat)	DIQMTQSPSSLSASVGDRVTITCR ASQSIYNYLNWYQQKPGKAPKL LIYAASSTQSGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQAFHV PITFGGGTKVEIK [SEQ ID NO:297] CDR1: RASQSIYNYLN [SEQ ID NO:397] CDR2: AASSTQS [SEQ ID NO:398] CDR3: QQAFHVPIT [SEQ ID NO:399]
scFv of Ab26	DIQMTQSPSSLSASVGDRVTITCRASQSIYNYLNWYQQKPGKAPKLLI YAASSTQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAFHVPIT FG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQP GGSLRLSCAASGFTFPGYWMSWVRQAPGK*C*LEWVANINQDGSEVY YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREANYYG NVGDDYWGQGTLVTVSS [SEQ ID NO:477]	

Table 1	VH	VL
	EVQLVESGGGLVQPGGSLRLSCAASGFTFPGYWMSWVRQAPGK***C***LEWVANINQDGSEVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREANYYGNVGDDYWGQGTLVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSSLSASVGDRVTITCRASQSIYNYLNWYQQKPGKAPKLLIYAASSTQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAFHVPITFG***C***GTKVEIK [SEQ ID NO:478]	
Exemplary nucleotide sequence of Ab26 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCTACAACTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGCCAGCAGCACCCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGCCTTCCACGTGCCCATCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCCCCGGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAACATCAACCAGGACGGCAGCGAGGTGTACTACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGGAGGCCAACTACTACGGCAACGTGGGCGACGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:519] GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCCCCGGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAACATCAACCAGGACGGCAGCGAGGTGTACTACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGGAGGCCAACTACTACGGCAACGTGGGCGACGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCTACAACTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGCCAGCAGCACCCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGCCTTCCACGTGCCCATCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:520]	
ADI-11828 [Ab27]	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANINQDGSEVYYVDSVKGRFTISRDNAKNSLYLQMNSL	DIQMTQSPSSLSASVGDRVTITCRASQSIYYYLNWYQQKPGKAPKLLIYAASSRQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYD

Table 1	VH	VL
	RAEDTAVYYCARDVGPGIAYQ GHFDYWGQGTLVTVSS [SEQ ID NO:298] CDR1: SYWMS [SEQ ID NO:400] or FTFSSYWMS [SEQ ID NO:560] (non-Kabat) CDR2: NINQDGSEVYYVDSVKG [SEQ ID NO:401] CDR3: DVGPGIAYQGHFDY [SEQ ID NO:402] or ARDVGPGIAYQGHFDY [SEQ ID NO:561] (non-Kabat)	TPLTFGGGTKVEIK [SEQ ID NO:299] CDR1: RASQSIYYYLN [SEQ ID NO:403] CDR2: AASSRQS [SEQ ID NO:404] CDR3: QQVYDTPLT [SEQ ID NO:405]
scFv of Ab27	DIQMTQSPSSLSASVGDRVTITCRASQSIYYYLNWYQQKPGKAPKLLI YAASSRQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYDTPL TFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LEWVANINQDGSEVY YVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDVGPGIA YQGHFDYWGQGTLVTVSS [SEQ ID NO:479] EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK*C*LE WVANINQDGSEVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCARDVGPGIAYQGHFDYWGQGTLVTVSS**GGGGSGGGGSGGG GSGGGGS**DIQMTQSPSSLSASVGDRVTITCRASQSIYYYLNWYQQKP GKAPKLLIYAASSRQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ QVYDTPLTFG*C*GTKVEIK [SEQ ID NO:480]
Exemplary nucleotide sequence of Ab27 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCAGGGCCAGCCAGAGCATCT ACTACTACCTGAACTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCAGCAGGCAGAGCGGCGTGCC CAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGA CCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCC AGCAGGTGTACGACACCCCCCTGACCTTCGGCTGCGGCACCAAGG TGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGGA GAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGA GCTGCGCCGCCAGCGGCTTCACCTTCAGCAGCTACTGGATGAGCT GGGTGAGGCAGGCCCCCGGCAAGTGCCTGGAGTGGGTGGCCAAC ATCAACCAGGACGGCAGCGAGGTGTACTACGTGGACAGCGTGAA GGGCAGGTTCACCATCAGCAGGGACAACGCCAAGAACAGCCTGT ACCTGCAGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGGGACGTGGGCCCCGGCATCGCCTACCAGGGCCAC TTCGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:521]	

Table 1	VH	VL
	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGG CGGCAGCCTGAGGCTGAGCTGCGCCGCCAGCGGCTTCACCTTCAG CAGCTACTGGATGAGCTGGGTGAGGCAGGCCCCCGGCAAGTGCC TGGAGTGGGTGGCCAACATCAACCAGGACGGCAGCGAGGTGTAC TACGTGGACAGCGTGAAGGGCAGGTTCACCATCAGCAGGGACAA CGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCG AGGACACCGCCGTGTACTACTGCGCCAGGGACGTGGGCCCCGGC ATCGCCTACCAGGGCCACTTCGACTACTGGGGCCAGGGCACCCTG GTGACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAG CGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGA CCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTG ACCATCACCTGCAGGGCCAGCCAGAGCATCTACTACCTGAACTGG TACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCC GCCAGCAGCAGGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAG CGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCC CGAGGACTTCGCCACCTACTACTGCCAGCAGGTGTACGACACCCC CCTGACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:522]	
ADI-11839 [Ab28]	QVQLVQSGAEVKKPGASVKVS CKASGYTFSNYYMHWVRQAPG QGLEWMGWINPFSGGTRYAQK FQGRVTMTRDTSTSTVYMELSS LRSEDTAVYYCARDVGSSAYY YMDVWGKGTTVTVSS [SEQ ID NO:300] CDR1: NYYMH [SEQ ID NO:406] or YTFSNYYMH [SEQ ID NO:562] (non-Kabat) CDR2: WINPFSGGTRYAQKFQG [SEQ ID NO:407] CDR3: DVGSSAYYYMDV [SEQ ID NO:408] or ARDVGSSAYYYMDV [SEQ ID NO:563] (non-Kabat)	DIQMTQSPSSVSASVGDRVTITCE ASKGISSWLAWYQQKPGKAPKL LIYAASDLQSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQAFL FPPTFGGGTKVEIK [SEQ ID NO:301] CDR1: EASKGISSWLA [SEQ ID NO:409] CDR2: AASDLQS [SEQ ID NO:410] CDR3: QQAFLFPPT [SEQ ID NO:411]
scFv of Ab28	DIQMTQSPSSVSASVGDRVTITCEASKGISSWLAWYQQKPGKAPKLL IYAASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAFLFPP TFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQSGAEVKK PGASVKVSCKASGYTFSNYYMHWVRQAPGQ*C*LEWMGWINPFSGGT RYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDVGSSA YYYMDVWGKGTTVTVSS [SEQ ID NO:481] QVQLVQSGAEVKKPGASVKVSCKASGYTFSNYYMHWVRQAPGQ*C*L EWMGWINPFSGGTRYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDT AVYYCARDVGSSAYYYMDVWGKGTTVTVSS**GGGGSGGGGSGGG GSGGGGS**DIQMTQSPSSVSASVGDRVTITCEASKGISSWLAWYQQK	

Table 1	VH	VL
	PGKAPKLLIYAASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQAFLFPPTFG*C*GTKVEIK [SEQ ID NO:482]	
Exemplary nucleotide sequence of Ab28 scFv	GACATCCAGATGACCCAGAGCCCCAGCAGCGTGAGCGCCAGCGT GGGCGACAGGGTGACCATCACCTGCGAGGCCAGCAAGGGCATCA GCAGCTGGCTGGCCTGGTACCAGCAGAAGCCCGGCAAGGCCCCC AAGCTGCTGATCTACGCCGCCAGCGACCTGCAGAGCGGCGTGCCC AGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGAC CATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCA GCAGGCCTTCCTGTTCCCCCCCACCTTCGGCTGCGGCACCAAGGT GGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGC GGCGGCGGCAGCGGCGGCGGCGGCAGCCAGGTGCAGCTGGTGCA GAGCGGCGCCGAGGTGAAGAAGCCCGGCGCCAGCGTGAAGGTGA GCTGCAAGGCCAGCGGCTACACCTTCAGCAACTACTACATGCACT GGGTGAGGCAGGCCCCCGGCCAGTGCCTGGAGTGGATGGGCTGG ATCAACCCCTTCAGCGGCGGCACCAGGTACGCCCAGAAGTTCCAG GGCAGGGTGACCATGACCAGGGACACCAGCACCAGCACCGTGTA CATGGAGCTGAGCAGCCTGAGGAGCGAGGACACCGCCGTGTACT ACTGCGCCAGGGACGTGGGCAGCAGCGCCTACTACTACATGGAC GTGTGGGGCAAGGGCACCACCGTGACCGTGAGCAGC [SEQ ID NO:523] CAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGG CGCCAGCGTGAAGGTGAGCTGCAAGGCCAGCGGCTACACCTTCA GCAACTACTACATGCACTGGGTGAGGCAGGCCCCCGGCCAGTGCC TGGAGTGGATGGGCTGGATCAACCCCTTCAGCGGCGGCACCAGGT ACGCCCAGAAGTTCCAGGGCAGGGTGACCATGACCAGGGACACC AGCACCAGCACCGTGTACATGGAGCTGAGCAGCCTGAGGAGCGA GGACACCGCCGTGTACTACTGCGCCAGGGACGTGGGCAGCAGCG CCTACTACTACATGGACGTGTGGGGCAAGGGCACCACCGTGACCG TGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGC GGCGGCAGCGGCGGCGGCGGCAGCGACATCCAGATGACCCAGAG CCCCAGCAGCGTGAGCGCCAGCGTGGGCGACAGGGTGACCATCA CCTGCGAGGCCAGCAAGGGCATCAGCAGCTGGCTGGCCTGGTAC CAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGC CAGCGACCTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCG GCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCG AGGACTTCGCCACCTACTACTGCCAGCAGGCCTTCCTGTTCCCCCC CACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:524]	
ADI-10152 [Ab29]	EVQLVQSGAEVKKPGESLKISC KGSGYSFTSYWIGWVRQMPGK GLEWMGSIYPGDSDTRYSPSFQ GQVTISADKSISTAYLQWSSLKA SDTAMYYCARELAYGDYKGGV DYWGQGTLVTVSS [SEQ ID NO:302]	EIVLTQSPGTLSLSPGERATLSCR ASQSVSSSFLAWYQQKPGQAPR LLIYGASSRATGIPDRFSGSGSGT DFTLTISRLEPEDFAVYYCQQLDS PPPTFGGGTKVEIK [SEQ ID NO:303] CDR1: RASQSVSSSFLA [SEQ ID

Table 1	VH	VL
	CDR1: SYWIG [SEQ ID NO:412] or YSFTSYWIG [SEQ ID NO:564] (non-Kabat) CDR2: SIYPGDSDTRYSPSFQG [SEQ ID NO:413] CDR3: ELAYGDYKGGVDY [SEQ ID NO:414] or ARELAYGDYKGGVDY [SEQ ID NO:565] (non-Kabat)	NO:415] CDR2: GASSRAT [SEQ ID NO:416] CDR3: QQLDSPPPT [SEQ ID NO:417]
scFv of Ab29	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQLDSPPPTFG*C*GTKVEIK**GGGGSGGGGSGGGGSGGGGS**EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGK*C*LEWMGSIYPGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARELAYGDYKGGVDYWGQGTLVTVSS [SEQ ID NO:483] EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGK*C*LEWMGSIYPGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARELAYGDYKGGVDYWGQGTLVTVSS**GGGGSGGGGSGGGGSGGGGS**EIVLTQSPGTLSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQLDSPPPTFG*C*GTKVEIK [SEQ ID NO:484]
Exemplary nucleotide sequence of Ab29 scFv	GAGATCGTGCTGACCCAGAGCCCCGGCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCACCCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCAGCTTCCTGGCCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCTACGGCGCCAGCAGCAGGGCCACCGGCATCCCCGACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGGCTGGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGCAGCTGGACAGCCCCCCCCCCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAGGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGGCGAGAGCCTGAAGATCAGCTGCAAGGGCAGCGGCTACAGCTTCACCAGCTACTGGATCGGCTGGGTGAGGCAGATGCCCGGCAAGTGCCTGGAGTGGATGGGCAGCATCTACCCCGGCGACAGCGACACCAGGTACAGCCCCAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACAAGAGCATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAAGGCCAGCGACACCGCCATGTACTACTGCGCCAGGGAGCTGGCCTACGGCGACTACAAGGGCGGCGTGGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC [SEQ ID NO:525] GAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCCGGCGAGAGCCTGAAGATCAGCTGCAAGGGCAGCGGCTACAGCTTCACCAGCTACTGGATCGGCTGGGTGAGGCAGATGCCCGGCAAGTGCCTGGAGTGGATGGGCAGCATCTACCCCGGCGACAGCGACACCAG

Table 1	VH	VL
	GTACAGCCCCAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACA AGAGCATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAAGGCC AGCGACACCGCCATGTACTACTGCGCCAGGGAGCTGGCCTACGGC GACTACAAGGGCGGCGTGGACTACTGGGGCCAGGGCACCCTGGT GACCGTGAGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCG GCGGCGGCGGCAGCGGCGGCGGCGGCAGCGAGATCGTGCTGACC CAGAGCCCCGGCACCCTGAGCCTGAGCCCCGGCGAGAGGGCCAC CCTGAGCTGCAGGGCCAGCCAGAGCGTGAGCAGCAGCTTCCTGG CCTGGTACCAGCAGAAGCCCGGCCAGGCCCCCAGGCTGCTGATCT ACGGCGCCAGCAGCAGGGCCACCGGCATCCCCGACAGGTTCAGC GGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGGCT GGAGCCCGAGGACTTCGCCGTGTACTACTGCCAGCAGCTGGACAG CCCCCCCCCCACCTTCGGCTGCGGCACCAAGGTGGAGATCAAG [SEQ ID NO:526]	
Clone 280-31-01 (mut) of WO2012045752	QVQLVQSGAEVKKPGSSVKVSC KASGGTFSDYAISWVRQAPGQG LEWMGRIIPILGVADYAQKFQG RVTITADKSTRTAYMELSSLRSE DTAVYYCARNWADAFDIWGQG TMVTVSS [SEQ ID NO:418] CDR1: DYAIS [SEQ ID NO:422] CDR2: RIIPILGVADYAQKFQG [SEQ ID NO:423] CDR3: NWADAFDI [SEQ ID NO:424]	DIQLTQSPSSLSASVGDRVTITCR ASQGISSVLAWYQQKPGKAPKL LIYDASSLESGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQFDSSI TFGQGTKLEIK [SEQ ID NO:419] CDR1: RASQGISSVLA [SEQ ID NO:425] CDR2: DASSLES [SEQ ID NO:426] CDR3: QQFDSSIT [SEQ ID NO:427]
scFv of clone 280-31-01 (mut) of WO2012045752	DIQLTQSPSSLSASVGDRVTITCRASQGISSVLAWYQQKPGKAPKLLI YDASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFDSSITF G*C*GTKLEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQSGAEVKKPG SSVKVSCKASGGTFSDYAISWVRQAPGQ*C*LEWMGRIIPILGVADYAQ KFQGRVTITADKSTRTAYMELSSLRSEDTAVYYCARNWADAFDIWG QGTMVTVSS [SEQ ID NO:485] QVQLVQSGAEVKKPGSSVKVSCKASGGTFSDYAISWVRQAPGQ*C*LE WMGRIIPILGVADYAQKFQGRVTITADKSTRTAYMELSSLRSEDTAV YYCARNWADAFDIWGQGTMVTVSS**GGGGSGGGGSGGGGSGGGG S**DIQLTQSPSSLSASVGDRVTITCRASQGISSVLAWYQQKPGKAPKLL IYDASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFDSSITF G*C*GTKLEIK [SEQ ID NO:486]	
lintuzumab	QVQLVQSGAEVKKPGSSVKVSC KASGYTFTDYNMHWVRQAPGQ GLEWIGYIYPYNGGTGYNQKFK SKATITADESTNTAYMELSSLRS EDTAVYYCARGRPAMDYWGQ	DIQMTQSPSSLSASVGDRVTITCR ASESVDNYGISFMNWFQQKPGK APKLLIYAASNQGSGVPSRFSGS GSGTDFTLTISSLQPDDFATYYCQ QSKEVPWTFGQGTKVEIK [SEQ

Table 1	VH	VL
	GTLVTVSS [SEQ ID NO:420] CDR1: DYNMH [SEQ ID NO:428] CDR2: YIYPYNGGTGYNQKFKS [SEQ ID NO:429] CDR3: GRPAMDY [SEQ ID NO:430]	ID NO:421] CDR1: RASESVDNYGISFMN [SEQ ID NO:431] CDR2: AASNQGS [SEQ ID NO:432] CDR3: QQSKEVPWT [SEQ ID NO:433]
scFv of lintuzumab	DIQMTQSPSSLSASVGDRVTITCRASESVDNYGISFMNWFQQKPGKAPKLLIYAASNQGSGVPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQSKEVPWTFG**C**GTKVEIK**GGGGSGGGGSGGGGSGGGGS**QVQLVQSGAEVKKPGSSVKVSCKASGYTFTDYNMHWVRQAPGQ**C**LEWIGYIYPYNGGTGYNQKFKSKATITADESTNTAYMELSSLRSEDTAVYYCARGRPAMDYWGQGTLVTVSS [SEQ ID NO:487] QVQLVQSGAEVKKPGSSVKVSCKASGYTFTDYNMHWVRQAPGQ**C**LEWIGYIYPYNGGTGYNQKFKSKATITADESTNTAYMELSSLRSEDTAVYYCARGRPAMDYWGQGTLVTVSS**GGGGSGGGGSGGGGSGGGG S**DIQMTQSPSSLSASVGDRVTITCRASESVDNYGISFMNWFQQKPGKAPKLLIYAASNQGSGVPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQSKEVPWTFG**C**GTKVEIK [SEQ ID NO:488]

An antigen binding site that binds an epitope on an extracellular domain of human CD33 and/or Cynomolgus/Rhesus (cyno) CD33

[0225] In one aspect, the invention provides an antigen binding site including a heavy chain variable domain that binds an epitope on an extracellular domain of human CD33 and/or Cynomolgus/Rhesus (cyno) CD33.

[0226] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYGMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVYYGMDVWGQGTTVTVSS [SEQ ID NO:1]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:1. In some embodiments, the heavy chain variable domain includes amino acid sequences FTFSSYGMS [SEQ ID NO:21]

as the first complementarity-determining region 1 ("CDR1"), NIKQDGSEKYYVDSVKG [SEQ ID NO:22] as the second CDR ("CDR2"), and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:23] as the third CDR ("CDR3") of SEQ ID NO:1. In some embodiments, the heavy chain variable domain includes amino acid sequences SYGMS [SEQ ID NO:434] as the first complementarity-determining region 1 ("CDR1"), NIKQDGSEKYYVDSVKG [SEQ ID NO:22] as the second CDR ("CDR2"), and EGGPYYDSSGYFVYYGMDV [SEQ ID NO:435] as the third CDR ("CDR3") of SEQ ID NO:1. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYESFPTFGGGTKVEIK [SEQ ID NO:2]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:2, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:24] as CDR1, DASSLES [SEQ ID NO:25] as CDR2, and QQYESFPT [SEQ ID NO:26] as CDR3 of SEQ ID NO:2.

[0227] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDG SEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ GTMVTVSS [SEQ ID NO:3]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:3. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:27] as

CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:28] as CDR2, and ARPLNAGELDV [SEQ ID NO:29] as CDR3 of SEQ ID NO:3. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:28] as CDR2, and PLNAGELDV [SEQ ID NO:436] as CDR3 of SEQ ID NO:3. In certain embodiments, the antibody heavy chain variable domain, which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3, is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQLESYPLTFGGGTKVEIK [SEQ ID NO:4]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:4, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:30] as CDR1, EASSLES [SEQ ID NO:31] as CDR2, and QQLESYPLT [SEQ ID NO:32] as CDR3 of SEQ ID NO:4.

[0228] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGKGLEWVSAIVGSGE STYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVY YGMDVWGQGTTVTVSS [SEQ ID NO:5]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:5. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSKYTMS [SEQ ID NO:33] as CDR1, AIVGSGESTYFADSVKG [SEQ ID NO:34] as CDR2, and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:35] as CDR3 of SEQ ID NO:5. In some

embodiments, the heavy chain variable domain incorporates amino acid sequences KYTMS [SEQ ID NO:183] as CDR1, AIVGSGESTYFADSVKG [SEQ ID NO:34] as CDR2, and EGGPYYDSSGYFVYYGMDV [SEQ ID NO:184] as CDR3 of SEQ ID NO:5. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFGGGTKVEIK [SEQ ID NO:6]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:36] as CDR1, KASSLES [SEQ ID NO:37] or KASSLE [SEQ ID NO:185] as CDR2, and QQYDDLPT [SEQ ID NO:38] as CDR3 of SEQ ID NO:6.

[0229] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQGLEWMGMINPS WGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAREAADGFVGERYF DLWGRGTLVTVSS [SEQ ID NO:7]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:7. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFSDYYMH [SEQ ID NO:39] as CDR1, MINPSWGSTSYAQKFQG [SEQ ID NO:40] as CDR2, and AREAADGFVGERYFDL [SEQ ID NO:41] as CDR3 of SEQ ID NO:7. In some embodiments, the heavy chain variable domain incorporates amino acid sequences DYYMH [SEQ ID NO:437] as CDR1, AIVGSGESTYFADSVKG [SEQ ID NO:34] as CDR2, and

EAADGFVGERYFDL [SEQ ID NO:438] as CDR3 of SEQ ID NO:7. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQSPQLLIYLGSN RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQDVALPITFGGGTKVEIK [SEQ ID NO:8]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8, which includes amino acid sequences RSSQSLLYSNGYNYLD [SEQ ID NO:42] as CDR1, LGSNRAS [SEQ ID NO:43] as CDR2, and MQDVALPIT [SEQ ID NO:44] as CDR3 of SEQ ID NO:8.

[0230] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPGKGLEWVATIKQDG SEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ GTMVTVSS [SEQ ID NO:9]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:9. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFGSYWMS [SEQ ID NO:45] as CDR1, TIKQDGSEKSYVDSVKG [SEQ ID NO:46] as CDR2, and ARPLNAGELDV [SEQ ID NO:47] as CDR3 of SEQ ID NO:9. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1, TIKQDGSEKSYVDSVKG [SEQ ID NO:46] as CDR2, and RPLNAGELDV [SEQ ID NO:182] as CDR3 of SEQ ID NO:9. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%,

92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIK [SEQ ID NO:10]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:10, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:48] as CDR1, EASSLES [SEQ ID NO:49] as CDR2, and QQSQSYPPIT [SEQ ID NO:50] as CDR3 of SEQ ID NO:10.

[0231] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFPSYWMSWVRQAPGKGLEWVATIKRDGS EKGYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQG TMVTVSS [SEQ ID NO:11]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:11. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFPSYWMS [SEQ ID NO:51] as CDR1, TIKRDGSEKGYVDSVKG [SEQ ID NO:52] as CDR2, and ARPLNAGELDV [SEQ ID NO:53] as CDR3 of SEQ ID NO:11. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1, TIKRDGSEKGYVDSVKG [SEQ ID NO:52] as CDR2, and PLNAGELDV [SEQ ID NO:439] as CDR3 of SEQ ID NO:11. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 is combined with a light chain variable domain to form an antigen-binding

site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIK [SEQ ID NO:12]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:12, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:54] as CDR1, EASSLES [SEQ ID NO:55] as CDR2, and QQSQSYPPIT [SEQ ID NO:56] as CDR3 of SEQ ID NO:12.

[0232] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQAPGQGLEWMGIINPSR GSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDV WGKGTTVTVSS [SEQ ID NO:13]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:13. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFGTYYMH [SEQ ID NO:57] as CDR1, IINPSRGSTVYAQKFQG [SEQ ID NO:58] as CDR2, and ARGAGYDDEDMDV [SEQ ID NO:59] as CDR3 of SEQ ID NO:13. In some embodiments, the heavy chain variable domain incorporates amino acid sequences TYYMH [SEQ ID NO:440] as CDR1, TIKRDGSEKGYVDSVKG [SEQ ID NO:52] as CDR2, and GAGYDDEDMDV [SEQ ID NO:441] as CDR3 of SEQ ID NO:13. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%)

identical to the amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPLTFGGGTKVEIK [SEQ ID NO:14]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14, which includes amino acid sequences RASQGIDSWLA [SEQ ID NO:60] as CDR1, AASSLQS [SEQ ID NO:61] as CDR2, and QQAHSYPLT [SEQ ID NO:62] as CDR3 of SEQ ID NO:14.

[0233] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSISSSSEG IYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVYY GMDVWGQGTTVTVSS [SEQ ID NO:15]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:15. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYAMS [SEQ ID NO:63] as CDR1, SISSSSEGIYYADSVKG [SEQ ID NO:64] as CDR2, and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:65] as CDR3 of SEQ ID NO:15. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYAMS [SEQ ID NO:442] as CDR1, SISSSSEGIYYADSVKG [SEQ ID NO:64] as CDR2, and EGGPYYDSSGYFVYYGMDV [SEQ ID NO:443] as CDR3 of SEQ ID NO:15. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASNSISSWLAWYQQKPGKAPKLLIYEASSTKSGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFGGGTKVEIK [SEQ ID NO:16]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:16, which includes amino acid sequences RASNSISSWLA [SEQ ID NO:66] as CDR1, EASSTKS [SEQ ID NO:67] as CDR2, and QQYDDLPT [SEQ ID NO:68] as CDR3 of SEQ ID NO:16.

[0234] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANINTDG SEVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDVGPGIAYQGHFD YWGQGTLVTVSS [SEQ ID NO:17]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:17. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:69] as CDR1, NINTDGSEVYYVDSVKG [SEQ ID NO:70] as CDR2, and ARDVGPGIAYQGHFDY [SEQ ID NO:71] as CDR3 of SEQ ID NO:17. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1, NINTDGSEVYYVDSVKG [SEQ ID NO:70] as CDR2, and DVGPGIAYQGHFDY [SEQ ID NO:444] as CDR3 of SEQ ID NO:17. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQVIYSYLNWYQQKPGKAPKLLIYAASSLKSGV

PSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYDTPLTFGGGTKVEIK [SEQ ID NO:18]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:18, which includes amino acid sequences RASQVIYSYLN [SEQ ID NO:72] as CDR1, AASSLKS [SEQ ID NO:73] as CDR2, and QQVYDTPLT [SEQ ID NO:74] as CDR3 of SEQ ID NO:18.

[0235] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno) CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QLQLQESGPGLVKPSETLSLTCTVSGGSISSTDYYWGWIRQPPGKGLEWIGSIGYSGT YYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARETAHDVHGMDVWGQG TTVTVSS [SEQ ID NO:19]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:19. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GSISSTDYYWG [SEQ ID NO:75] as CDR1, SIGYSGTYYNPSLKS [SEQ ID NO:76] as CDR2, and ARETAHDVHGMDV [SEQ ID NO:77] as CDR3 of SEQ ID NO:19. In some embodiments, the heavy chain variable domain incorporates amino acid sequences STDYYWG [SEQ ID NO:445] as CDR1, SIGYSGTYYNPSLKS [SEQ ID NO:76] as CDR2, and ETAHDVHGMDV [SEQ ID NO:446] as CDR3 of SEQ ID NO:19. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence EIVLTQSPATLSLSPGERATLSCRASHSVYSYLAWYQQKPGQAPRLLIYDASNRATGI PARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLPTFGGGTKVEIK [SEQ ID NO:20]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*,

at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:20, which includes amino acid sequences RASHSVYSYLA [SEQ ID NO:78] as CDR1, DASNRAT [SEQ ID NO:79] as CDR2, and QQYDNLPT [SEQ ID NO:80] as CDR3 of SEQ ID NO:20.

[0236] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:304 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:306 as CDR3 of SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:528 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:529 as CDR3 of SEQ ID NO:266. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267, which includes amino acid sequences SEQ ID NO:307 as CDR1, SEQ ID NO:308 as CDR2, and SEQ ID NO:309 as CDR3 of SEQ ID NO:267.

[0237] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*,

at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:310 as CDR1, SEQ ID NO:311 as CDR2, and SEQ ID NO:312 as CDR3 of SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:530 as CDR1, SEQ ID NO:311 as CDR2, and SEQ ID NO:531 as CDR3 of SEQ ID NO:268. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269, which includes amino acid sequences SEQ ID NO:313 as CDR1, SEQ ID NO:314 as CDR2, and SEQ ID NO:315 as CDR3 of SEQ ID NO:269.

[0238] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:316 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:318 as CDR3 of SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:532 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:533 as CDR3 of SEQ ID NO:270. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%,

or 100%) identical to the amino acid sequence of SEQ ID NO:270 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271, which includes amino acid sequences SEQ ID NO:319 as CDR1, SEQ ID NO:320 as CDR2, and SEQ ID NO:321 as CDR3 of SEQ ID NO:271.

[0239] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:322 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:324 as CDR3 of SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:534 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:535 as CDR3 of SEQ ID NO:272. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with

an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273, which includes amino acid sequences SEQ ID NO:325 as CDR1, SEQ ID NO:326 as CDR2, and SEQ ID NO:327 as CDR3 of SEQ ID NO:273.

[0240] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:328 as CDR1, SEQ ID NO:329 as CDR2, and SEQ ID NO:330 as CDR3 of SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:536 as CDR1, SEQ ID NO:329 as CDR2, and SEQ ID NO:537 as CDR3 of SEQ ID NO:274. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275, which includes amino acid sequences SEQ ID NO:331 as CDR1, SEQ ID NO:332 as CDR2, and SEQ ID NO:333 as CDR3 of SEQ ID NO:275.

[0241] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276. In some embodiments, the antibody heavy chain variable

domain is at least 95% identical to SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:334 as CDR1, SEQ ID NO:335 as CDR2, and SEQ ID NO:336 as CDR3 of SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:538 as CDR1, SEQ ID NO:335 as CDR2, and SEQ ID NO:539 as CDR3 of SEQ ID NO:276. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277, which includes amino acid sequences SEQ ID NO:337 as CDR1, SEQ ID NO:338 as CDR2, and SEQ ID NO:339 as CDR3 of SEQ ID NO:277.

[0242] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:340 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:342 as CDR3 of SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:540 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:541 as CDR3 of SEQ ID NO:278. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For

example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279, which includes amino acid sequences SEQ ID NO:343 as CDR1, SEQ ID NO:344 as CDR2, and SEQ ID NO:345 as CDR3 of SEQ ID NO:279.

[0243] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:346 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:348 as CDR3 of SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:542 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:543 as CDR3 of SEQ ID NO:280. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID

NO:281, which includes amino acid sequences SEQ ID NO:349 as CDR1, SEQ ID NO:350 as CDR2, and SEQ ID NO:351 as CDR3 of SEQ ID NO:281.

[0244] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:352 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:354 as CDR3 of SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:544 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:545 as CDR3 of SEQ ID NO:282. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283, which includes amino acid sequences SEQ ID NO:355 as CDR1, SEQ ID NO:356 as CDR2, and SEQ ID NO:357 as CDR3 of SEQ ID NO:283.

[0245] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:358 as CDR1, SEQ ID

NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:546 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:547. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285, which includes amino acid sequences SEQ ID NO:361 as CDR1, SEQ ID NO:362 as CDR2, and SEQ ID NO:363 as CDR3 of SEQ ID NO:285.

[0246] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:364 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:366 as CDR3 of SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:548 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:549 as CDR3 of SEQ ID NO:286. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of

SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287, which includes amino acid sequences SEQ ID NO:367 as CDR1, SEQ ID NO:368 as CDR2, and SEQ ID NO:369 as CDR3 of SEQ ID NO:287.

[0247] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:370 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:372 as CDR3 of SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:550 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:551 as CDR3 of SEQ ID NO:288. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, which includes amino acid sequences SEQ ID NO:373 as CDR1, SEQ ID NO:374 as CDR2, and SEQ ID NO:375 as CDR3 of SEQ ID NO:289.

[0248] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:376 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:378 as CDR3 of SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:552 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:553 as CDR3 of SEQ ID NO:290. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291, which includes amino acid sequences SEQ ID NO:379 as CDR1, SEQ ID NO:380 as CDR2, and SEQ ID NO:381 as CDR3 of SEQ ID NO:291.

[0249] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:382 as CDR1, SEQ ID NO:383 as CDR2, and SEQ ID NO:384 as CDR3 of SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:554 as

CDR1, SEQ ID NO:383 as CDR2, and SEQ ID NO:555 as CDR3 of SEQ ID NO:292. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293, which includes amino acid sequences SEQ ID NO:385 as CDR1, SEQ ID NO:386 as CDR2, and SEQ ID NO:387 as CDR3 of SEQ ID NO:293.

[0250] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:388 as CDR1, SEQ ID NO:389 as CDR2, and SEQ ID NO:390 as CDR3 of SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:556 as CDR1, SEQ ID NO:389 as CDR2, and SEQ ID NO:557 as CDR3 of SEQ ID NO:294. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the

amino acid sequence of SEQ ID NO:295. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295, which includes amino acid sequences SEQ ID NO:391 as CDR1, SEQ ID NO:392 as CDR2, and SEQ ID NO:393 as CDR3 of SEQ ID NO:295.

[0251] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:394 as CDR1, SEQ ID NO:395 as CDR2, and SEQ ID NO:396 as CDR3 of SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:558 as CDR1, SEQ ID NO:395 as CDR2, and SEQ ID NO:559 as CDR3 of SEQ ID NO:296. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297, which includes amino acid sequences SEQ ID NO:397 as CDR1, SEQ ID NO:398 as CDR2, and SEQ ID NO:399 as CDR3 of SEQ ID NO:297.

[0252] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33 and Cynomolgus/Rhesus (cyno)

CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:400 as CDR1, SEQ ID NO:401 as CDR2, and SEQ ID NO:402 as CDR3 of SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:560 as CDR1, SEQ ID NO:401 as CDR2, and SEQ ID NO:561 as CDR3 of SEQ ID NO:298. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299, which includes amino acid sequences SEQ ID NO:403 as CDR1, SEQ ID NO:404 as CDR2, and SEQ ID NO:405 as CDR3 of SEQ ID NO:299.

[0253] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:406 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:408 as CDR3 of SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:562 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:563 as CDR3 of SEQ ID NO:300. In

certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301, which includes amino acid sequences SEQ ID NO:409 as CDR1, SEQ ID NO:410 as CDR2, and SEQ ID NO:411 as CDR3 of SEQ ID NO:301.

[0254] In certain embodiments, the present invention provides an antigen binding site that binds an epitope on an extracellular domain of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:412 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:414 as CDR3 of SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:564 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:565 as CDR3 of SEQ ID NO:302. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303. In certain embodiments, an antibody heavy chain

variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303, which includes amino acid sequences SEQ ID NO:415 as CDR1, SEQ ID NO:416 as CDR2, and SEQ ID NO:417 as CDR3 of SEQ ID NO:303.

An antigen binding site that recognizes and binds a conformational epitope on an extracellular domain of the human CD33 and/or the Cynomolgus/Rhesus (cyno) CD33

[0255] In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain that recognizes and binds one or more conformational epitopes on the extracellular domain of the human CD33 and/or the Cynomolgus/Rhesus (cyno) CD33.

[0256] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds a conformational epitope partially located in the V domain of human CD33 extracellular domain; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDG SEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ GTMVTVSS [SEQ ID NO:3]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:3. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:27] as CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:28] as CDR2, and ARPLNAGELDV [SEQ ID NO:29] as CDR3 of SEQ ID NO:3. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV

PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQLESYPLTFGGGTKVEIK [SEQ ID NO:4]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:4, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:30] as CDR1, EASSLES [SEQ ID NO:31] as CDR2, and QQLESYPLT [SEQ ID NO:32] as CDR3 of SEQ ID NO:4.

[0257] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds a conformational epitope partially located in the V domain of the human CD33 extracellular domain; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFPSYWMSWVRQAPGKGLEWVATIKRDGS EKGYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQG TMVTVSS [SEQ ID NO:11]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:11. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFPSYWMS [SEQ ID NO:51] as CDR1, TIKRDGSEKGYVDSVKG [SEQ ID NO:52] as CDR2, and ARPLNAGELDV [SEQ ID NO:53] as CDR3 of SEQ ID NO:11. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIK [SEQ ID NO:12]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the

amino acid sequence of SEQ ID NO:12, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:54] as CDR1, EASSLES [SEQ ID NO:55] as CDR2, and QQSQSYPPIT [SEQ ID NO:56] as CDR3 of SEQ ID NO:12.

[0258] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds a conformational epitope partially located in the V domain of the human CD33 extracellular domain; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSISSSSEG IYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVYY GMDVWGQGTTVTVSS [SEQ ID NO:15]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:15. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYAMS [SEQ ID NO:63] as CDR1, SISSSSEGIYYADSVKG [SEQ ID NO:64] as CDR2, and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:65] as CDR3 of SEQ ID NO:15. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASNSISSWLAWYQQKPGKAPKLLIYEASSTKSGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFGGGTKVEIK [SEQ ID NO:16]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:16, which includes amino acid sequences RASNSISSWLA [SEQ ID NO:66] as CDR1, EASSTKS [SEQ ID NO:67] as CDR2, and QQYDDLPT [SEQ ID NO:68] as CDR3 of SEQ ID NO:16.

[0259] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds a conformational epitope partially located in the V domain of the human

CD33 extracellular domain; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:316 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:318 as CDR3 of SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:532 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:533 as CDR3 of SEQ ID NO:270. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271, which includes amino acid sequences SEQ ID NO:319 as CDR1, SEQ ID NO:320 as CDR2, and SEQ ID NO:321 as CDR3 of SEQ ID NO:271.

[0260] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds a conformational epitope partially located in the V domain of the human CD33 extracellular domain; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:322 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:324 as CDR3 of SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:534 as CDR1, SEQ ID NO:323 as CDR2,

and SEQ ID NO:535 as CDR3 of SEQ ID NO:272. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273, which includes amino acid sequences SEQ ID NO:325 as CDR1, SEQ ID NO:326 as CDR2, and SEQ ID NO:327 as CDR3 of SEQ ID NO:273.

[0261] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds a conformational epitope partially located in the V domain of the human CD33 extracellular domain; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:346 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:348 as CDR3 of SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:542 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:543 as CDR3 of SEQ ID NO:280. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%,

95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281, which includes amino acid sequences SEQ ID NO:349 as CDR1, SEQ ID NO:350 as CDR2, and SEQ ID NO:351 as CDR3 of SEQ ID NO:281.

An antigen binding site that recognizes and binds a conformational epitope on an extracellular domain of the human CD33 but not a conformational epitope on an extracellular domain of the Cynomolgus/Rhesus (cyno) CD33

[0262] In one aspect, the present invention provides an antigen binding site that recognizes and binds one or more conformational epitopes on the extracellular domain of the human CD33 but does not recognize and/or bind one or more conformational epitopes on the extracellular domain of the cyno CD33.

[0263] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds one or more conformational epitopes on the extracellular domain of the human CD33 but does not recognize and/or bind one or more conformational epitopes on the extracellular domain of the cyno CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQGLEWMGMINPS WGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAREAADGFVGERYF DLWGRGTLVTVSS [SEQ ID NO:7]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:7. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFSDYYMH [SEQ ID NO:39] as CDR1, MINPSWGSTSYAQKFQG [SEQ ID NO:40] as CDR2, and AREAADGFVGERYFDL [SEQ ID NO:41] as CDR3 of SEQ ID NO:7. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%,

97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQSPQLLIYLGSN RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQDVALPITFGGGTKVEIK [SEQ ID NO:8]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8, which includes amino acid sequences RSSQSLLYSNGYNYLD [SEQ ID NO:42] as CDR1, LGSNRAS [SEQ ID NO:43] as CDR2, and MQDVALPIT [SEQ ID NO:44] as CDR3 of SEQ ID NO:8.

[0264] In certain embodiments, the present invention provides an antigen binding site that recognizes and binds one or more conformational epitopes on the extracellular domain of the human CD33 but does not recognize and/or bind one or more conformational epitopes on the extracellular domain of the cyno CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQAPGQGLEWMGIINPSR GSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDV WGKGTTVTVSS [SEQ ID NO:13]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:13. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFGTYYMH [SEQ ID NO:57] as CDR1, IINPSRGSTVYAQKFQG [SEQ ID NO:58] as CDR2, and ARGAGYDDEDMDV [SEQ ID NO:59] as CDR3 of SEQ ID NO:13. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSG

VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPLTFGGGTKVEIK [SEQ ID NO:14]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14, which includes amino acid sequences RASQGIDSWLA [SEQ ID NO:60] as CDR1, AASSLQS [SEQ ID NO:61] as CDR2, and QQAHSYPLT [SEQ ID NO:62] as CDR3 of SEQ ID NO:14.

[0265] In certain embodiments, an antibody binding site that includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQAPGQGLEWMGIINPSR GSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDV WGKGTTVTVSS [SEQ ID NO:13] binds to the full-length extracellular domain of human CD33, but does not bind human CD33 V domain or C domain individually, and does not cross-block binding to human CD33 with lintuzumab. In certain embodiments, an antibody binding site that includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13, and is paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPLTFGGGTKVEIK [SEQ ID NO:14], binds to the full-length extracellular domain of human CD33, but does not bind human CD33 V domain or C domain individually, and does not cross-block binding to human CD33 with lintuzumab. In certain embodiments, an antibody binding site that includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13, and is paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14, which includes amino acid sequences RASQGIDSWLA [SEQ ID NO:60] as CDR1, AASSLQS [SEQ ID NO:61] as CDR2, and QQAHSYPLT [SEQ ID NO:62] as CDR3 of SEQ ID NO:14, binds to the full-length extracellular domain of

human CD33, but does not bind human CD33 V domain or C domain individually, and does not cross-block binding to human CD33 with lintuzumab.

An antigen binding site that binds to the R69G allele of human CD33

[0266] In one aspect, the present invention provides an antigen binding site that binds to the R69G allele of human CD33. In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYGMSWVRQAPGKGLEWVANIKQDGS EKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVY YGMDVWGQGTTVTVSS [SEQ ID NO:1]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:1. In some embodiments, the heavy chain variable domain includes amino acid sequences FTFSSYGMS [SEQ ID NO:21] as the first complementarity-determining region 1 ("CDR1"), NIKQDGSEKYYVDSVKG [SEQ ID NO:22] as the second CDR ("CDR2"), and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:23] as the third CDR ("CDR3") of SEQ ID NO:1. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYESFPTFGGGTKVEIK [SEQ ID NO:2]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:2, which includes amino acid sequences RASQSISSWLA

[SEQ ID NO:24] as CDR1, DASSLES [SEQ ID NO:25] as CDR2, and QQYESFPT [SEQ ID NO:26] as CDR3 of SEQ ID NO:2.

[0267] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDG SEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ GTMVTVSS [SEQ ID NO:3]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:3. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:27] as CDR1, NIKQDGSEKYYVDSVKG [SEQ ID NO:28] as CDR2, and ARPLNAGELDV [SEQ ID NO:29] as CDR3 of SEQ ID NO:3. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQLESYPLTFGGGTKVEIK [SEQ ID NO:4]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:4, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:30] as CDR1, EASSLES [SEQ ID NO:31] as CDR2, and QQLESYPLT [SEQ ID NO:32] as CDR3 of SEQ ID NO:4.

[0268] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGKGLEWVSAIVGSGE STYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVY YGMDVWGQGTTVTVSS [SEQ ID NO:5]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:5. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSKYTMS [SEQ ID NO:33] as CDR1, AIVGSGESTYFADSVKG [SEQ ID NO:34] as CDR2, and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:35] as CDR3 of SEQ ID NO:5. In some embodiments, the heavy chain variable domain incorporates amino acid sequences KYTMS [SEQ ID NO:183] as CDR1, AIVGSGESTYFADSVKG [SEQ ID NO:34] as CDR2, and EGGPYYDSSGYFVYYGMDV [SEQ ID NO:184] as CDR3 of SEQ ID NO:5. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFGGGTKVEIK [SEQ ID NO:6]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:36] as CDR1, KASSLES [SEQ ID NO:37] or KASSLE [SEQ ID NO:185] as CDR2, and QQYDDLPT [SEQ ID NO:38] as CDR3 of SEQ ID NO:6.

[0269] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPGKGLEWVATIKQDG SEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ GTMVTVSS [SEQ ID NO:9]. In some embodiments, the antibody heavy chain variable

domain is at least 95% identical to SEQ ID NO:9. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFGSYWMS [SEQ ID NO:45] as CDR1, TIKQDGSEKSYVDSVKG [SEQ ID NO:46] as CDR2, and ARPLNAGELDV [SEQ ID NO:47] as CDR3 of SEQ ID NO:9. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SYWMS [SEQ ID NO:181] as CDR1, TIKQDGSEKSYVDSVKG [SEQ ID NO:46] as CDR2, and RPLNAGELDV [SEQ ID NO:182] as CDR3 of SEQ ID NO:9. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIK [SEQ ID NO:10]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:10, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:48] as CDR1, EASSLES [SEQ ID NO:49] as CDR2, and QQSQSYPPIT [SEQ ID NO:50] as CDR3 of SEQ ID NO:10.

[0270] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFPSYWMSWVRQAPGKGLEWVATIKRDGS EKGYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQG TMVTVSS [SEQ ID NO:11]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:11. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFPSYWMS [SEQ ID NO:51] as CDR1, TIKRDGSEKGYVDSVKG [SEQ ID NO:52] as CDR2, and ARPLNAGELDV [SEQ

ID NO:53] as CDR3 of SEQ ID NO:11. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIK [SEQ ID NO:12]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:12, which includes amino acid sequences RASQSISSWLA [SEQ ID NO:54] as CDR1, EASSLES [SEQ ID NO:55] as CDR2, and QQSQSYPPIT [SEQ ID NO:56] as CDR3 of SEQ ID NO:12.

[0271] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQAPGQGLEWMGIINPSR GSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDV WGKGTTVTVSS [SEQ ID NO:13]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:13. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFGTYYMH [SEQ ID NO:57] as CDR1, IINPSRGSTVYAQKFQG [SEQ ID NO:58] as CDR2, and ARGAGYDDEDMDV [SEQ ID NO:59] as CDR3 of SEQ ID NO:13. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the

amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPLTFGGGTKVEIK [SEQ ID NO:14]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14, which includes amino acid sequences RASQGIDSWLA [SEQ ID NO:60] as CDR1, AASSLQS [SEQ ID NO:61] as CDR2, and QQAHSYPLT [SEQ ID NO:62] as CDR3 of SEQ ID NO:14.

[0272] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSISSSSEG IYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVYY GMDVWGQGTTVTVSS [SEQ ID NO:15]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:15. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYAMS [SEQ ID NO:63] as CDR1, SISSSSEGIYYADSVKG [SEQ ID NO:64] as CDR2, and AREGGPYYDSSGYFVYYGMDV [SEQ ID NO:65] as CDR3 of SEQ ID NO:15. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSTLSASVGDRVTITCRASNSISSWLAWYQQKPGKAPKLLIYEASSTKSGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFGGGTKVEIK [SEQ ID NO:16]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:16, which includes amino acid sequences RASNSISSWLA [SEQ ID NO:66] as CDR1, EASSTKS [SEQ ID NO:67] as CDR2, and QQYDDLPT [SEQ ID NO:68] as CDR3 of SEQ ID NO:16.

[0273] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANINTDG SEVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDVGPGIAYQGHFD YWGQGTLVTVSS [SEQ ID NO:17]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:17. In some embodiments, the heavy chain variable domain incorporates amino acid sequences FTFSSYWMS [SEQ ID NO:69] as CDR1, NINTDGSEVYYVDSVKG [SEQ ID NO:70] as CDR2, and ARDVGPGIAYQGHFDY [SEQ ID NO:71] as CDR3 of SEQ ID NO:17. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQVIYSYLNWYQQKPGKAPKLLIYAASSLKSGV PSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYDTPLTFGGGTKVEIK [SEQ ID NO:18]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:18, which includes amino acid sequences RASQVIYSYLN [SEQ ID NO:72] as CDR1, AASSLKS [SEQ ID NO:73] as CDR2, and QQVYDTPLT [SEQ ID NO:74] as CDR3 of SEQ ID NO:18.

[0274] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QLQLQESGPGLVKPSETLSLTCTVSGGSISSTDYYWGWIRQPPGKGLEWIGSIGYSGT YYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARETAHDVHGMDVWGQG TTVTVSS [SEQ ID NO:19]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:19. In some embodiments, the heavy chain variable domain incorporates amino acid sequences GSISSTDYYWG [SEQ ID NO:75] as CDR1, SIGYSGTYYNPSLKS [SEQ ID NO:76] as CDR2, and ARETAHDVHGMDV [SEQ ID NO:77] as CDR3 of SEQ ID NO:19. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence EIVLTQSPATLSLSPGERATLSCRASHSVYSYLAWYQQKPGQAPRLLIYDASNRATGI PARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLPTFGGGTKVEIK [SEQ ID NO:20]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:20, which includes amino acid sequences RASHSVYSYLA [SEQ ID NO:78] as CDR1, DASNRAT [SEQ ID NO:79] as CDR2, and QQYDNLPT [SEQ ID NO:80] as CDR3 of SEQ ID NO:20.

[0275] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:266. In some embodiments, the heavy chain variable domain

incorporates amino acid sequences SEQ ID NO:304 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:306 as CDR3 of SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:528 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:529 as CDR3 of SEQ ID NO:266. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267, which includes amino acid sequences SEQ ID NO:307 as CDR1, SEQ ID NO:308 as CDR2, and SEQ ID NO:309 as CDR3 of SEQ ID NO:267.

[0276] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:310 as CDR1, SEQ ID NO:311 as CDR2, and SEQ ID NO:312 as CDR3 of SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:530 as CDR1, SEQ ID NO:311 as CDR2, and SEQ ID NO:531 as CDR3 of SEQ ID NO:268. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269, which includes amino acid sequences SEQ ID NO:313 as CDR1, SEQ ID NO:314 as CDR2, and SEQ ID NO:315 as CDR3 of SEQ ID NO:269.

[0277] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:316 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:318 as CDR3 of SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:532 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:533 as CDR3 of SEQ ID NO:270. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID

NO:271, which includes amino acid sequences SEQ ID NO:319 as CDR1, SEQ ID NO:320 as CDR2, and SEQ ID NO:321 as CDR3 of SEQ ID NO:271.

[0278] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:322 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:324 as CDR3 of SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:534 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:535 as CDR3 of SEQ ID NO:272. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273, which includes amino acid sequences SEQ ID NO:325 as CDR1, SEQ ID NO:326 as CDR2, and SEQ ID NO:327 as CDR3 of SEQ ID NO:273.

[0279] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:328 as CDR1, SEQ ID NO:329 as CDR2,

and SEQ ID NO:330 as CDR3 of SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:536 as CDR1, SEQ ID NO:329 as CDR2, and SEQ ID NO:537 as CDR3 of SEQ ID NO:274. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275, which includes amino acid sequences SEQ ID NO:331 as CDR1, SEQ ID NO:332 as CDR2, and SEQ ID NO:333 as CDR3 of SEQ ID NO:275.

[0280] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:334 as CDR1, SEQ ID NO:335 as CDR2, and SEQ ID NO:336 as CDR3 of SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:538 as CDR1, SEQ ID NO:335 as CDR2, and SEQ ID NO:539 as CDR3 of SEQ ID NO:276. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of

SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277, which includes amino acid sequences SEQ ID NO:337 as CDR1, SEQ ID NO:338 as CDR2, and SEQ ID NO:339 as CDR3 of SEQ ID NO:277.

[0281] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:340 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:342 as CDR3 of SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:540 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:541 as CDR3 of SEQ ID NO:278. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279, which includes amino acid sequences SEQ ID NO:343 as CDR1, SEQ ID NO:344 as CDR2, and SEQ ID NO:345 as CDR3 of SEQ ID NO:279.

[0282] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:346 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:348 as CDR3 of SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:542 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:543 as CDR3 of SEQ ID NO:280. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281, which includes amino acid sequences SEQ ID NO:349 as CDR1, SEQ ID NO:350 as CDR2, and SEQ ID NO:351 as CDR3 of SEQ ID NO:281.

[0283] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:352 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:354 as CDR3 of SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:544 as CDR1, SEQ ID

NO:353 as CDR2, and SEQ ID NO:545 as CDR3 of SEQ ID NO:282. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283, which includes amino acid sequences SEQ ID NO:355 as CDR1, SEQ ID NO:356 as CDR2, and SEQ ID NO:357 as CDR3 of SEQ ID NO:283.

[0284] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:358 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:546 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:547. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the

amino acid sequence of SEQ ID NO:285. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285, which includes amino acid sequences SEQ ID NO:361 as CDR1, SEQ ID NO:362 as CDR2, and SEQ ID NO:363 as CDR3 of SEQ ID NO:285.

[0285] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:364 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:366 as CDR3 of SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:548 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:549 as CDR3 of SEQ ID NO:286. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287, which includes amino acid sequences SEQ ID NO:367 as CDR1, SEQ ID NO:368 as CDR2, and SEQ ID NO:369 as CDR3 of SEQ ID NO:287.

[0286] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain

variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:382 as CDR1, SEQ ID NO:383 as CDR2, and SEQ ID NO:384 as CDR3 of SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:554 as CDR1, SEQ ID NO:383 as CDR2, and SEQ ID NO:555 as CDR3 of SEQ ID NO:292. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293, which includes amino acid sequences SEQ ID NO:385 as CDR1, SEQ ID NO:386 as CDR2, and SEQ ID NO:387 as CDR3 of SEQ ID NO:293.

[0287] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:388 as CDR1, SEQ ID NO:389 as CDR2, and SEQ ID NO:390 as CDR3 of SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:556 as CDR1, SEQ ID NO:389 as CDR2, and SEQ ID NO:557 as CDR3 of SEQ ID NO:294. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid

sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295, which includes amino acid sequences SEQ ID NO:391 as CDR1, SEQ ID NO:392 as CDR2, and SEQ ID NO:393 as CDR3 of SEQ ID NO:295.

[0288] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:394 as CDR1, SEQ ID NO:395 as CDR2, and SEQ ID NO:396 as CDR3 of SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:558 as CDR1, SEQ ID NO:395 as CDR2, and SEQ ID NO:559 as CDR3 of SEQ ID NO:296. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%,

99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297, which includes amino acid sequences SEQ ID NO:397 as CDR1, SEQ ID NO:398 as CDR2, and SEQ ID NO:399 as CDR3 of SEQ ID NO:297.

[0289] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:400 as CDR1, SEQ ID NO:401 as CDR2, and SEQ ID NO:402 as CDR3 of SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:560 as CDR1, SEQ ID NO:401 as CDR2, and SEQ ID NO:561 as CDR3 of SEQ ID NO:298. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299, which includes amino acid sequences SEQ ID NO:403 as CDR1, SEQ ID NO:404 as CDR2, and SEQ ID NO:405 as CDR3 of SEQ ID NO:299.

[0290] In certain embodiments, the present invention provides an antigen binding site that binds to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of

SEQ ID NO:302. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:412 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:414 as CDR3 of SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:564 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:565 as CDR3 of SEQ ID NO:302. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303, which includes amino acid sequences SEQ ID NO:415 as CDR1, SEQ ID NO:416 as CDR2, and SEQ ID NO:417 as CDR3 of SEQ ID NO:303.

An antigen binding site that does not bind to the R69G allele of human CD33

[0291] In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain that binds wild-type human CD33, but not the R69G allele of human CD33. In certain embodiments, the present invention provides an antigen binding site that does not bind to the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQGLEWMGMINPS WGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAREAADGFVGERYF DLWGRGTLVTVSS [SEQ ID NO:7]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:7. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFSDYYMH [SEQ ID NO:39]

as CDR1, MINPSWGSTSYAQKFQG [SEQ ID NO:40] as CDR2, and AREAADGFVGERYFDL [SEQ ID NO:41] as CDR3 of SEQ ID NO:7. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90%(*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQSPQLLIYLGSN RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQDVALPITFGGGTKVEIK [SEQ ID NO:8]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8, which includes amino acid sequences RSSQSLLYSNGYNYLD [SEQ ID NO:42] as CDR1, LGSNRAS [SEQ ID NO:43] as CDR2, and MQDVALPIT [SEQ ID NO:44] as CDR3 of SEQ ID NO:8.

[0292] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:370 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:372 as CDR3 of SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:550 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:551 as CDR3 of SEQ ID NO:288. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, which includes amino acid sequences SEQ ID NO:373 as CDR1, SEQ ID NO:374 as CDR2, and SEQ ID NO:375 as CDR3 of SEQ ID NO:289.

[0293] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:376 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:378 as CDR3 of SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:552 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:553 as CDR3 of SEQ ID NO:290. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of

SEQ ID NO:291, which includes amino acid sequences SEQ ID NO:379 as CDR1, SEQ ID NO:380 as CDR2, and SEQ ID NO:381 as CDR3 of SEQ ID NO:291.

[0294] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the R69G allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:406 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:408 as CDR3 of SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:562 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:563 as CDR3 of SEQ ID NO:300. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301, which includes amino acid sequences SEQ ID NO:409 as CDR1, SEQ ID NO:410 as CDR2, and SEQ ID NO:411 as CDR3 of SEQ ID NO:301.

An antigen binding site that binds to a unique epitope including R69 on human CD33

[0295] In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain that binds to a unique epitope on human CD33 that includes R69. In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes R69; the antigen binding site

includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQGLEWMGMINPS WGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAREAADGFVGERYF DLWGRGTLVTVSS [SEQ ID NO:7]. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:7. In some embodiments, the heavy chain variable domain incorporates amino acid sequences YTFSDYYMH [SEQ ID NO:39] as CDR1, MINPSWGSTSYAQKFQG [SEQ ID NO:40] as CDR2, and AREAADGFVGERYFDL [SEQ ID NO:41] as CDR3 of SEQ ID NO:7. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQSPQLLIYLGSN RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQDVALPITFGGGTKVEIK [SEQ ID NO:8]. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8, which includes amino acid sequences RSSQSLLYSNGYNYLD [SEQ ID NO:42] as CDR1, LGSNRAS [SEQ ID NO:43] as CDR2, and MQDVALPIT [SEQ ID NO:44] as CDR3 of SEQ ID NO:8.

[0296] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes R69; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:288. In some embodiments, the heavy chain

variable domain incorporates amino acid sequences SEQ ID NO:370 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:372 as CDR3 of SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:550 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:551 as CDR3 of SEQ ID NO:288. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, which includes amino acid sequences SEQ ID NO:373 as CDR1, SEQ ID NO:374 as CDR2, and SEQ ID NO:375 as CDR3 of SEQ ID NO:289.

[0297] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes R69; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:376 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:378 as CDR3 of SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:552 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:553 as CDR3 of SEQ ID NO:290. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291, which includes amino acid sequences SEQ ID NO:379 as CDR1, SEQ ID NO:380 as CDR2, and SEQ ID NO:381 as CDR3 of SEQ ID NO:291.

[0298] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes R69; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:406 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:408 as CDR3 of SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:562 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:563 as CDR3 of SEQ ID NO:300. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID

NO:301, which includes amino acid sequences SEQ ID NO:409 as CDR1, SEQ ID NO:410 as CDR2, and SEQ ID NO:411 as CDR3 of SEQ ID NO:301.

An antigen binding site that binds to the S128N allele of human CD33

[0299] In one aspect, the present invention provides an antigen binding site that binds to the S128N allele of human CD33.

[0300] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:310 as CDR1, SEQ ID NO:311 as CDR2, and SEQ ID NO:312 as CDR3 of SEQ ID NO:268. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:530 as CDR1, SEQ ID NO:311 as CDR2, and SEQ ID NO:531 as CDR3 of SEQ ID NO:268. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:268 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:269, which includes amino acid sequences SEQ ID NO:313 as CDR1, SEQ ID NO:314 as CDR2, and SEQ ID NO:315 as CDR3 of SEQ ID NO:269.

[0301] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:328 as CDR1, SEQ ID NO:329 as CDR2, and SEQ ID NO:330 as CDR3 of SEQ ID NO:274. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:536 as CDR1, SEQ ID NO:329 as CDR2, and SEQ ID NO:537 as CDR3 of SEQ ID NO:274. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:274 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:275, which includes amino acid sequences SEQ ID NO:331 as CDR1, SEQ ID NO:332 as CDR2, and SEQ ID NO:333 as CDR3 of SEQ ID NO:275.

[0302] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:334 as CDR1, SEQ ID NO:335 as CDR2, and SEQ ID NO:336 as CDR3 of SEQ ID NO:276. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:538 as CDR1, SEQ ID NO:335 as CDR2, and SEQ ID NO:539 as CDR3 of SEQ ID NO:276. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100%) identical to the amino acid sequence of SEQ ID NO:276 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:276 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:277, which includes amino acid sequences SEQ ID NO:337 as CDR1, SEQ ID NO:338 as CDR2, and SEQ ID NO:339 as CDR3 of SEQ ID NO:277.

[0303] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:382 as CDR1, SEQ ID NO:383 as CDR2, and SEQ ID NO:384 as CDR3 of SEQ ID NO:292. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:554 as CDR1, SEQ ID NO:383 as CDR2, and SEQ ID NO:555 as CDR3 of SEQ ID NO:292. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:292 can be paired with

an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:293, which includes amino acid sequences SEQ ID NO:385 as CDR1, SEQ ID NO:386 as CDR2, and SEQ ID NO:387 as CDR3 of SEQ ID NO:293.

[0304] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:388 as CDR1, SEQ ID NO:389 as CDR2, and SEQ ID NO:390 as CDR3 of SEQ ID NO:294. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:556 as CDR1, SEQ ID NO:389 as CDR2, and SEQ ID NO:557 as CDR3 of SEQ ID NO:294. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:294 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:295, which includes amino acid sequences SEQ ID NO:391 as CDR1, SEQ ID NO:392 as CDR2, and SEQ ID NO:393 as CDR3 of SEQ ID NO:295.

[0305] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296. In some embodiments, the antibody heavy chain variable domain is at least

95% identical to SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:394 as CDR1, SEQ ID NO:395 as CDR2, and SEQ ID NO:396 as CDR3 of SEQ ID NO:296. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:558 as CDR1, SEQ ID NO:395 as CDR2, and SEQ ID NO:559 as CDR3 of SEQ ID NO:296. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:296 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:297, which includes amino acid sequences SEQ ID NO:397 as CDR1, SEQ ID NO:398 as CDR2, and SEQ ID NO:399 as CDR3 of SEQ ID NO:297.

[0306] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:400 as CDR1, SEQ ID NO:401 as CDR2, and SEQ ID NO:402 as CDR3 of SEQ ID NO:298. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:560 as CDR1, SEQ ID NO:401 as CDR2, and SEQ ID NO:561 as CDR3 of SEQ ID NO:298. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For

example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:298 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:299, which includes amino acid sequences SEQ ID NO:403 as CDR1, SEQ ID NO:404 as CDR2, and SEQ ID NO:405 as CDR3 of SEQ ID NO:299.

[0307] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:376 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:378 as CDR3 of SEQ ID NO:290. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:552 as CDR1, SEQ ID NO:377 as CDR2, and SEQ ID NO:553 as CDR3 of SEQ ID NO:290. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:291. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:290 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID

NO:291, which includes amino acid sequences SEQ ID NO:379 as CDR1, SEQ ID NO:380 as CDR2, and SEQ ID NO:381 as CDR3 of SEQ ID NO:291.

[0308] In certain embodiments, the present invention provides an antigen binding site that binds to the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:406 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:408 as CDR3 of SEQ ID NO:300. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:562 as CDR1, SEQ ID NO:407 as CDR2, and SEQ ID NO:563 as CDR3 of SEQ ID NO:300. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:300 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:301, which includes amino acid sequences SEQ ID NO:409 as CDR1, SEQ ID NO:410 as CDR2, and SEQ ID NO:411 as CDR3 of SEQ ID NO:301.

An antigen binding site that does not bind to the S128N allele of human CD33

[0309] In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain that binds to wild-type human CD33 but not the S128N allele of human CD33.

[0310] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen

binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:412 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:414 as CDR3 of SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:564 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:565 as CDR3 of SEQ ID NO:302. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303, which includes amino acid sequences SEQ ID NO:415 as CDR1, SEQ ID NO:416 as CDR2, and SEQ ID NO:417 as CDR3 of SEQ ID NO:303.

[0311] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:304 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:306 as CDR3 of SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:528 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:529 as CDR3 of SEQ ID NO:266. In certain embodiments, the antibody heavy chain variable domain which includes

an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267, which includes amino acid sequences SEQ ID NO:307 as CDR1, SEQ ID NO:308 as CDR2, and SEQ ID NO:309 as CDR3 of SEQ ID NO:267.

[0312] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:316 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:318 as CDR3 of SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:532 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:533 as CDR3 of SEQ ID NO:270. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%,

96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271, which includes amino acid sequences SEQ ID NO:319 as CDR1, SEQ ID NO:320 as CDR2, and SEQ ID NO:321 as CDR3 of SEQ ID NO:271.

[0313] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:322 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:324 as CDR3 of SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:534 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:535 as CDR3 of SEQ ID NO:272. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273, which includes amino acid sequences SEQ ID NO:325 as CDR1, SEQ ID NO:326 as CDR2, and SEQ ID NO:327 as CDR3 of SEQ ID NO:273.

[0314] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to

the amino acid sequence of SEQ ID NO:278. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:340 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:342 as CDR3 of SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:540 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:541 as CDR3 of SEQ ID NO:278. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279, which includes amino acid sequences SEQ ID NO:343 as CDR1, SEQ ID NO:344 as CDR2, and SEQ ID NO:345 as CDR3 of SEQ ID NO:279.

[0315] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:346 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:348 as CDR3 of SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:542 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:543 as CDR3 of SEQ ID NO:280. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 is combined

with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281, which includes amino acid sequences SEQ ID NO:349 as CDR1, SEQ ID NO:350 as CDR2, and SEQ ID NO:351 as CDR3 of SEQ ID NO:281.

[0316] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:352 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:354 as CDR3 of SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:544 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:545 as CDR3 of SEQ ID NO:282. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283, which includes amino acid sequences SEQ ID NO:355 as CDR1, SEQ ID NO:356 as CDR2, and SEQ ID NO:357 as CDR3 of SEQ ID NO:283.

[0317] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:358 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:546 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:547. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285, which includes amino acid sequences SEQ ID NO:361 as CDR1, SEQ ID NO:362 as CDR2, and SEQ ID NO:363 as CDR3 of SEQ ID NO:285.

[0318] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:286. In some embodiments,

the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:364 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:366 as CDR3 of SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:548 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:549 as CDR3 of SEQ ID NO:286. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287, which includes amino acid sequences SEQ ID NO:367 as CDR1, SEQ ID NO:368 as CDR2, and SEQ ID NO:369 as CDR3 of SEQ ID NO:287.

[0319] In certain embodiments, the present invention provides an antigen binding site that binds to wild-type human CD33 but not the S128N allele of human CD33; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:370 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:372 as CDR3 of SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:550 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:551 as CDR3 of SEQ ID NO:288. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, which includes amino acid sequences SEQ ID NO:373 as CDR1, SEQ ID NO:374 as CDR2, and SEQ ID NO:375 as CDR3 of SEQ ID NO:289.

An antigen binding site that binds to a unique epitope including S128 on human CD33

[0320] In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain that binds to a unique epitope on human CD33 that includes S128.

[0321] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:412 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:414 as CDR3 of SEQ ID NO:302. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:564 as CDR1, SEQ ID NO:413 as CDR2, and SEQ ID NO:565 as CDR3 of SEQ ID NO:302. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303. In certain embodiments, an antibody heavy chain

variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:302 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:303, which includes amino acid sequences SEQ ID NO:415 as CDR1, SEQ ID NO:416 as CDR2, and SEQ ID NO:417 as CDR3 of SEQ ID NO:303.

[0322] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:304 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:306 as CDR3 of SEQ ID NO:266. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:528 as CDR1, SEQ ID NO:305 as CDR2, and SEQ ID NO:529 as CDR3 of SEQ ID NO:266. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:266 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:267, which includes amino acid sequences SEQ ID NO:307 as CDR1, SEQ ID NO:308 as CDR2, and SEQ ID NO:309 as CDR3 of SEQ ID NO:267.

[0323] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*,

at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:316 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:318 as CDR3 of SEQ ID NO:270. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:532 as CDR1, SEQ ID NO:317 as CDR2, and SEQ ID NO:533 as CDR3 of SEQ ID NO:270. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:270 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:271, which includes amino acid sequences SEQ ID NO:319 as CDR1, SEQ ID NO:320 as CDR2, and SEQ ID NO:321 as CDR3 of SEQ ID NO:271.

[0324] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:322 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:324 as CDR3 of SEQ ID NO:272. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:534 as CDR1, SEQ ID NO:323 as CDR2, and SEQ ID NO:535 as CDR3 of SEQ ID NO:272. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%,

or 100%) identical to the amino acid sequence of SEQ ID NO:272 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:272 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:273, which includes amino acid sequences SEQ ID NO:325 as CDR1, SEQ ID NO:326 as CDR2, and SEQ ID NO:327 as CDR3 of SEQ ID NO:273.

[0325] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:340 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:342 as CDR3 of SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:540 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:541 as CDR3 of SEQ ID NO:278. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with

an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279, which includes amino acid sequences SEQ ID NO:343 as CDR1, SEQ ID NO:344 as CDR2, and SEQ ID NO:345 as CDR3 of SEQ ID NO:279.

[0326] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:346 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:348 as CDR3 of SEQ ID NO:280. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:542 as CDR1, SEQ ID NO:347 as CDR2, and SEQ ID NO:543 as CDR3 of SEQ ID NO:280. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:280 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:281, which includes amino acid sequences SEQ ID NO:349 as CDR1, SEQ ID NO:350 as CDR2, and SEQ ID NO:351 as CDR3 of SEQ ID NO:281.

[0327] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282. In some embodiments, the antibody heavy chain variable

domain is at least 95% identical to SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:352 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:354 as CDR3 of SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:544 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:545 as CDR3 of SEQ ID NO:282. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283, which includes amino acid sequences SEQ ID NO:355 as CDR1, SEQ ID NO:356 as CDR2, and SEQ ID NO:357 as CDR3 of SEQ ID NO:283.

[0328] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:358 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:546 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:547. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For

example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285, which includes amino acid sequences SEQ ID NO:361 as CDR1, SEQ ID NO:362 as CDR2, and SEQ ID NO:363 as CDR3 of SEQ ID NO:285.

[0329] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:364 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:366 as CDR3 of SEQ ID NO:286. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:548 as CDR1, SEQ ID NO:365 as CDR2, and SEQ ID NO:549 as CDR3 of SEQ ID NO:286. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:287. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:286 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID

NO:287, which includes amino acid sequences SEQ ID NO:367 as CDR1, SEQ ID NO:368 as CDR2, and SEQ ID NO:369 as CDR3 of SEQ ID NO:287.

[0330] In certain embodiments, the present invention provides an antigen binding site that binds to a unique epitope on human CD33 that includes S128; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:370 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:372 as CDR3 of SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:550 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:551 as CDR3 of SEQ ID NO:288. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, which includes amino acid sequences SEQ ID NO:373 as CDR1, SEQ ID NO:374 as CDR2, and SEQ ID NO:375 as CDR3 of SEQ ID NO:289.

An antigen binding site binds to the V domain of human CD33 in a glycosylation sensitive manner

[0331] In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain that binds to the V domain of human CD33 in a glycosylation sensitive manner, *e.g.*, binds to the V domain of CD33 only when the V domain is deglycosylated.

[0332] In certain embodiments, the present invention provides an antigen binding site that binds an epitope in the V domain of human CD33 only when the V domain is deglycosylated; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:340 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:342 as CDR3 of SEQ ID NO:278. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:540 as CDR1, SEQ ID NO:341 as CDR2, and SEQ ID NO:541 as CDR3 of SEQ ID NO:278. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:278 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:279, which includes amino acid sequences SEQ ID NO:343 as CDR1, SEQ ID NO:344 as CDR2, and SEQ ID NO:345 as CDR3 of SEQ ID NO:279.

[0333] In certain embodiments, the present invention provides an antigen binding site that binds an epitope in the V domain of human CD33 only when the V domain is deglycosylated; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:352 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:354 as CDR3 of SEQ ID

NO:282. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:544 as CDR1, SEQ ID NO:353 as CDR2, and SEQ ID NO:545 as CDR3 of SEQ ID NO:282. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:282 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:283, which includes amino acid sequences SEQ ID NO:355 as CDR1, SEQ ID NO:356 as CDR2, and SEQ ID NO:357 as CDR3 of SEQ ID NO:283.

[0334] In certain embodiments, the present invention provides an antigen binding site that binds an epitope in the V domain of human CD33 only when the V domain is deglycosylated; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:358 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:284. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:546 as CDR1, SEQ ID NO:359 as CDR2, and SEQ ID NO:360 as CDR3 of SEQ ID NO:547. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to

the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:284 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:285, which includes amino acid sequences SEQ ID NO:361 as CDR1, SEQ ID NO:362 as CDR2, and SEQ ID NO:363 as CDR3 of SEQ ID NO:285.

[0335] In certain embodiments, the present invention provides an antigen binding site that binds an epitope in the V domain of human CD33 only when the V domain is deglycosylated; the antigen binding site includes a heavy chain variable domain including an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288. In some embodiments, the antibody heavy chain variable domain is at least 95% identical to SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:370 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:372 as CDR3 of SEQ ID NO:288. In some embodiments, the heavy chain variable domain incorporates amino acid sequences SEQ ID NO:550 as CDR1, SEQ ID NO:371 as CDR2, and SEQ ID NO:551 as CDR3 of SEQ ID NO:288. In certain embodiments, the antibody heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 is combined with a light chain variable domain to form an antigen-binding site capable of binding to CD33. For example, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289. In certain embodiments, an antibody heavy chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:288 can be paired with an antibody light chain variable domain at least 90% (*e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:289, which includes amino acid sequences SEQ ID

NO:373 as CDR1, SEQ ID NO:374 as CDR2, and SEQ ID NO:375 as CDR3 of SEQ ID NO:289.

An antigen binding site that binds to the extracellular domain in human CD33 and/or cyno CD33, irrespective of the glycosylation profile of the targeted CD33

[0336] In one aspect, the present invention provides an antigen binding site including a heavy chain variable domain which includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, or 302, which binds to the extracellular domain in human CD33 irrespective of the glycosylation profile of the targeted CD33.

[0337] In certain embodiments, the present invention provides an antigen binding site including a heavy chain variable domain that binds to the extracellular domain in human CD33 and/or cyno CD33, such that the epitopes are unique compared to the epitopes targeted by one or more known anti-CD33 antibodies in the art. In certain embodiments, the present invention provides an antigen binding site including a heavy chain variable domain that binds to the extracellular domain in human CD33 and/or cyno CD33, which shows human or Cynomolgus/Rhesus (cyno) CD33 cross reactivity and high affinity binding to the target CD33.

A second antigen binding site same or different from the antigen-binding site that binds human CD33

[0338] In certain embodiments, the present invention provides a protein that includes a human CD33 antigen-binding site including a heavy chain variable domain, which includes an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, or 302, and further comprises a second antigen binding site same or different from the antigen-binding site that binds to human CD33.

Proteins with antigen-binding sites

[0339] An antibody heavy chain variable domain of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296,

298, 300, and/or 302 can optionally be coupled to an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an antibody constant region, such as an IgG constant region including hinge, CH2 and CH3 domains with or without a CH1 domain. In some embodiments, the amino acid sequence of the constant region is at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) 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% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) 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.

[0340] 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.

II. Multi-specific Binding Proteins

[0341] In certain embodiments, the present invention provides an antigen-binding site in a protein (*e.g.*, a multi-specific binding protein) that binds to CD33 on a cancer cell, and the NKG2D receptor and CD16 receptor on natural killer cells to activate the natural killer cell. As used herein, the term "antibody" encompasses proteins (*e.g.*, multi-specific binding proteins) that comprise one or more antigen-binding sites (*e.g.*, an antigen-binding site that binds CD33), and is not limited to single-specific antibodies. In certain embodiments, the

protein (*e.g.*, multi-specific binding protein) or antibody is a trispecific antibody, also called Trispecific NK cell Engagement Therapy (TriNKET). The protein (*e.g.*, a multi-specific binding protein) is useful in the pharmaceutical compositions and therapeutic methods described herein. Binding of the protein including an antigen-binding site that binds to CD33, and to NKG2D receptor and CD16 receptor on natural killer cell enhances the activity of the natural killer cell toward destruction of a cancer cell. Binding of the protein including an antigen-binding site that binds to CD33 (*e.g.*, a multi-specific binding protein) on a cancer cell brings the cancer cell into proximity to the natural killer cell, which facilitates direct and indirect destruction of the cancer cell by the natural killer cell. Further description of exemplary multi-specific binding proteins is provided below.

[0342] In certain embodiments of the present disclosure, the first component of the multi-specific binding proteins binds to CD33-expressing cells, which can include but are not limited to AML, myelodysplastic syndromes, chronic myelomonocytic leukemia, myeloid blast crisis of chronic myeloid leukemia, and ALLs.

[0343] In certain embodiments of the present disclosure, the second 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 and MICA, from binding to NKG2D and activating NKG2D receptors.

[0344] In certain embodiments of the present disclosure, 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.

[0345] Another aspect of the present invention provides a protein comprising an antigen-binding site that binds NKG2D, the antigen-binding site comprising a heavy chain variable domain comprising:

CDR1 comprising the amino acid sequence of SYSMN [SEQ ID NO:192];

CDR2 comprising the amino acid sequence of SISSSSSYIYYADSVKG [SEQ ID NO:112]; and

CDR3 comprising the amino acid sequence of GAPXGAAAGWFDP [SEQ ID NO:527], wherein X is A, V, L, I, P, F, W, G, S, T, C, N, Q, or Y; and

a light chain variable domain comprising:

CDR1 comprising the amino acid sequence of RASQGISSWLA [SEQ ID NO:114],

CDR2 comprising the amino acid sequence of AASSLQS [SEQ ID NO:115], and CDR3 comprising the amino acid sequence of QQGVSFPRT [SEQ ID NO:116].

[0346] In certain embodiments, X is A, V, L, I, P, F, or W. In certain embodiments, X is V, L, or I. In certain embodiments, the amino acid sequence of CDR3 in the heavy chain variable domain comprises the sequence of SEQ ID NO:195.

[0347] In certain embodiments, the antigen-binding site comprises a heavy chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) identical to the amino acid sequence of SEQ ID NO:191; and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) identical to the amino acid sequence of SEQ ID NO:81. In certain embodiments, the antigen-binding site comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:191; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:81.

[0348] In certain embodiments, the antigen-binding site that binds NKG2D is in the form of an Fab fragment. In certain embodiments, the antigen-binding site that binds NKG2D is in the form of an scFv.

[0349] In certain embodiments, the present invention provides a protein comprising (a) a first antigen-binding site comprising an Fab fragment that binds NKG2D as disclosed herein; (b) a second antigen-binding site comprising a single-chain variable fragment (scFv) that binds a tumor associated antigen (*e.g.*, CD33); and (c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16.

[0350] The multi-specific binding proteins described herein can take various formats. For example, one format is a heterodimeric, multi-specific antibody which includes a first immunoglobulin heavy chain, a first immunoglobulin light chain, a second immunoglobulin heavy chain and a second immunoglobulin light chain. 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 CD33. 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 NKG2D. The first Fc domain and second Fc domain together are able to bind to CD16.

[0351] Another exemplary format involves a heterodimeric, multi-specific antibody which includes a first immunoglobulin heavy chain, a second immunoglobulin heavy chain and an immunoglobulin light chain. 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 variable domain and light chain variable domain which pair and bind CD33 or NKG2D. 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 constant light chain domain. The second immunoglobulin heavy chain pairs with the immunoglobulin light chain and binds to NKG2D or CD33. The first Fc domain and the second Fc domain together are able to bind to CD16.

[0352] 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 site could be a single-chain or disulfide-stabilized variable region (scFv) or could form a tetravalent or trivalent molecule.

[0353] 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.

[0354] 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 FcgammaRs. *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.

[0355] 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.

[0356] 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, without any changes being made to the other Fab.

[0357] 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 Fabs binding to targets 1 and target 2 fused to the Fc. Heterodimerization is ensured by electrostatic steering mutations in the Fc.

[0358] In some embodiments, the multi-specific binding protein is in the κλ-Body form, which is an heterodimeric constructs with two different Fabs fused to Fc stabilized by heterodimerization mutations: Fab1 targeting antigen 1 contains kappa LC, while second Fab 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.

[0359] 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). 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)). 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).

[0360] 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).

[0361] In some embodiments, the multi-specific binding protein is in an Oasc-Fab heterodimeric form that includes Fab binding to target 1, and scFab binding to target 2 fused to Fc. Heterodimerization is ensured by mutations in the Fc.

[0362] In some embodiments, the multi-specific binding protein is in a DuetMab form, which is an heterodimeric construct containing two different Fabs binding to antigens 1 and 2, and Fc stabilized by heterodimerization mutations. Fab 1 and 2 contain differential S-S bridges that ensure correct LC and HC pairing.

[0363] In some embodiments, the multi-specific binding protein is in a CrossmAb form, which is an heterodimeric construct with two different Fabs 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.

[0364] In some embodiments, the multi-specific binding protein is in a Fit-Ig form, which is a homodimeric constructs where Fab binding to antigen 2 is fused to the N terminus of HC of Fab that binds to antigen 1. The construct contains wild-type Fc.

[0365] Additional formats of the multi-specific binding proteins can be devised by combining various formats of CD33 binding-fragments described herein.

[0366] In certain embodiments of the present disclosure, the third component for the multi-specific binding proteins is an antibody constant region. In certain embodiments, each of the two immunoglobulin heavy chains of the antibody constant region includes a constant region with an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to human IgG1 constant region. In certain

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, L351, S354, E356, E357, K360, Q362, S364, T366, L368, K370, K392, T394, D399, S400, D401, F405, Y407, K409, T411 and K439; and 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, Y349, L351, S354, E356, E357, S364, T366, L368, K370, N390, K392, T394, D399, D401, F405, Y407, K409, T411 and K439.

[0367] In certain embodiments of the present disclosure, the NKG2D-antigen binding site comprises:

(1) a heavy chain variable domain comprising 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:81 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:82 [ADI-29379];

(2) a heavy chain variable domain comprising 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:83 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:84 [ADI-29463];

(3) a heavy chain variable domain comprising 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:85 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:86 [ADI-27744];

(4) a heavy chain variable domain comprising 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:87 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:88 [ADI-27749];

(5) a heavy chain variable domain comprising 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:191 and a light chain variable domain comprising an amino acid sequence at least 90%

(*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:88 [A49MI]; or

(6) a heavy chain variable domain comprising 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:89 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:90 [ADI-29378].

[0368] In certain embodiments of the present disclosure, the NKG2D-antigen binding site comprises:

(1) a heavy chain variable domain comprising 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:124 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:125 [ADI-27705];

(2) a heavy chain variable domain comprising 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:129 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:130 [ADI-27724];

(3) a heavy chain variable domain comprising 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:131 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:132 [ADI-27740];

(4) a heavy chain variable domain comprising 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:133 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:134 [ADI-27741];

(5) a heavy chain variable domain comprising 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:135 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:136 [ADI-27743];

(6) a heavy chain variable domain comprising 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:137 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:138 [ADI-28153];

(7) a heavy chain variable domain comprising 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:139 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:140 [ADI-28226 (C26)];

(8) a heavy chain variable domain comprising 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:141 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:142;

(9) a heavy chain variable domain comprising 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:143 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:144;

(10) a heavy chain variable domain comprising 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:145 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:146;

(11) a heavy chain variable domain comprising 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:147 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:148;

(12) a heavy chain variable domain comprising 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:149 and a light chain variable domain comprising an amino acid sequence at least 90%

(*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:150;

(13) a heavy chain variable domain comprising 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:151 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:152;

(14) a heavy chain variable domain comprising 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:153 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:154;

(15) a heavy chain variable domain comprising 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:155 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:156;

(16) a heavy chain variable domain comprising 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:157 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:158;

(17) a heavy chain variable domain comprising 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:159 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:160;

(18) a heavy chain variable domain comprising 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:161 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:162;

(19) a heavy chain variable domain comprising 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:163 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:164;

(20) a heavy chain variable domain comprising 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:165 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:166;

(21) a heavy chain variable domain comprising 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:167 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:168;

(22) a heavy chain variable domain comprising 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:175 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:176;

(23) a heavy chain variable domain comprising 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:583 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:584; or

(24) a heavy chain variable domain comprising 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:585 and a light chain variable domain comprising an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to a SEQ ID NO:580.

[0369] Table 2 lists peptide sequences of heavy chain variable domains and light chain variable domains that, in combination, can bind to NKG2D. Unless indicated otherwise, the CDR sequences provided in Table 2 are determined under Kabat. The NKG2D-binding domains can vary in their binding affinity to NKG2D, nevertheless, they all activate human NKG2D and NK cells.

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
ADI-29379 (E79)	QVQLVQSGAEVKKPGASVKVSCKAS GYTFTSYYMHWVRQAPGQGLEWMGI INPSGGSTSYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCARGAPNY GDTTHDYYYMDVWGKGTTVTVSS [SEQ ID NO:81] CDR1: YTFTSYYMH [SEQ ID NO:93] (non-Kabat) or SYYMH [SEQ ID NO:566] CDR2: IINPSGGSTSYAQKFQG [SEQ ID NO:94] CDR3: ARGAPNYGDTTHDYYYMDV [SEQ ID NO:95] (non-Kabat) or GAPNYGDTTHDYYYMDV [SEQ ID NO:567]	EIVMTQSPATLSVSPGERATLS CRASQSVSSNLAWYQQKPGQA PRLLIYGASTRATGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQ QYDDWPFTFGGGTKVEIK [SEQ ID NO:82] CDR1: RASQSVSSNLA [SEQ ID NO:96] CDR2: GASTRAT [SEQ ID NO:97] CDR3: QQYDDWPFT [SEQ ID NO:98]
ADI-29463 (F63)	QVQLVQSGAEVKKPGASVKVSCKAS GYTFTGYYMHWVRQAPGQGLEWMG WINPNSGGTNYAQKFQGRVTMTRDT SISTAYMELSRLRSDDTAVYYCARDT GEYYDTDDHGMDVWGQGTTVTVSS [SEQ ID NO:83] CDR1: YTFTGYYMH [SEQ ID NO:99] (non-Kabat) or GYYMH [SEQ ID NO:568] CDR2: WINPNSGGTNYAQKFQG [SEQ ID NO:100] CDR3: ARDTGEYYDTDDHGMDV [SEQ ID NO:101] (non-Kabat) or DTGEYYDTDDHGMDV [SEQ ID	EIVLTQSPGTLSLSPGERATLSC RASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGS GTEFTLTISSLQSEDFAVYYCQ QDDYWPPTFGGGTKVEIK [SEQ ID NO:84] CDR1: RASQSVSSNLA [SEQ ID NO:102] CDR2: GASTRAT [SEQ ID NO:103] CDR3: QQDDYWPPT [SEQ ID NO:104]

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	NO:569]	
ADI-27744 (A44)	EVQLLESGGGLVQPGGSLRLSCAASG FTFSSYAMSWVRQAPGKGLEWVSAIS GSGGSTYYADSVKGRFTISRDNSKNT LYLQMNSLRAEDTAVYYCAKDGGYY DSGAGDYWGQGTLVTVSS [SEQ ID NO:85] CDR1: FTFSSYAMS [SEQ ID NO:105] (non-Kabat) or SYAMS [SEQ ID NO:570] CDR2: AISGSGGSTYYADSVKG [SEQ ID NO:106] CDR3: AKDGGYYDSGAGDY [SEQ ID NO:107] (non-Kabat) or DGGYYDSGAGDY [SEQ ID NO:571]	DIQMTQSPSSVSASVGDRVTIT CRASQGIDSWLAWYQQKPGK APKLLIYAASSLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYC QQGVSYPRTFGGGTKVEIK [SEQ ID NO:86] CDR1: RASQGIDSWLA [SEQ ID NO:108] CDR2: AASSLQS [SEQ ID NO:109] CDR3: QQGVSYPRT [SEQ ID NO:110]
ADI-27749 (A49)	EVQLVESGGGLVKPGGSLRLSCAASG FTFSSYSMNWVRQAPGKGLEWVSSIS SSSSYIYYADSVKGRFTISRDNAKNSL YLQMNSLRAEDTAVYYCARGAPMGA AAGWFDPWGQGTLVTVSS [SEQ ID NO:87] CDR1: FTFSSYSMN [SEQ ID NO:111] or SYSMN [SEQ ID NO:192] CDR2: SISSSSSYIYYADSVKG [SEQ ID NO:112] CDR3: ARGAPMGAAAGWFDP [SEQ ID NO:113] or	DIQMTQSPSSVSASVGDRVTIT CRASQGISSWLAWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQ QGVSFPRTFGGGTKVEIK [SEQ ID NO:88] CDR1: RASQGISSWLA [SEQ ID NO:114] CDR2: AASSLQS [SEQ ID NO:115] CDR3: QQGVSFPRT [SEQ ID NO:116]

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	GAPMGAAAGWFDP [SEQ ID NO:193]	
A49MI	EVQLVESGGGLVKPGGSLRLSCAASG FTFSSYSMNWVRQAPGKGLEWVSSIS SSSSYIYYADSVKGRFTISRDNAKNSL YLQMNSLRAEDTAVYYCARGAPIGA AAGWFDPWGQGTLVTVSS [SEQ ID NO:191] CDR1: FTFSSYSMN [SEQ ID NO:111] or SYSMN [SEQ ID NO:192] CDR2: SISSSSSYIYYADSVKG [SEQ ID NO:112] CDR3: ARGAPIGAAAGWFDP [SEQ ID NO:194] or GAPIGAAAGWFDP [SEQ ID NO:195]	DIQMTQSPSSVSASVGDRVTIT CRASQGISSWLAWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQ QGVSFPRTFGGGTKVEIK [SEQ ID NO:88] CDR1: RASQGISSWLA [SEQ ID NO:114] CDR2: AASSLQS [SEQ ID NO:115] CDR3: QQGVSFPRT [SEQ ID NO:116]
A49MQ	EVQLVESGGGLVKPGGSLRLSCAASG FTFSSYSMNWVRQAPGKGLEWVSSIS SSSSYIYYADSVKGRFTISRDNAKNSL YLQMNSLRAEDTAVYYCARGAP**Q**GA AAGWFDPWGQGTLVTVSS (SEQ ID NO:586) CDR1 (non-Kabat) (SEQ ID NO:111) - FTFSSYSMN or CDR1 (SEQ ID NO:192) - SYSMN CDR2 (SEQ ID NO:112) - SISSSSSYIYYADSVKG CDR3 (non-Kabat) (SEQ ID NO:587) - ARGAP**Q**GAAAGWFDP or CDR3 (SEQ ID NO:588) - GAP**Q**GAAAGWFDP	DIQMTQSPSSVSASVGDRVTIT CRASQGISSWLAWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQ QGVSFPRTFGGGTKVEIK (SEQ ID NO:88) CDR1 (SEQ ID NO:114) - RASQGISSWLA CDR2 (SEQ ID NO:115) - AASSLQS CDR3 (SEQ ID NO:116) - QQGVSFPRT
A49ML	EVQLVESGGGLVKPGGSLRLSCAASG	DIQMTQSPSSVSASVGDRVTIT

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	FTFSSYSMNWVRQAPGKGLEWVSSIS SSSSYIYYADSVKGRFTISRDNAKNSL YLQMNSLRAEDTAVYYCARGAP**L**GA AAGWFDPWGQGTLVTVSS (SEQ ID NO:589) CDR1 (non-Kabat) (SEQ ID NO:111) - FTFSSYSMN or CDR1 (SEQ ID NO:192) - SYSMN CDR2 (SEQ ID NO:112) - SISSSSSYIYYADSVKG CDR3 (non-Kabat) (SEQ ID NO:590) - ARGAP**L**GAAAGWFDP or CDR3 (SEQ ID NO:591) - GAP**L**GAAAGWFDP	CRASQGISSWLAWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQ QGVSFPRTFGGGTKVEIK (SEQ ID NO:88) CDR1 (SEQ ID NO:114) - RASQGISSWLA CDR2 (SEQ ID NO:115) - AASSLQS CDR3 (SEQ ID NO:116) - QQGVSFPRT
A49MF	EVQLVESGGGLVKPGGSLRLSCAASG FTFSSYSMNWVRQAPGKGLEWVSSIS SSSSYIYYADSVKGRFTISRDNAKNSL YLQMNSLRAEDTAVYYCARGAP**F**GA AAGWFDPWGQGTLVTVSS (SEQ ID NO:592) CDR1 (non-Kabat) (SEQ ID NO:111) - FTFSSYSMN or CDR1 (SEQ ID NO:192) - SYSMN CDR2 (SEQ ID NO:112) - SISSSSSYIYYADSVKG CDR3 (non-Kabat) (SEQ ID NO:593) - ARGAP**F**GAAAGWFDP or CDR3 (SEQ ID NO:594) - GAP**F**GAAAGWFDP	DIQMTQSPSSVSASVGDRVTIT CRASQGISSWLAWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQ QGVSFPRTFGGGTKVEIK [SEQ ID NO:88] CDR1: RASQGISSWLA [SEQ ID NO:114] CDR2: AASSLQS [SEQ ID NO:115] CDR3: QQGVSFPRT [SEQ ID NO:116]
A49MV	EVQLVESGGGLVKPGGSLRLSCAASG FTFSSYSMNWVRQAPGKGLEWVSSIS SSSSYIYYADSVKGRFTISRDNAKNSL YLQMNSLRAEDTAVYYCARGAP**V**GA AAGWFDPWGQGTLVTVSS (SEQ ID NO:595) CDR1 (non-Kabat) (SEQ ID NO:111) -	DIQMTQSPSSVSASVGDRVTIT CRASQGISSWLAWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQ QGVSFPRTFGGGTKVEIK [SEQ ID NO:88]

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	FTFSSYSMN or CDR1 (SEQ ID NO:192) - SYSMN CDR2 (SEQ ID NO:112) - SISSSSSYIYYADSVKG CDR3 (non-Kabat) (SEQ ID NO:596) - ARGAP**V**GAAAGWFDP or CDR3 (SEQ ID NO:597) - GAP**V**GAAAGWFDP	CDR1: RASQGISSWLA [SEQ ID NO:114] CDR2: AASSLQS [SEQ ID NO:115] CDR3: QQGVSFPRT [SEQ ID NO:116]
A49-consensus	EVQLVESGGGLVKPGGSLRLSCAASG FTFSSYSMNWVRQAPGKGLEWVSSIS SSSSYIYYADSVKGRFTISRDNAKNSL YLQMNSLRAEDTAVYYCARGAP**X**GA AAGWFDPWGQGTLVTVSS, wherein X is M, L, I, V, Q, or F (SEQ ID NO:91) CDR1 (non-Kabat) (SEQ ID NO:111) - FTFSSYSMN or CDR1 (SEQ ID NO:192) - SYSMN CDR2 (SEQ ID NO:112) - SISSSSSYIYYADSVKG CDR3 (non-Kabat) (SEQ ID NO:92) - ARGAP**X**GAAAGWFDP or CDR3 (SEQ ID NO:123) – GAP**X**GAAAGWFDP, wherein X is M, L, I, V, Q, or F	DIQMTQSPSSVSASVGDRVTIT CRASQGISSWLAWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQ QGVSFPRTFGGGTKVEIK [SEQ ID NO:88] CDR1: RASQGISSWLA [SEQ ID NO:114] CDR2: AASSLQS [SEQ ID NO:115] CDR3: QQGVSFPRT [SEQ ID NO:116]
ADI-29378 (E78)	QVQLVQSGAEVKKPGASVKVSCKAS GYTFTSYYMHWVRQAPGQGLEWMGI INPSGGSTSYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCAREGAGF AYGMDYYYMDVWGKGTTVTVSS [SEQ ID NO:89] CDR1: YTFTSYYMH [SEQ ID NO:117] (non-Kabat) or SYYMH [SEQ ID NO:572]	EIVLTQSPATLSLSPGERATLSC RASQSVSSYLAWYQQKPGQAP RLLIYDASNRATGIPARFSGSGS GTDFTLTISSLEPEDFAVYYCQ QSDNWPFTFGGGTKVEIK [SEQ ID NO:90] CDR1: RASQSVSSYLA [SEQ ID NO:120]

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	CDR2: IINPSGGSTSYAQKFQG [SEQ ID NO:118] CDR3: AREGAGFAYGMDYYYMDV [SEQ ID NO:119] (non-Kabat) or EGAGFAYGMDYYYMDV [SEQ ID NO:573]	CDR2: DASNRAT [SEQ ID NO:121] CDR3: QQSDNWPFT [SEQ ID NO:122]
ADI-27705	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:124] CDR1: GSFSGYYWS [SEQ ID NO:126] (non-Kabat) or GYYWS [SEQ ID NO:574] CDR2: EIDHSGSTNYNPSLKS [SEQ ID NO:127] CDR3: ARARGPWSFDP [SEQ ID NO:128] (non-Kabat) or ARGPWSFDP [SEQ ID NO:575]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYNSYPITFGGGTKVEIK [SEQ ID NO:125]
ADI-27724	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:129]	EIVLTQSPGTLSLSPGERATLSC RASQSVSSSYLAWYQQKPGQA PRLLIYGASSRATGIPDRFSGSG SGTDFTLTISRLEPEDFAVYYC QQYGSSPITFGGGTKVEIK [SEQ ID NO:130]
ADI-27740 (A40)	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	DPWGQGTLVTVSS [SEQ ID NO:131]	QYHSFYTFGGGTKVEIK [SEQ ID NO:132]
ADI-27741	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:133]	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QSNSYYTFGGGTKVEIK [SEQ ID NO:134]
ADI-27743	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:135]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYNSYPTFGGGTKVEIK [SEQ ID NO:136]
ADI-28153	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWG FDPWGQGTLVTVSS [SEQ ID NO:137]	ELQMTQSPSSLSASVGDRVTIT CRTSQSISSYLNWYQQKPGQPP KLLIYWASTRESGVPDRFSGSG SGTDFTLTISSLQPEDSATYYCQ QSYDIPYTFGQGTKLEIK [SEQ ID NO:138]
ADI-28226 (C26)	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:139]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYGSFPITFGGGTKVEIK [SEQ ID NO:140]
ADI-28154	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTDFTLTISSLQPDDFATYYC QQSKEVPWTFGQGTKVEIK

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	[SEQ ID NO:141]	[SEQ ID NO:142]
ADI-29399	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:143]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYNSFPTFGGGTKVEIK [SEQ ID NO:144]
ADI-29401	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:145]	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYDIYPTFGGGTKVEIK [SEQ ID NO:146]
ADI-29403	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:147]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYDSYPTFGGGTKVEIK [SEQ ID NO:148]
ADI-29405	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:149]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYGSFPTFGGGTKVEIK [SEQ ID NO:150]
ADI-29407	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:151]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYQSFPTFGGGTKVEIK [SEQ ID NO:152]

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
ADI-29419	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:153]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYSSFSTFGGGTKVEIK [SEQ ID NO:154]
ADI-29421	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:155]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYESYSTFGGGTKVEIK [SEQ ID NO:156]
ADI-29424	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:157]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYDSFITFGGGTKVEIK [SEQ ID NO:158]
ADI-29425	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:159]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYQSYPTFGGGTKVEIK [SEQ ID NO:160]
ADI-29426	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:161]	DIQMTQSPSTLSASVGDRVTIT CRASQSIGSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYHSFPTFGGGTKVEIK [SEQ ID NO:162]
ADI-	QVQLQQWGAGLLKPSETLSLTCAVY	DIQMTQSPSTLSASVGDRVTIT

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
29429	GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:163]	CRASQSIGSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYELYSYTFGGGTKVEIK [SEQ ID NO:164]
ADI-29447 (F47)	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:165]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQ QYDTFITFGGGTKVEIK [SEQ ID NO:166]
ADI-27727	QVQLVQSGAEVKKPGSSVKVSCKAS GGTFSSYAISWVRQAPGQGLEWMGGI IPIFGTANYAQKFQGRVTITADESTST AYMELSSLRSEDTAVYYCARGDSSIR HAYYYYGMDVWGQGTTVTVSS [SEQ ID NO:167] CDR1: GTFSSYAIS [SEQ ID NO:169] (non-Kabat) or SYAIS [SEQ ID NO:576] CDR2: GIIPIFGTANYAQKFQG [SEQ ID NO:170] CDR3: ARGDSSIRHAYYYYGMDV [SEQ ID NO:171] (non-Kabat) or GDSSIRHAYYYYGMDV [SEQ ID NO:577]	DIVMTQSPDSLAVSLGERATIN CKSSQSVLYSSNNKNYLAWYQ QKPGQPPKLLIYWASTRESGVP DRFSGSGSGTDFTLTISSLQAED VAVYYCQQYYSTPITFGGGTK VEIK [SEQ ID NO:168] CDR1: KSSQSVLYSSNNKNYLA [SEQ ID NO:172] CDR2: WASTRES [SEQ ID NO:173] CDR3: QQYYSTPIT [SEQ ID NO:174]
ADI-29443 (F43)	QLQLQESGPGLVKPSETLSLTCTVSGG SISSSSYYWGWIRQPPGKGLEWIGSIY YSGSTYYNPSLKSRVTISVDTSKNQFS LKLSSVTAADTAVYYCARGSDRFHPY FDYWGQGTLVTVSS	EIVLTQSPATLSLSPGERATLSC RASQSVSRYLAWYQQKPGQAP RLLIYDASNRATGIPARFSGSGS GTDFTLTISSLEPEDFAVYYCQ QFDTWPPTFGGGTKVEIK

Table 2

Clones	Heavy chain variable region amino acid sequence	Light chain variable region amino acid sequence
	[SEQ ID NO:175] CDR1: GSISSSSYYWG [SEQ ID NO:177] (non-Kabat) or SSSYYWG [SEQ ID NO:578] CDR2: SIYYSGSTYYNPSLKS [SEQ ID NO:178] CDR3: ARGSDRFHPYFDY [SEQ ID NO:179] (non-Kabat) or GSDRFHPYFDY [SEQ ID NO:579]	[SEQ ID NO:176] CDR1: RASQSVSRYLA [SEQ ID NO:180] CDR2: DASNRAT [SEQ ID NO:581] CDR3: QQFDTWPPT [SEQ ID NO:582]
ADI-29404 (F04)	QVQLQQWGAGLLKPSETLSLTCAVY GGSFSGYYWSWIRQPPGKGLEWIGEI DHSGSTNYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARARGPWSF DPWGQGTLVTVSS [SEQ ID NO:583]	DIQMTQSPSTLSASVGDRVTIT CRASQSISSWLAWYQQKPGKA PKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCE QYDSYPTFGGGTKVEIK [SEQ ID NO:584]
ADI-28200	QVQLVQSGAEVKKPGSSVKVSCKAS GGTFSSYAISWVRQAPGQGLEWMGGI IPIFGTANYAQKFQGRVTITADESTST AYMELSSLRSEDTAVYYCARRGRKAS GSFYYYYGMDVWGQGTTVTVSS [SEQ ID NO:585]	DIVMTQSPDSLAVSLGERATIN CESSQSLLNSGNQKNYLTWYQ QKPGQPPKPLIYWASTRESGVP DRFSGSGSGTDFTLTISSLQAED VAVYYCQNDYSYPYTFGQGTK LEIK [SEQ ID NO:580]

[0370] The antibody molecule may have a heavy chain constant region chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.*, the (*e.g.*, human) heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In another embodiment, the antibody molecule has a light chain constant region chosen from, *e.g.*, the (*e.g.*, human) light chain constant regions of kappa or lambda. The constant region can be altered, *e.g.*, mutated, to modify the properties of the antibody (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the

number of cysteine residues, effector cell function, and/or complement function). In one embodiment the antibody has effector function and can fix complement. In other embodiments the antibody does not recruit effector cells or fix complement. In another embodiment, the antibody has reduced or no ability to bind an Fc receptor. For example, it is an isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, *e.g.*, it has a mutagenized or deleted Fc receptor binding region.

[0371] 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.

[0372] In some embodiments, the antibody constant domain comprises a CH2 domain and a CH3 domain of an IgG antibody, for example, a human IgG1 antibody. In some embodiments, mutations are introduced in the antibody constant domain to enable heterdimerization with another antibody constant domain. For example, if the antibody constant domain is derived from the constant domain of a human IgG1, the antibody constant domain can comprise an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to amino acids 234-332 of a human IgG1 antibody, 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, and K439. All the amino acid positions in an Fc domain or hinge region disclosed herein are numbered according to EU numbering.

[0373] 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.

[0374] 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.

[0375] An antibody heavy chain variable domain of the invention can optionally be coupled to an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) 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% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) 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% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) 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.

[0376] 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.

[0377] Alternatively, amino acid substitutions could be selected from the following sets of substitutions shown in Table 3.

Table 3

	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

[0378] Alternatively, amino acid substitutions could be selected from the following sets of substitutions shown in Table 4.

Table 4

	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

[0379] Alternatively, amino acid substitutions could be selected from the following set of substitutions shown in Table 5.

Table 5		
	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

[0380] Alternatively, at least one amino acid substitution in each polypeptide chain could be selected from Table 6.

Table 6	
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

[0381] Alternatively, at least one amino acid substitutions could be selected from the following set of substitutions in Table 7, 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 7	
First Polypeptide	**Second Polypeptide**
K392, K370, K409, or K439	D399, E356, or E357

[0382] Alternatively, at least one amino acid substitutions could be selected from the following set of in Table 8, 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 8	
First Polypeptide	**Second Polypeptide**
D399, E356, or E357	K409, K439, K370, or K392

[0383] Alternatively, amino acid substitutions could be selected from the following set of in Table 9.

Table 9	
First Polypeptide	**Second Polypeptide**
T350V, L351Y, F405A, and Y407V	T350V, T366L, K392L, and T394W

[0384] Alternatively, or in addition, the structural stability of heterodimeric heavy chains within the multi-specific binding proteins can 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.

[0385] In certain embodiments of the present disclosure, 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.

[0386] In certain embodiments of the present disclosure, 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.

[0387] In certain embodiments of the present disclosure, 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.

[0388] In certain embodiments of the present disclosure, 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.

[0389] In certain embodiments of the present disclosure, 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.

[0390] In certain embodiments of the present disclosure, 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.

[0391] In certain embodiments of the present disclosure, 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.

[0392] In certain embodiments of the present disclosure, 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.

[0393] In certain embodiments of the present disclosure, 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.

[0394] In certain embodiments of the present disclosure, 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.

[0395] In certain embodiments of the present disclosure, 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.

[0396] In certain embodiments of the present disclosure, 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.

[0397] In certain embodiments of the present disclosure, 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.

[0398] In certain embodiments of the present disclosure, 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.

[0399] In certain embodiments of the present disclosure, 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 Q347R, D399V and F405T substitutions.

[0400] In certain embodiments of the present disclosure, 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.

[0401] In certain embodiments of the present disclosure, 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.

[0402] In certain embodiments of the present disclosure, 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.

[0403] In certain embodiments of the present disclosure, 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.

[0404] In certain embodiments of the present disclosure, 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.

[0405] Listed below are examples of CD33-binding F3'-TriNKETs comprising: a CD33-binding single-chain variable fragment (scFv) linked to an Fc domain via a hinge comprising Ala-Ser; and an NKG2D-binding Fab fragment ("A49" or "A49MI") comprising a heavy chain portion comprising an heavy chain variable domain (SEQ ID NO:87 or SEQ ID NO:191) and a CH1 domain, and a light chain portion comprising a light chain variable domain (SEQ ID NO:88) and a light chain constant domain, wherein the heavy chain variable domain is connected to the CH1 domain, and the CH1 domain is connected to an Fc domain. The CDR sequences are underlined.

[0406] In each of the examples, the Fc domain linked to the CD33-binding scFv comprises Q347R, D399V, and F405T substitutions for forming a heterodimer with the Fc domain linked to the Fab comprising K360E and K409W substitutions. These substitutions in the Fc domains are bold-underlined in the sequences described below. Alternatively, in an exemplary embodiment, the Fc domain linked to the NKG2D-binding Fab fragment includes the mutations of Q347R, D399V, and F405T, and the Fc domain linked to the CD33-binding scFv comprises matching mutations K360E and K409W for forming a heterodimer.

[0407] Additionally, the Fc domain linked to the CD33-binding scFv comprises S354C substitution, and the Fc domain linked to the Fab comprises Y349C substitution, thereby stabilizing the interaction between the two Fc domains via a S-S bridge. These substitutions in the Fc domains are bold-italics-underlined in the sequences below.

[0408] Alternatively, in an exemplary embodiment, the Fc domain linked to the NKG2D-binding Fab fragment includes a S354C substitution in the CH3 domain, which forms a disulfide bond with a Y349C substitution on the Fc linked to the CD33-binding scFv.

[0409] A CD33-binding scFv of the present disclosure can include a heavy chain variable domain connected to a light chain variable domain with a $(G4S)_4$ linker. The scFv is linked to an Fc domain via a hinge comprising Ala-Ser (bolded-underlined). SEQ ID NOs:188, 198, and 206-223 are exemplary sequences of such CD33-binding scFv polypeptides. The V_L and V_H comprised within the scFv (*e.g.*, SEQ ID NOs:188, 198 or 206-223) contain $100V_L$ - $44V_H$ S-S bridge (resulting from G100C and G44C substitutions, respectively) (cysteine

residues are in bold-italics-underlined in the sequences below). $(G4S)_4$ is the bold-underlined sequence GGGGSGGGGSGGGGSGGGGS [SEQ ID NO:186] in SEQ ID NOs:188, 198, and 206-243.

[0410] Exemplary sequences of CD33-binding scFvs linked to an Fc domain via a hinge comprising Ala-Ser are provided below.

Ab1 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYESFPTFG***C***GTKVEIK**GGGGSGGGGS**
GGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYGMSWVRQAPGK***C***L
EWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREG
GPYYDSSGYFVYYGMDVWGQGTTVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:224]

Ab1 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYGMSWVRQAPGK***C***LEWVANIKQDGS
EKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVY
YGMDVWGQGTTVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSTLSASVGDR
VTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTEFTLTISS
LQPDDFATYYCQQYESFPTFG***C***GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:225]

Ab2 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQLESYPLTFG***C***GTKVEIK**GGGGSGGGG**
SGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK***C***
LEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPL
NAGELDVWGQGTMVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPG [SEQ ID NO:226]

Ab2 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK***C***LEWVANIKQDG
SEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ
GTMVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSTLSASVGDRVTITCRASQ
SISSWLAWYQQKPGKAPKLLIYEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATY
YCQQLESYPLTFG***C***GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT

PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:227]

H76 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFG***C***GTKVEIK**GGGGSGGGG**
SGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGK***C***
LEWVSAIVGSGESTYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREG
GPYYDSSGYFVYYGMDVWGQGTTVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:197]

H76 scFv (HC-LC) -Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGK***C***LEWVSAIVGSGE
STYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVY
YGMDVWGQGTTVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSTLSASVGDR
VTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPSRFSGSGSGTEFTLTISS
LQPDDFATYYCQQYDDLPTFG***C***GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:228]

H76 scFc (LC-HC)-Fc (K360E, K409W, and Y349C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFG***C***GTKVEIK**GGGGSGGGG**
SGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGK***C***
LEWVSAIVGSGESTYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREG
GPYYDSSGYFVYYGMDVWGQGTTVTVSS**AS**TKGPSVFPLAPSSKSTSGGTAALGCL
VKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN
HKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC
VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQV***C***TLPPSRDELT**E**NQVSLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS**W**LTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPG [SEQ ID NO:243]

Ab4 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQSPQLLIYLGSN
RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQDVALPITFG***C***GTKVEIK**GGG**
GSGGGGSGGGGSGGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHW
VRQAPGQ***C***LEWMGMINPSWGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDT
AVYYCAREAADGFVGERYFDLWGRGTLVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RD

ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVD
KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:229]

Ab4 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

QVQLVQSGAEVKKPGASVKVSCKASGYTFSDYYMHWVRQAPGQ***C***LEWMGMINPS
WGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCAREAADGFVGERYF
DLWGRGTLVTVSS**GGGGSGGGGSGGGGSGGGGS**DIVMTQSPLSLPVTPGEPASISC
RSSQSLLYSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKIS
RVEAEDVGVYYCMQDVALPITFG***C***GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDEL
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:230]

I07 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFG***C***GTKVEIK**GGGGSGGG**
GSGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPG
K***C***LEWVATIKQDGSEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
PLNAGELDVWGQGTMVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:187]

I07 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPGK***C***LEWVATIKQDG
SEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ
GTMVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSTLSASVGDRVTITCRASQ
SISSWLAWYQQKPGKAPKLLIYEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATY
YCQQSQSYPPITFG***C***GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:231]

I07 scFc (LC-HC)-Fc (K360E, K409W, and Y349C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFG***C***GTKVEIK**GGGGSGGG**
GSGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPG
K***C***LEWVATIKQDGSEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
PLNAGELDVWGQGTMVTVSS**AS**TKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE
DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQV***C***TLPPSRDELT**E**NQVSLTCLVKGFYPSDIAVEW

ESNGQPENNYKTTPPVLDSDGSFFLYS**W**LTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPG [SEQ ID NO:242]

Ab6 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFG***C***GTKVEIK**GGGGSGGG**
GSGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFPSYWMSWVRQAPGK
CLEWVATIKRDGSEKGYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARP
LNAGELDVWGQGTMVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT
PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:232]

Ab6 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVQPGGSLRLSCAASGFTFPSYWMSWVRQAPGK***C***LEWVATIKRDGS
EKGYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQG
TMVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSTLSASVGDRVTITCRASQSI
SSWLAWYQQKPGKAPKLLIYEASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYY
CQQSQSYPPITFG***C***GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPG [SEQ ID NO:233]

Ab7 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSSVSASVGDRVTITCRASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHSYPLTFG***C***GTKVEIK**GGGGSGG**
GGSGGGGSGGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQA
PGQ***C***LEWMGIINPSRGSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYC
ARGAGYDDEDMDVWGKGTTVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQV
SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:234]

Ab7 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

QVQLVQSGAEVKKPGASVKVSCKASGYTFGTYYMHWVRQAPGQ***C***LEWMGIINPSR
GSTVYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGAGYDDEDMDV
WGKGTTVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSSVSASVGDRVTITCR
ASQGIDSWLAWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPED
FATYYCQQAHSYPLTFG***C***GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:235]

Ab8 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASNSISSWLAWYQQKPGKAPKLLIYEASSTKSGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFG**C**GTKVEIK**GGGGSGGGG**
SGGGGSGGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYAMSWVRQAPGK**C**
LEWVSSISSSSEGIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGG
PYYDSSGYFVYYGMDVWGQGTTVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:236]

Ab8 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYAMSWVRQAPGK**C**LEWVSSISSSSEGI
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGPYYDSSGYFVYY
GMDVWGQGTTVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSTLSASVGDRV
TITCRASNSISSWLAWYQQKPGKAPKLLIYEASSTKSGVPSRFSGSGSGTEFTLTISSL
QPDDFATYYCQQYDDLPTFG**C**GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:237]

Ab9 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSSLSASVGDRVTITCRASQVIYSYLNWYQQKPGKAPKLLIYAASSLKSGV
PSRFSGSGSGTDFTLTISSLQPEDFATYYCQQVYDTPLTFG**C**GTKVEIK**GGGGSGGG**
GSGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK
CLEWVANINTDGSEVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARD
VGPGIAYQGHFDYWGQGTLVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:238]

Ab9 scFv (HC-LC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGK**C**LEWVANINTDGS
EVYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDVGPGIAYQGHFD
YWGQGTLVTVSS**GGGGSGGGGSGGGGSGGGGS**DIQMTQSPSSLSASVGDRVTITC
RASQVIYSYLNWYQQKPGKAPKLLIYAASSLKSGVPSRFSGSGSGTDFTLTISSLQPE
DFATYYCQQVYDTPLTFG**C**GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKNQV
SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPG [SEQ ID NO:239]

Ab10 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

EIVLTQSPATLSLSPGERATLSCRASHSVYSYLAWYQQKPGQAPRLLIYDASNRATGI
PARFSGSGSGTDFTLTISSLEPEDFAVYYCQQYDNLPTFG**C**GTKVEIK**GGGGSGGGG**
SGGGGSGGGGSQLQLQESGPGLVKPSETLSLTCTVSGGSISSTDYYWGWIRQPPGK**C**
LEWIGSIGYSGTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARETAHDV
HGMDVWGQGTTVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV
TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPG [SEQ ID NO:240]

Ab10 scFv (HC-LC) -Fc (Q347R, D399V, F405T, and S354C substitutions)

QLQLQESGPGLVKPSETLSLTCTVSGGSISSTDYYWGWIRQPPGK**C**LEWIGSIGYSGT
YYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARETAHDVHGMDVWGQG
TTVTVSS**GGGGSGGGGSGGGGSGGGGS**EIVLTQSPATLSLSPGERATLSCRASHSV
YSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYY
CQQYDNLPTFG**C**GTKVEIK**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPG [SEQ ID NO:241]

[0411] A TriNKET of the present disclosure is A49-F3'-TriNKET-I07, comprising a first polypeptide chain, named "I07 scFv-Fc," which comprises a CD33-binding scFv linked to an Fc domain via an Ala-Ser linker; a second polypeptide chain, named "A49 VH-CH1-Fc," which comprises an NKG2D-targeting heavy chain; and a third polypeptide chain, named "A49 VL-CL," which comprises an NKG2D-targeting light chain. The amino acid sequence of I07 scFv-Fc comprises:

I07 scFv (LC-HC)-Fc (Q347R, D399V, F405T, and S354C substitutions)

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFG**C**GTKVEIK**GGGGSGGG**
GSGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPG
K**C**LEWVATIKQDGSEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
PLNAGELDVWGQGTMVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKNQVSLTC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPG
[SEQ ID NO:187]

[0412] The amino acid sequence of the scFv portion of I07 scFv-Fc comprises:

I07 scFv

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFG***C***GTKVEIK**GGGGSGGG**
GSGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPG
K***C***LEWVATIKQDGSEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
PLNAGELDVWGQGTMVTVSS
[SEQ ID NO:188]

[0413] A49 VH-CH1-Fc comprises A49 VH [SEQ ID NO:87] linked to a CH1 domain and an Fc domain (including hinge, CH2, and CH3 domains). The amino acid sequence of A49 VH-CH1-Fc comprises:

A49 VH-CH1-Fc (K360E, K409W, and Y349C substitutions)

EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYI
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGAPMGAAAGWFDPW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT
SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQV***C***TLPPSRDELT**E**NQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYS**W**LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
[SEQ ID NO:189]

A49 VH-CH1-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYI
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGAPMGAAAGWFDPW
GQGTLVTVSSASDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTCLVKGFYPSDIA
VEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSL [SEQ ID NO:244]

[0414] A49 VL-CL comprises A49 VL [SEQ ID NO:88] linked to a light chain constant domain (CL). The amino acid sequence of A49 VL-CL comprises:

A49 VL-CL

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGVSFPRTFGGGTKVEIKRTVAAPSVF
IFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY
SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
[SEQ ID NO:190]

[0415] Another TriNKET of the present disclosure is A49MI-F3'-TriNKET-I07, comprising a first polypeptide chain, named "I07 scFv-Fc," as described above [SEQ ID NO:187]; a second polypeptide chain, named "A49MI VH-CH1-Fc," that comprises an NKG2D-targeting heavy chain with an Fc domain; and a third polypeptide chain, named "A49 VL-CL," as described above [SEQ ID NO:190]. A49MI-F3'-TriNKET-I07 is identical to A49-F3'-TriNKET-I07 except for a substitution of I for M in CDR3 of the NKG2D-targeting VH. This substitution is bold-italic (and underlined because it is part of a CDR) in the sequence below. A49MI VH-CH1-Fc comprises A49MI VH [SEQ ID NO:191] linked to a CH1 domain and an Fc domain (including hinge, CH2, and CH3 domains). The amino acid sequence of A49MI VH-CH1-Fc comprises:

A49MI VH-CH1-Fc (K360E, K409W, and Y349C substitutions)

EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYI
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGAP***I***GAAAGWFDPWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS
GVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDK
THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQV**C**TLPPSRDELT**E**NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYS**W**LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
[SEQ ID NO:196]

A49MI VH-CH1-Fc (Q347R, D399V, F405T, and S354C substitutions)

EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYI
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGAP***I***GAAAGWFDPWG
QGTLVTVSSASDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVFSCSVMHEALHN
HYTQKSLSL [SEQ ID NO:245]

[0416] Another TriNKET of the present disclosure is A49-F3'-TriNKET-I07(si), comprising a first polypeptide chain, named "I07 scFv-Fc(si)," which comprises a CD33-binding scFv linked to a silent Fc domain via an Ala-Ser linker; a second polypeptide chain, named "A49 VH-CH1-Fc(si)," which comprises an NKG2D-targeting heavy chain with a silent Fc domain; and a third polypeptide chain, named "A49 VL-CL," as described above [SEQ ID NO: 190]. A49-F3'-TriNKET-I07(si) is identical to A49-F3'-TriNKET-I07 except for L234A, L235A, and P329A substitutions in both Fc domains. These substitutions are

bold-italic in the two sequences below. The amino acid sequence of I07 scFv-Fc(si) comprises:

I07 scFv-Fc(si)
DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFG***C***GTKVEIK**GGGGSGGG**
GSGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPG
K***C***LEWVATIKQDGSEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
PLNAGELDVWGQGTMVTVSS**AS**DKTHTCPPCPAPE***AA***GGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKAL***G***APIEKTISKAKGQPREP**R**VYTLPP***C***RDELTKNQVSLTC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPG
[SEQ ID NO:204]

[0417] The amino acid sequence of the scFv portion of I07 scFv-Fc(si) is identical to that of the scFv portion of I07 scFv-Fc as described above [SEQ ID NO:188].

[0418] The amino acid sequence of A49 VH-CH1-Fc(si) comprises:

A49 VH-CH1-Fc(si)
EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYI
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGAPMGAAAGWFDPW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT
SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPE***AA***GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL***G***APIE
KTISKAKGQPREPQV***C***TLPPSRDELT**E**NQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLYS**W**LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
[SEQ ID NO:205]

[0419] Another TriNKET of the present disclosure is A49-F3'-TriNKET-H76, comprising a first polypeptide chain, named "H76 scFv-Fc," that comprises a CD33-binding scFv linked to an Fc domain via an Ala-Ser linker; a second polypeptide chain, named "A49 VH-CH1-Fc," as described above [SEQ ID NO:189]; and a third polypeptide chain, named "A49 VL-CL," as described above [SEQ ID NO:190]. The amino acid sequence of H76 scFv-Fc comprises:

H76 scFv-Fc
DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFG***C***GTKVEIK**GGGGSGGGG**
SGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGK***C***
LEWVSAIVGSGESTYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREG
GPYYDSSGYFVYYGMDVWGQGTTVTVSS**AS**DKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV

VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP**R**VYTLPP**C**RDELT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**V**SDGSF**T**LYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPG
[SEQ ID NO:197]

[0420] The amino acid sequence of the scFv portion of H76 scFv-Fc comprises:

H76 scFv
DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYDDLPTFG**C**GTKVEIK**GGGGSGGGG**
SGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSKYTMSWVRQAPGK**C**
LEWVSAIVGSGESTYFADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREG
GPYYDSSGYFVYYGMDVWGQGTTVTVSS
[SEQ ID NO:198]

[0421] In other embodiments of the present disclosure, the CD33-binding scFv of the multi-specific binding protein (*e.g.*, TriNKET) comprises the heavy chain variable domain CDR1, CDR2, and CDR3, and light chain variable domain CDR1, CDR2, and CDR3, of any one of the antibodies provided in Table 1. In certain embodiments, the amino acid sequence of the heavy chain variable domain is identical to the VH sequence of an antibody in Table 1 except for a substitution of Cys at position 44, and the amino acid sequence of the light chain variable domain is identical to the VL sequence of the same antibody except for a substitution of Cys at position 100. In certain embodiments, the heavy chain variable domain is connected to the light chain variable domain with a $(G4S)_4$ linker. The heavy chain variable domain can be N-terminal to the light chain variable domain or C-terminal to the light chain variable domain. The scFv is linked to an Fc domain via a hinge comprising Ala-Ser.

[0422] The multi-specific binding 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 first immunoglobulin light chain can be cloned into a third expression vector; a fourth nucleic acid sequence encoding the second immunoglobulin light chain can be cloned into a fourth expression vector; the first, second, third and fourth expression vectors can be stably transfected together into host cells to produce the multimeric proteins.

[0423] To achieve the highest yield of the multi-specific binding proteins, different ratios of the first, second, third and fourth expression vectors 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.

[0424] Clones can be cultured under conditions suitable for bio-reactor scale-up and maintained expression of the multi-specific protein. The multi-specific binding 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.

[0425] In certain embodiments, the antibody binds CD33 with a K_D of 20 nM, 15 nM, 10 nM, 9 nM, 8 nM, 7 nM, 6 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM or lower, as measured using standard binding assays, for example, surface plasmon resonance or bio-layer interferometry. In certain embodiments the antibody binds EBI3 from a body fluid, tissue and/or cell of a subject.

[0426] Competition assays for determining whether an antibody binds to the same epitope as, or competes for binding with a disclosed antibody, *e.g.,* the Ab1 antibody, the Ab2 antibody, the Ab3 antibody, the Ab4 antibody, or the Ab5 antibody, are known in the art. Exemplary competition assays include immunoassays (*e.g.*, ELISA assays, RIA assays), surface plasmon resonance (*e.g.,* BIAcore analysis), bio-layer interferometry, and flow cytometry.

[0427] Typically, a competition assay involves the use of an antigen (*e.g.*, a human CD33 protein or fragment thereof) bound to a solid surface or expressed on a cell surface, a test CD33-binding antibody and a reference antibody. The reference antibody is labeled and the test antibody is unlabeled. Competitive inhibition is measured by determining the amount of labeled reference antibody bound to the solid surface or cells in the presence of the test antibody. Usually the test antibody is present in excess (*e.g.*, 1x, 5x, 10x, 20x or 100x). Antibodies identified by competition assay (*e.g.*, competing antibodies) include antibodies binding to the same epitope, or similar (*e.g.*, overlapping) epitopes, as the reference antibody, and antibodies binding to an adjacent epitope sufficiently proximal to the epitope bound by the reference antibody for steric hindrance to occur.

[0428] A competition assay can be conducted in both directions to ensure that the presence of the label does not interfere or otherwise inhibit binding. For example, in the first direction the reference antibody is labeled and the test antibody is unlabeled, and in the second direction, the test antibody is labeled and the reference antibody is unlabeled.

[0429] A test antibody competes with the reference antibody for specific binding to the antigen if an excess of one antibody (*e.g.*, 1x, 5x, 10x, 20x or 100x) inhibits binding of the other antibody, *e.g.*, by at least 50%, 75%, 90%, 95% or 99% as measured in a competitive binding assay.

[0430] Two antibodies may be determined to bind to the same epitope if essentially all amino acid mutations in the antigen that reduce or eliminate binding of one antibody reduce or eliminate binding of the other. Two antibodies may be determined to bind to overlapping epitopes if only a subset of the amino acid mutations that reduce or eliminate binding of one antibody reduce or eliminate binding of the other.

[0431] The antibodies disclosed herein may be further optimized (*e.g.*, affinity-matured) to improve biochemical characteristics including affinity and/or specificity, improve biophysical properties including aggregation, stability, precipitation and/or non-specific interactions, and/or to reduce immunogenicity. Affinity-maturation procedures are within ordinary skill in the art. For example, diversity can be introduced into an immunoglobulin heavy chain and/or an immunoglobulin light chain by DNA shuffling, chain shuffling, CDR shuffling, random mutagenesis and/or site-specific mutagenesis.

[0432] In certain embodiments, isolated human antibodies contain one or more somatic mutations. In these cases, antibodies can be modified to a human germline sequence to optimize the antibody (*e.g.*, by a process referred to as germlining).

[0433] Generally, an optimized antibody has at least the same, or substantially the same, affinity for the antigen as the non-optimized (or parental) antibody from which it was derived. Preferably, an optimized antibody has a higher affinity for the antigen when compared to the parental antibody.

[0434] If the antibody is for use as a therapeutic, it can be conjugated to an effector agent such as a small molecule toxin or a radionuclide using standard *in vitro* conjugation chemistries. If the effector agent is a polypeptide, the antibody can be chemically conjugated to the effector or joined to the effector as a fusion protein. Construction of fusion proteins is within ordinary skill in the art.

[0435] The antibody can be conjugated to an effector moiety such as a small molecule toxin or a radionuclide using standard *in vitro* conjugation chemistries. If the effector moiety is a polypeptide, the antibody can be chemically conjugated to the effector or joined to the effector as a fusion protein. Construction of fusion proteins is within ordinary skill in the art.

[0436] In certain embodiments, the protein (*e.g.*, multi-specific binding protein) of the present disclosure is not substantially internalized by a CD33-expressing cell. A low level of

internalization may improve the pharmacokinetics of the protein, thereby reducing the dose required to engage CD33-expressing target cells with effector cells (*e.g.*, NK cells). Internalization can be measured by any method known in the art, *e.g.*, the methods described in Examples 5 and 10 of the present disclosure. For example, in certain embodiments, internalization of the protein (*e.g.*, multi-specific binding protein) by EOL-1 cells is lower than 25%, 30%, 35%, 40%, 45%, or 50% after a two-hour incubation, as assessed by the methods disclosed herein. In certain embodiments, internalization of the protein (*e.g.*, multi-specific binding protein) by EOL-1 cells is lower than 25%, 30%, 35%, 40%, 45%, or 50% after a 24-hour incubation, as assessed by the methods disclosed herein. In certain embodiments, internalization of the protein (*e.g.*, multi-specific binding protein) by Molm-13 cells is lower than 25%, 30%, 35%, 40%, 45%, or 50% after a two-hour incubation, as assessed by the methods disclosed herein.

[0437] KHYG-1 cells express surface NKG2D, but do not express CD16. In certain embodiments, TriNKET mediated killings of Molm-13 and THP-1 cells are dependent upon NKG2D-mediated activation of the KHYG-1 effector cells. In certain embodiments, TriNKETs of the present disclosure mediate KHYG-1 effector cell killing of Molm-13 (FIG. 15A), EOL-1 (FIG. 16), and THP-1 (FIG. 17A) human AML target cell lines.

[0438] In certain embodiments, TriNKETs of the present disclosure mediate cytotoxicity of rested human NK cells against Molm-13 or THP-1 human AML cells. FIG. 15B and 38A show that TriNKETs of the present disclosure mediate rested human NK cell killing of Molm-13 human AML cells. The rested human NK effector cell (E) to target cancer cell (T) ratio (E:T) was 10:1 in FIG. 15B and 5:1 in FIG. 38A. The E:T ratio may reflect differences in the maximal % lysis.

[0439] In certain embodiments, TriNKETs of the present disclosure mediate rested human NK cell killing of EOL-1 human AML cells. FIG. 38B shows that TriNKETs mediate rested human NK cell killing of EOL-1 cells at an E:T of 5:1. In certain embodiments, TriNKETs of the present disclosure mediate rested human NK cell killing of THP-1 target cells, which express the high-affinity FcγRI. FIGs. 17B, 38C, and 38D show that TriNKETs mediate rested human NK cell killing of THP-1 human AML cells using an E:T of 5:1.

[0440] In certain embodiments, TriNKETs of the present disclosure mediate human $CD8^+$ T cell killing of Molm-13 target cells. FIGs. 40A-40B show that TriNKETs mediate human $CD8^+$ T cell killing of Molm-13 cells at an E:T of 50:1.

A protein comprising an antigen-binding site that competes with the CD33-binding sites described herein

[0441] In one aspect, the present invention provides a protein that includes an antigen-binding site that competes with the CD33-binding sites described herein to bind to CD33. In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:1 and an antibody light chain having the amino acid sequence of SEQ ID NO:2.

[0442] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:3 and an antibody light chain having the amino acid sequence of SEQ ID NO:4.

[0443] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:5 and an antibody light chain having the amino acid sequence of SEQ ID NO:6.

[0444] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:7 and an antibody light chain having the amino acid sequence of SEQ ID NO:8.

[0445] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:9 and an antibody light chain having the amino acid sequence of SEQ ID NO:10.

[0446] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:11 and an antibody light chain having the amino acid sequence of SEQ ID NO:12.

[0447] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:13 and an antibody light chain having the amino acid sequence of SEQ ID NO:14.

[0448] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an

antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:15 and an antibody light chain having the amino acid sequence of SEQ ID NO:16.

[0449] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:17 and an antibody light chain having the amino acid sequence of SEQ ID NO:18.

[0450] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody heavy chain having the amino acid sequence of SEQ ID NO:19 and an antibody light chain having the amino acid sequence of SEQ ID NO:20.

[0451] In some embodiments, an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:2. In some embodiments, an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:4.

[0452] In some embodiments, an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6.

[0453] In some embodiments, an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7 and a

light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8.

[0454] In some embodiments an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:10.

[0455] In some embodiments an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:12.

[0456] In some embodiments an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14.

[0457] In some embodiments an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:16.

[0458] In some embodiments an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%,

96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:18.

[0459] In some embodiments an antigen-binding site of the protein that competes with the CD33-binding sites includes a heavy chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19 and a light chain variable domain having an amino acid sequence at least at least 50% (*e.g.*, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:20.

[0460] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antigen-binding site that binds a tumor-associated antigen.

[0461] In certain embodiments, the present invention provides a protein that includes an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody that includes an antibody constant region or a portion thereof capable of binding CD16.

CAR T cells, CD33/CD3-directed bispecific T-cell engagers, immunocytokines, antibody-drug conjugates, and immunotoxins

[0462] Another aspect of the present invention provides a molecule or complex comprising an antigen-binding site that binds CD33 as disclosed herein. Exemplary molecules or complexes include but are not limited to chimeric antigen receptors (CARs), T-cell engagers (*e.g.*, CD33/CD3-directed bispecific T-cell engagers), immunocytokines, antibody-drug conjugates, and immunotoxins.

[0463] Any antigen-binding site that binds CD33 as disclosed herein can be used, including but not limited to the antigen-binding site that binds CD33 as disclosed in Section I. Antigen-Binding Site. In certain embodiments, the amino acid sequence(s) of the antigen-binding site that binds CD33 are provided in Table 1. In certain embodiments, the antigen-binding site that binds CD33 is an scFv. In certain embodiments, the scFv comprises an amino acid sequence at least 90% (*e.g.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID

NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484. In certain embodiments, the scFv comprises an amino acid sequence selected from SEQ ID NO:188, SEQ ID NO:198, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:447, SEQ ID NO:448, SEQ ID NO:449, SEQ ID NO:450, SEQ ID NO:451, SEQ ID NO:452, SEQ ID NO:453, SEQ ID NO:454, SEQ ID NO:455, SEQ ID NO:456, SEQ ID NO:457, SEQ ID NO:458, SEQ ID NO:459, SEQ ID NO:460, SEQ ID NO:461, SEQ ID NO:462, SEQ ID NO:463, SEQ ID NO:464, SEQ ID NO:465, SEQ ID NO:466, SEQ ID NO:467, SEQ ID NO:468, SEQ ID NO:469, SEQ ID NO:470, SEQ ID NO:471, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, and SEQ ID NO:484.

[0464] In certain embodiments, the antigen-binding site that binds CD33 comprises a heavy chain variable domain comprising CDR1, CDR2, and CDR3 sequences represented by the amino acid sequences of SEQ ID NOs:181, 46, and 182, respectively; and a light chain variable domain comprising CDR1, CDR2, and CDR3 sequences represented by the amino acid sequences of SEQ ID NOs:48, 49, and 50, respectively. In certain embodiments, the antigen-binding site comprises a heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9; and a light chain variable domain with an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:10. In certain embodiments, the antigen-

binding site comprises an scFv comprising 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:188.

[0465] In other embodiments of any one of the foregoing aspects in this subsection, the antigen-binding site that binds CD33 comprises a heavy chain variable domain comprising CDR1, CDR2, and CDR3 sequences represented by the amino acid sequences of SEQ ID NOs:183, 34, and 184, respectively; and a light chain variable domain comprising CDR1, CDR2, and CDR3 sequences represented by the amino acid sequences of SEQ ID NOs:36, 185, and 38, respectively. In certain embodiments, the antigen-binding site comprises a heavy chain variable domain with an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5; and a light chain variable domain with an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6. In certain embodiments, the antigen-binding site comprises an scFv comprising 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:198.

Chimeric antigen receptors (CARs)

[0466] In certain embodiments, the present invention provides a CD33-targeting CAR comprising an antigen-binding site that binds CD33 as disclosed herein (*see, e.g.,* Table 1). The CD33-targeting CAR can comprise an Fab fragment or an scFv.

[0467] The term "chimeric antigen receptor" or alternatively a "CAR" refers to a recombinant polypeptide construct comprising at least an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a stimulatory molecule (also referred to herein as a "primary signaling domain").

[0468] Accordingly, in certain embodiments, the CAR comprises an extracellular antigen-binding site that binds CD33 as disclosed herein, a transmembrane domain, and an intracellular signaling domain comprising a primary signaling domain. In certain embodiments, the CAR further comprises one or more functional signaling domains derived from at least one costimulatory molecule (also referred to as a "costimulatory signaling domain").

[0469] In one embodiment, the CAR comprises a chimeric fusion protein comprising a CD33-binding domain (*e.g.*, CD33-binding scFv domain) comprising CDR1, CDR2, and CDR3 of a heavy chain variable domain and CDR1, CDR2, and CDR3 of a light chain

variable domain listed in Table 1 as an extracellular antigen binding domain, a transmembrane domain, and an intracellular signaling domain comprising a primary signaling domain. In one embodiment, the CAR comprises a chimeric fusion protein comprising a CD33-binding domain (*e.g.*, CD33-binding scFv domain) comprising CDR1, CDR2, and CDR3 of a heavy chain variable domain and CDR1, CDR2, and CDR3 of a light chain variable domain listed in Table 1 as an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising a costimulatory signaling domain and a primary signaling domain. In one aspect, the CAR comprises a chimeric fusion protein comprising a CD33-binding domain (*e.g.*, CD33-binding scFv domain) comprising CDR1, CDR2, and CDR3 of a heavy chain variable domain and CDR1, CDR2, and CDR3 of a light chain variable domain listed in Table 1 as an extracellular antigen binding domain, a transmembrane domain, and an intracellular signaling domain comprising two costimulatory signaling domains and a primary signaling domain. In one embodiment, the CAR comprises a chimeric fusion protein comprising a CD33-binding domain comprising CDR1, CDR2, and CDR3 of a heavy chain variable domain and CDR1, CDR2, and CDR3 of a light chain variable domain listed in Table 1 as an extracellular antigen binding domain, a transmembrane domain, and an intracellular signaling domain comprising at least two costimulatory signaling domains and a primary signaling domain.

[0470] For example, in certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 434, 22, and 435, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 24, 25, and 26, respectively. In certain embodiments, the heavy chain variable domain comprises 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 the light chain variable domain comprises 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:2. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:206 or SEQ ID NO:207.

[0471] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 181, 28, and 436, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively. In certain

embodiments, the heavy chain variable domain comprises 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:3, and the light chain variable domain comprises 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:4. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:208 or SEQ ID NO:209.

[0472] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 183, 34, and 184, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 36, 37, and 38, respectively. In certain embodiments, the heavy chain variable domain comprises 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:5, and the light chain variable domain comprises 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:6. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:198 or SEQ ID NO:210.

[0473] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 437, 40, and 438, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 42, 43, and 44, respectively. In certain embodiments, the heavy chain variable domain comprises 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:7, and the light chain variable domain comprises 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:8. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:211 or SEQ ID NO:212.

[0474] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 181, 46, and 182, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 48, 49, and 50, respectively. In certain embodiments, the heavy chain variable domain comprises 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:9, and the light chain variable domain comprises 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:10. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:188 or SEQ ID NO:213.

[0475] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 181, 52, and 439, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 54, 55, and 56, respectively. In certain embodiments, the heavy chain variable domain comprises 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:11, and the light chain variable domain comprises 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:12. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:214 or SEQ ID NO:215.

[0476] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 440, 58, and 441, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 60, 61, and 62, respectively. In certain embodiments, the heavy chain variable domain comprises 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:13, and the light chain variable domain comprises 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:14. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:216 or SEQ ID NO:217.

[0477] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 442, 64, and 443, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 66, 67, and 68, respectively. In certain embodiments, the heavy chain variable domain comprises 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:15, and the light chain variable domain comprises 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:16. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:218 or SEQ ID NO:219.

[0478] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 181, 70, and 444, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 72, 73, and 74, respectively. In certain embodiments, the heavy chain variable domain comprises 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:17, and the light chain variable domain comprises 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:18. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:220 or SEQ ID NO:221.

[0479] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 445, 76, and 446, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 78, 79, and 80, respectively. In certain embodiments, the heavy chain variable domain comprises 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:19, and the light chain variable domain comprises 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:20. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:222 or SEQ ID NO:223.

[0480] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 528, 305, and 529, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 307, 308, and 309, respectively. In certain embodiments, the heavy chain variable domain comprises 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:266, and the light chain variable domain comprises 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:267. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:447 or SEQ ID NO:448.

[0481] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 530, 311, and 531, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 313, 314, and 315, respectively. In certain embodiments, the heavy chain variable domain comprises 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:268, and the light chain variable domain comprises 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:269. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:449 or SEQ ID NO:450.

[0482] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 532, 317, and 533, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 319, 320, and 321, respectively. In certain embodiments, the heavy chain variable domain comprises 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:270, and the light chain variable domain comprises 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:271. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:451 or SEQ ID NO:452.

[0483] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 534, 323, and 535, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 325, 326, and 327, respectively. In certain embodiments, the heavy chain variable domain comprises 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:272, and the light chain variable domain comprises 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:273. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:453 or SEQ ID NO:454.

[0484] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 536, 329, and 537, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 331, 332, and 333, respectively. In certain embodiments, the heavy chain variable domain comprises 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:274, and the light chain variable domain comprises 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:275. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:455 or SEQ ID NO:456.

[0485] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 538, 335, and 539, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 337, 338, and 339, respectively. In certain embodiments, the heavy chain variable domain comprises 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:276, and the light chain variable domain comprises 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:277. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:457 or SEQ ID NO:458.

[0486] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 540, 341, and 541, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 343, 344, and 345, respectively. In certain embodiments, the heavy chain variable domain comprises 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:278, and the light chain variable domain comprises 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:279. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:459 or SEQ ID NO:460.

[0487] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 542, 347, and 543, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 349, 350, and 351, respectively. In certain embodiments, the heavy chain variable domain comprises 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:280, and the light chain variable domain comprises 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:281. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:461 or SEQ ID NO:462.

[0488] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 544, 353, and 545, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 355, 356, and 357, respectively. In certain embodiments, the heavy chain variable domain comprises 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:282, and the light chain variable domain comprises 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:283. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:463 or SEQ ID NO:464.

[0489] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 546, 359, and 547, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 361, 362, and 363, respectively. In certain embodiments, the heavy chain variable domain comprises 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:284, and the light chain variable domain comprises 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:285. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:465 or SEQ ID NO:466.

[0490] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 548, 365, and 549, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 367, 368, and 369, respectively. In certain embodiments, the heavy chain variable domain comprises 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:286, and the light chain variable domain comprises 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:287. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:467 or SEQ ID NO:468.

[0491] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 550, 371, and 551, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 373, 374, and 375, respectively. In certain embodiments, the heavy chain variable domain comprises 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:288, and the light chain variable domain comprises 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:289. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:469 or SEQ ID NO:470.

[0492] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 552, 377, and 553, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 379, 380, and 381, respectively. In certain embodiments, the heavy chain variable domain comprises 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:290, and the light chain variable domain comprises 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:291. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:471 or SEQ ID NO:472.

[0493] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 554, 383, and 555, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 385, 386, and 387, respectively. In certain embodiments, the heavy chain variable domain comprises 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:292, and the light chain variable domain comprises 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:293. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:473 or SEQ ID NO:474.

[0494] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 556, 389, and 557, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 391, 392, and 393, respectively. In certain embodiments, the heavy chain variable domain comprises 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:294, and the light chain variable domain comprises 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:295. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:475 or SEQ ID NO:476.

[0495] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 558, 395, and 559, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 397, 398, and 399, respectively. In certain embodiments, the heavy chain variable domain comprises 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:296, and the light chain variable domain comprises 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:297. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:477 or SEQ ID NO:478.

[0496] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 560, 401, and 561, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 403, 404, and 405, respectively. In certain embodiments, the heavy chain variable domain comprises 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:298, and the light chain variable domain comprises 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:299. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:479 or SEQ ID NO:480.

[0497] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 562, 407, and 563, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 409, 410, and 411, respectively. In certain embodiments, the heavy chain variable domain comprises 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:300, and the light chain variable domain comprises 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:301. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:481 or SEQ ID NO:482.

[0498] In certain embodiments, the extracellular antigen binding domain comprises an antigen-binding site (*e.g.*, an scFv) comprising a heavy chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 564, 413, and 565, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 having the amino acid sequences of SEQ ID NOs: 415, 416, and 417, respectively. In certain embodiments, the heavy chain variable domain comprises 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:302, and the light chain variable domain comprises 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:303. In certain embodiments, the extracellular antigen binding domain comprises an scFv having the amino acid sequence of SEQ ID NO:483 or SEQ ID NO:484.

[0499] With respect to the transmembrane domain, in various embodiments, the CAR is designed to comprise a transmembrane domain that is fused to the extracellular domain of the CAR. In one embodiment, the transmembrane domain is one that naturally is associated with one of the domains in the CAR. In some instances, the transmembrane domain can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins to minimize interactions with other members of the receptor complex. In another embodiment, the transmembrane domain is capable of homodimerization with another CAR on the CAR T cell surface. In another embodiment, the amino acid sequence of the transmembrane domain may be modified or substituted so as to minimize interactions with the binding domains of the native binding partner present in the same CAR T cell.

[0500] The transmembrane domain may be derived from any naturally occurring membrane-bound or transmembrane protein. In one embodiment, the transmembrane region is capable of signaling to the intracellular domain(s) whenever the CAR has bound to a target. In some embodiments, the transmembrane domain comprises the transmembrane region(s) of one or more proteins selected from the group consisting of TCR α chain, TCR β chain, TCR ζ chain, CD28, CD3ε, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, and CD154. In some embodiments, the transmembrane domain comprises the transmembrane region(s) of one or more proteins selected from the group consisting of KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, IL2Rβ, IL2Rγ, IL7Rα, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKG2D, and NKG2C.

[0501] The extracellular CD33-binding domain (*e.g.*, CD33-binding scFv domain) domain can be connected to the transmembrane domain by a hinge region. A variety of hinges can be employed, including but not limited to the human Ig (immunoglobulin) hinge

(*e.g.*, an IgG4 hinge, an IgD hinge), a Gly-Ser linker, a $(G_4S)_4$ linker, a KIR2DS2 hinge, and a CD8α hinge.

[0502] The intracellular signaling domain of the CAR of the invention is responsible for activation of at least one of the specialized functions of the immune cell (*e.g.*, cytolytic activity or helper activity, including the secretion of cytokines, of a T cell) in which the CAR has been placed in. Thus, as used herein, the term "intracellular signaling domain" refers to the portion of a protein which transduces an effector function signal and directs the cell to perform a specialized function. While usually the entire intracellular signaling domain can be employed, in many cases it is not necessary to use the entire chain. To the extent that a truncated portion of the intracellular signaling domain is used, such truncated portion may be used in place of the intact chain as long as it transduces the effector function signal. The term intracellular signaling domain is thus meant to include any truncated portion of the intracellular signaling domain sufficient to transduce the effector function signal.

[0503] The intracellular signaling domain of the CAR comprises a primary signaling domain (*i.e.*, a functional signaling domain derived from a stimulatory molecule) and one or more costimulatory signaling domains (*i.e.*, functional signaling domains derived from at least one costimulatory molecule).

[0504] As used herein, the term "stimulatory molecule" refers to a molecule expressed by an immune cell, *e.g.*, a T cell, an NK cell, or a B cell, that provide the cytoplasmic signaling sequence(s) that regulate activation of the immune cell in a stimulatory way for at least some aspect of the immune cell signaling pathway. In one embodiment, the signal is a primary signal that is initiated by, for instance, binding of a TCR/CD3 complex with an MHC molecule loaded with a peptide, and which leads to mediation of a T cell response, including, but not limited to, proliferation, activation, differentiation, and the like.

[0505] Primary signaling domains that act in a stimulatory manner may contain signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs. Examples of ITAM containing cytoplasmic signaling sequences that are of particular use in the invention include those derived from CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12. In one embodiment, the primary signaling domain in any one or more CARs of the invention comprises a cytoplasmic signaling sequence derived from CD3-zeta.

[0506] In some embodiments, the primary signaling domain is a functional signaling domain of TCR zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta, CD3 epsilon, CD5,

CD22, CD79a, CD79b, CD66d, 4-1BB, and/or CD3-zeta. In an embodiment, the intracellular signaling domain comprises a functional signaling domain of CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and/or DAP12. In a particular embodiment, the primary signaling domain is a functional signaling domain of the zeta chain associated with the T cell receptor complex.

[0507] As used herein, the term "costimulatory molecule" refers to a cognate binding partner on a T cell that specifically binds with a costimulatory ligand, thereby mediating a costimulatory response by the T cell, such as, but not limited to, proliferation. A costimulatory molecule is a cell surface molecule other than an antigen receptor or its ligands that is required for an efficient response of lymphocytes to an antigen. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1, CD11a/CD18), CD2, CD7, CD258 (LIGHT), NKG2C, B7-H3, and a ligand that specifically binds with CD83, and the like. Further examples of such costimulatory molecules include CD5, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, and a ligand that specifically binds with CD83. In some embodiments, the costimulatory signaling domain of the CAR is a functional signaling domain of a costimulatory molecule described herein, e.g., OX40, CD27, CD28, CD30, CD40, PD-1, CD2, CD7, CD258, NKG2C, B7-H3, a ligand that binds to CD83, ICAM-1, LFA-1 (CD11a/CD18), ICOS and 4-1BB (CD137), or any combination thereof.

[0508] As used herein, the term "signaling domain" refers to the functional portion of a protein which acts by transmitting information within the cell to regulate cellular activity via defined signaling pathways by generating second messengers or functioning as effectors by responding to such messengers.

[0509] The cytoplasmic signaling sequences within the cytoplasmic signaling portion of the CAR of the invention may be linked to each other in a random or specified order.

Optionally, a short oligo- or polypeptide linker, for example, between 2 and 10 amino acids in length may form the linkage.

[0510] Another aspect of the present invention provides a nucleic acid encoding a CD33-targeting CAR disclosed herein. The nucleic acid is useful for expressing the CAR in an effector cell (*e.g.*, T cell) by introducing the nucleic acid to the cell.

[0511] Exemplary nucleic acid sequences encoding the extracellular portions of the CARs are disclosed herein, *e.g.*, as SEQ ID NOs:246-265. Modifications may be made in the sequence to create an equivalent or improved variant of the invention, for example, by changing one or more of the codons according to the codon degeneracy table. A DNA codon degeneracy table is provided in Table 10.

Table 10. Amino Acid Codons

Amino Acids	One letter code	Three letter code	Codons
Alanine	A	Ala	GCA GCC GCG GCU
Cysteine	C	Cys	UGC UGU
Aspartic acid	D	Asp	GAC GAU
Glutamic acid	E	Glu	GAA GAG
Phenylalanine	F	Phe	UUC UUU
Glycine	G	Gly	GGA GGC GGG GGU
Histidine	H	His	CAC CAU
Isoleucine	I	Iso	AUA AUC AUU
Lysine	K	Lys	AAA AAG
Leucine	L	Leu	UUA UUG CUA CUC CUG CUU
Methionine	M	Met	AUG
Asparagine	N	Asn	AAC AAU
Proline	P	Pro	CCA CCC CCG CCU
Glutamine	Q	Gln	CAA CAG
Arginine	R	Arg	AGA AGG CGA CGC CGG CGU
Serine	S	Ser	AGC AGU UCA UCC UCG UCU
Threonine	T	Thr	ACA ACC ACG ACU
Valine	V	Val	GUA GUC GUG GUU
Tryptophan	W	Trp	UGG
Tyrosine	Y	Tyr	UAC UAU

[0512] In certain embodiments, the nucleic acid is a DNA molecule (*e.g.*, a cDNA molecule). In certain embodiments, the nucleic acid further comprises an expression control sequence (*e.g.*, promoter and/or enhancer) operably linked to the CAR coding sequence. In certain embodiments, the present invention provides a vector comprising the nucleic acid.

The vector can be a viral vector (*e.g.*, AAV vector, lentiviral vector, or adenoviral vector) or a non-viral vector (*e.g.*, plasmid).

[0513] In certain embodiments, the nucleic acid is an RNA molecule (*e.g.*, an mRNA molecule). A method for generating mRNA for use in transfection can involve *in vitro* transcription of a template with specially designed primers, followed by polyA addition, to produce an RNA construct containing 3' and 5' untranslated sequences, a 5' cap and/or Internal Ribosome Entry Site (IRES), the nucleic acid to be expressed, and a polyA tail, typically 50-2000 bases in length. The RNA molecule can be further modified to increase translational efficiency and/or stability, *e.g.*, as disclosed in U.S. Patent Nos. 8,278,036; 8,883,506, and 8,716,465. RNA molecules so produced can efficiently transfect different kinds of cells.

[0514] In one embodiment, the nucleic acid encodes an amino acid sequence comprising a signal peptide at the amino-terminus of the CAR. Such signal peptide can facilitate the cell surface localization of the CAR when it is expressed in an effector cell, and is cleaved from the CAR during cellular processing. In one embodiment, the nucleic acid encodes an amino acid sequence comprising a signal peptide at the N-terminus of the extracellular CD33-binding domain (*e.g.*, CD33-binding scFv domain).

[0515] RNA or DNA can be introduced into target cells using any of a number of different methods, for instance, commercially available methods which include, but are not limited to, electroporation, cationic liposome mediated transfection using lipofection, polymer encapsulation, peptide mediated transfection, or biolistic particle delivery systems such as "gene guns" (see, for example, Nishikawa, et al. Hum Gene Ther., 12(8):861-70 (2001)).

[0516] Another aspect of the present invention provides an immune effector cell expressing the CD33-targeting CAR. Also provided is an immune effector cell comprising the nucleic acid encoding the CD33-targeting CAR. The immune effector cells include but are not limited to T cells and NK cells. In certain embodiments, the T cell is selected from a $CD8^+$ T cell, a $CD4^+$ T cell, and an NKT cell. The T cell or NK cell can be a primary cell or a cell line.

[0517] The immune effector cells can be obtained from a number of sources, including peripheral blood mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors, by methods known in the art. The immune effector cells can also be differentiated *in vitro* from a pluripotent or multipotent cell (*e.g.*, a hematopoietic stem cell). In some embodiments, the

present invention provides a pluripotent or multipotent cell (*e.g.*, a hematopoietic stem cell) expressing the CD33-targeting CAR or comprising a nucleic acid disclosed herein.

[0518] In certain embodiments, the immune effector cells are isolated and/or purified. For example, regulatory T cells can be removed from a T cell population using a CD25-binding ligand. Effector cells expressing a checkpoint protein (*e.g.*, PD-1, LAG-3, or TIM-3) can be removed by similar methods. In certain embodiments, the effector cells are isolated by a positive selection step. For example, a population of T cells can be isolated by incubation with anti-CD3/anti-CD28-conjugated beads. Other cell surface markers, such as IFN-7, TNF-α, IL-17A, IL-2, IL-3, IL-4, GM-CSF, IL-10, IL-13, granzyme B, and perforin, can also be used for positive selection.

[0519] Immune effector cells may be activated and expanded generally using methods known in the art, *e.g.*, as described in U.S. Patent Nos. 6,352,694; 6,534,055; 6,905,680; 6,692,964; 5,858,358; 6,887,466; 6,905,681; 7,144,575; 7,067,318; 7,172,869; 7,232,566; 7,175,843; 5,883,223; 6,905,874; 6,797,514; 6,867,041; and U.S. Patent Application Publications Nos. 2006/0121005 and 2016/0340406. For example, in certain embodiments, T cells can be expanded and/or activated by contact with an anti-CD3 antibody and an anti-CD28 antibody, under conditions appropriate for stimulating proliferation of the T cells. The cells can be expanded in culture for a period of several hours (*e.g.*, about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21 hours) to about 14 days (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days). In one embodiment, the cells are expanded for a period of 4 to 9 days. Multiple cycles of stimulation may be desirable for prolonged cell culture (*e.g.*, culture for a period of 60 days or more). In certain embodiments, the cell culture comprises serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, TGFβ, TNF-α, or a combination thereof. Other additives for the growth of cells known to the skilled person, *e.g.*, surfactant, plasmanate, and reducing agents such as N-acetyl-cysteine and 2-mercaptoethanol, can also be included in the cell culture. In certain embodiments, the immune effector cell of the present invention is a cell obtained from *in vitro* expansion.

[0520] Further embodiments of the CD33-targeting CAR (*e.g.*, regulatable CAR), nucleic acid encoding the CAR, and effector cells expressing the CAR or comprising the nucleic acid are provided in U.S. Patent Nos. 7,446,190 and 9,181,527, U.S. Patent Application Publication Nos. 2016/0340406 and 2017/0049819, and International Patent Application Publication No. WO2018/140725.

CD33/CD3-directed bispecific T-cell engagers

[0521] In certain embodiments, the present invention provides a CD33/CD3-directed bispecific T-cell engager comprising an antigen-binding site that binds CD33 disclosed herein. In certain embodiments, the CD33/CD3-directed bispecific T-cell engager comprises 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:187. In certain embodiments, the CD33/CD3-directed bispecific T-cell engager comprises 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:197.

[0522] In certain embodiments, the CD33/CD3-directed bispecific T-cell engager further comprises an antigen-binding site that binds CD3. Exemplary antigen-binding sites that bind CD3 are disclosed in International Patent Application Publication Nos. WO2014/051433 and WO2017/097723.

[0523] Another aspect of the present invention provides a nucleic acid encoding at least one polypeptide of the CD33/CD3-directed bispecific T-cell engager, wherein the polypeptide comprises an antigen binding site that binds CD33. In certain embodiments, the nucleic acid further comprises a nucleotide sequence encoding a signal peptide that, when expressed, is at the N-terminus of one or more of the polypeptides of the CD33/CD3-directed bispecific T-cell engager. Also provided is a vector (*e.g.*, a viral vector) comprising the nucleic acid, a producer cell comprising the nucleic acid or vector, and a producer cell expressing the CD33/CD3-directed bispecific T-cell engager.

Immunocytokines

[0524] In certain embodiments, the present invention provides an immunocytokine comprising an antigen-binding site that binds CD33 disclosed herein and a cytokine. Any cytokine (*e.g.*, pro-inflammatory cytokines) known in the art can be used, including but not limited to IL-2, IL-4, IL-10, IL-12, IL-15, TNF, IFNα, IFNγ, and GM-CSF. More exemplary cytokines are disclosed in U.S. Patent No. 9,567,399. In certain embodiments, the antigen-binding site is connected to the cytokine by chemical conjugation (*e.g.*, covalent or noncovalent chemical conjugation). In certain embodiments, the antigen-binding site is connected to the cytokine by fusion of polypeptide. The immunocytokine can further comprise an Fc domain connected to the antigen-binding site that binds CD33. In certain embodiments, the immunocytokine comprises 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:187. In certain embodiments, the immunocytokine comprises 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:197. In certain embodiments, the cytokine is connected to the Fc domain directly or via a linker.

[0525] Another aspect of the present invention provides a nucleic acid encoding at least one polypeptide of the immunocytokine, wherein the polypeptide comprises an antigen binding site that binds CD33. In certain embodiments, the nucleic acid further comprises a nucleotide sequence encoding a signal peptide that, when expressed, is at the N-terminus of one or more of the polypeptides of the immunocytokine. Also provided is a vector (*e.g.*, a viral vector) comprising the nucleic acid, a producer cell comprising the nucleic acid or vector, and a producer cell expressing the immunocytokine.

Antibody-drug conjugates

[0526] In certain embodiments, the present invention provides an antibody-drug conjugate comprising an antigen-binding site that binds CD33 disclosed herein and a cytotoxic drug moiety. Exemplary cytotoxic drug moieties are disclosed in International Patent Application Publication Nos. WO2014/160160 and WO2015/143382. In certain embodiments, the cytotoxic drug moiety is selected from auristatin, N-acetyl-γ calicheamicin, maytansinoid, pyrrolobenzodiazepine, and SN-38. The antigen-binding site can be connected to the cytotoxic drug moiety by chemical conjugation (*e.g.*, covalent or noncovalent chemical conjugation). In certain embodiments, the antibody-drug conjugate further comprises an Fc domain connected to the antigen-binding site that binds CD33. In certain embodiments, the antibody-drug conjugate comprises 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:187. In certain embodiments, the antibody-drug conjugate comprises 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:197. In certain embodiments, the cytotoxic drug moiety is connected to the Fc domain directly or via a linker.

Immunotoxins

[0527] In certain embodiments, the present invention provides an immunotoxin comprising an antigen-binding site that binds CD33 disclosed herein and a cytotoxic peptide moiety. Any cytotoxic peptide moiety known in the art can be used, including but not limited to ricin, *Diphtheria* toxin, and *Pseudomonas* exotoxin A. More exemplary cytotoxic peptides are disclosed in International Patent Application Publication Nos. WO2012/154530 and

WO2014/164680. In certain embodiments, the cytotoxic peptide moiety is connected to the protein by chemical conjugation (*e.g.*, covalent or noncovalent chemical conjugation). In certain embodiments, the cytotoxic peptide moiety is connected to the protein by fusion of polypeptide. The immunotoxin can further comprise an Fc domain connected to the antigen-binding site that binds CD33. In certain embodiments, the immunotoxin comprises 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:187. In certain embodiments, the immunotoxin comprises 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:197. In certain embodiments, the cytotoxic peptide moiety is connected to the Fc domain directly or via a linker.

[0528] Another aspect of the present invention provides a nucleic acid encoding at least one polypeptide of the immunotoxin, wherein the polypeptide comprises an antigen binding site that binds CD33. In certain embodiments, the nucleic acid further comprises a nucleotide sequence encoding a signal peptide that, when expressed, is at the N-terminus of one or more of the polypeptides of the immunotoxin. Also provided is a vector (*e.g.*, a viral vector) comprising the nucleic acid, a producer cell comprising the nucleic acid or vector, and a producer cell expressing the immunotoxin.

III. Therapeutic Compositions and Their Use

[0529] 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 CD33 by administering to a patient in need thereof a therapeutically effective amount of a multi-specific binding protein described herein.

[0530] The therapeutic method can be characterized according to the cancer to be treated. For example, in certain embodiments, the cancers are AML, myelodysplastic syndromes, chronic myelomonocytic leukemia, myeloid blast crisis of chronic myeloid leukemia, and ALLs.

[0531] For example, in certain embodiments, the cancer is a solid tumor. In certain other embodiments, the cancer is brain cancer, bladder cancer, breast cancer, cervical cancer, colon cancer, colorectal cancer, endometrial cancer, esophageal cancer, leukemia, lung cancer, liver cancer, melanoma, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, renal 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.

[0532] 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.

[0533] 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 CD33: 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.

[0534] In embodiments of the present invention, the cancer to be treated is selected from acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), acute lymphoblastic leukemia (ALL), myeloproliferative neoplasms (MPNs), lymphoma, non-Hodgkin lymphomas, and classical Hodgkin lymphoma.

[0535] In some embodiments of the present invention, the cancer to be treated is AML. In some embodiments of the present invention, the AML is selected from undifferentiated acute myeloblastic leukemia, acute myeloblastic leukemia with minimal maturation, acute myeloblastic leukemia with maturation, acute promyelocytic leukemia (APL), acute myelomonocytic leukemia, acute myelomonocytic leukemia with eosinophilia, acute monocytic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia (AMKL), acute basophilic leukemia, acute panmyelosis with fibrosis, and blastic plasmacytoid dendritic cell neoplasm (BPDCN). In some embodiments of the present invention, the AML

is characterized by expression of CLL-1 on the AML leukemia stem cells (LSCs). In some embodiments of the present invention, the LSCs in an AML subject further express a membrane marker selected from CD34, CD38, CD123, TIM3, CD25, CD32, and CD96. In some embodiments of the present invention, the AML is characterized as a minimal residual disease (MRD). In some embodiments of the present invention, the MRD of AML is characterized by the presence or absence of a mutation selected from *FLT3-ITD* ((Fms-like tyrosine kinase 3)-internal tandem duplications (ITD)), *NPM1* (Nucleophosmin 1), *DNMT3A* (DNA methyltransferase gene *DNMT3A)*, and *IDH* (Isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2)).

[0536] In certain embodiments of the present invention, the cancer is MDS selected from MDS with multilineage dysplasia (MDS-MLD), MDS with single lineage dysplasia (MDS-SLD), MDS with ring sideroblasts (MDS-RS), MDS with excess blasts (MDS-EB), MDS with isolated del(5q), and MDS, unclassified (MDS-U).

[0537] It is contemplated that the multi-specific binding proteins and/or pharmaceutical compositions of the present disclosure can be used to treat a variety of cancers, not limited to cancers in which the cancer cells express CD33. For example, in certain embodiments, the multi-specific binding proteins and/or pharmaceutical compositions disclosed herein can be used to treat cancers that are associated with CD33-expressing immune cells. CD33 is expressed on many myeloid lineages, and tumor-infiltrating myeloid cells (*e.g.*, tumor-associated macrophages) may contribute to cancer progression and metastasis. Therefore, the methods disclosed herein may be used to treat a variety of cancers in which CD33 is expressed, whether on cancer cells or on immune cells.

[0538] In certain embodiments, the multi-specific binding proteins and/or pharmaceutical compositions of the present disclosure can be used to treat cancers that express an Fc receptor with a higher binding affinity to Fc (*e.g.*, IgG1 Fc) than CD16. In certain embodiments, the Fc receptor is FcγRI. In certain embodiments, the Fc receptor is expressed on cancer cells and/or other cells in the tumor microenvironment.

[0539] In certain embodiments, the patient has effector cells (*e.g.*, NK cells) that express a CD16 variant with V158F substitution. In certain embodiments, the patient has a single nucleotide polymorphism (SNP) in the CD16 gene that causes V158F substitution. In certain embodiments, the patient has such an SNP in only one allele. In certain embodiments, the patient has such an SNP or SNPs in both alleles.

IV. Combination Therapy

[0540] Another aspect of the invention provides for combination therapy. Multi-specific binding proteins described herein be used in combination with additional therapeutic agents to treat the cancer.

[0541] 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, 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.

[0542] 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.

[0543] 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).

[0544] 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.

[0545] Proteins of the invention can also be used as an adjunct to surgical removal of the primary lesion.

[0546] 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

[0547] 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).

[0548] In one aspect, the present disclosure provides a formulation of a protein, which contains a CD33-binding site described herein, and a pharmaceutically acceptable carrier.

[0549] In certain embodiments, the pharmaceutical composition includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:1, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:2. In certain

embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:3, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:4. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:5, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:6. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:7, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:8. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:9, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:10. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:11, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:12. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:13, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:14. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a

heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:15, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:16. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:17, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:18. In certain embodiments, the formulation includes a protein that includes an antigen-binding site with a heavy chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:19, and a light chain variable domain having an amino acid sequence at least 90% (*e.g.*, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to the amino acid sequence of SEQ ID NO:20.

[0550] The composition can be formulated for use in a variety of drug delivery systems. One or more physiologically acceptable excipients or carriers can 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).

[0551] For example, this present disclosure could exist in an aqueous pharmaceutical formulation including a therapeutically effective amount of the protein in a buffered solution forming a formulation. Aqueous carriers can 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. In certain embodiments, an aqueous formulation is prepared including the protein disclosed herein in a pH-buffered solution. 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. 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. 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. 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.

[0552] In some embodiments, the formulation include an aqueous carrier, 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.

[0553] 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.

[0554] 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 edi., 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.

[0555] 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, which is 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.

[0556] In some 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.

[0557] 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 NH3 from a protein forming a succinimide intermediate that can undergo hydrolysis. The succinimide intermediate results in a 17 u mass decrease of the parent peptide. The subsequent hydrolysis results in an 18 u mass increase. Isolation of the succinimide intermediate is difficult due to instability under aqueous conditions. As such, deamidation is typically detectable as 1 u 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. 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.

[0558] In some embodiment, the formulation is a lyophilized formulation. In certain embodiments, the formulation is freeze-dried (lyophilized) and contained in about 12-60 vials. In certain embodiments, the formulation is 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 is 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. The formulation may be a liquid formulation. In some embodiments, a liquid formulation is stored as about 250 mg/vial to about 1000 mg/vial. In certain embodiments, the liquid formulation is stored as about 600 mg/vial. In certain embodiments, the liquid formulation is stored as about 250 mg/vial.

[0559] In some embodiments, the lyophilized formulation includes the proteins described herein 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. 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.

[0560] 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. 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.

[0561] 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.

[0562] In certain embodiments, the lyophilized protein product is 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. 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. 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).

[0563] The protein 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 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.

[0564] 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.

[0565] 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).

[0566] 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. 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.

[0567] 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.

[0568] 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.

[0569] In the application, where an element or component is said to be included in and/or selected from a list of recited elements or components, it should be understood that the element or component can be any one of the recited elements or components, or the element or component can be selected from a group consisting of two or more of the recited elements or components.

[0570] Further, it should be understood that elements and/or features of a composition or a method described herein can be combined in a variety of ways without departing from the spirit and scope of the present invention, whether explicit or implicit herein. For example, where reference is made to a particular compound, that compound can be used in various embodiments of compositions of the present invention and/or in methods of the present invention, unless otherwise understood from the context. In other words, within this application, embodiments have been described and depicted in a way that enables a clear and concise application to be written and drawn, but it is intended and will be appreciated that embodiments may be variously combined or separated without parting from the present teachings and invention(s). For example, it will be appreciated that all features described and depicted herein can be applicable to all aspects of the invention(s) described and depicted herein.

[0571] It should be understood that the expression “at least one of” includes individually each of the recited objects after the expression and the various combinations of two or more of the recited objects unless otherwise understood from the context and use. The expression “and/or” in connection with three or more recited objects should be understood to have the same meaning unless otherwise understood from the context.

[0572] The use of the term "include," "includes," "including," "have," "has," "having," "contain," "contains," or "containing," including grammatical equivalents thereof, should be understood generally as open-ended and non-limiting, for example, not excluding additional unrecited elements or steps, unless otherwise specifically stated or understood from the context.

[0573] Where the use of the term "about" is before a quantitative value, the present invention also includes the specific quantitative value itself, unless specifically stated otherwise. As used herein, the term "about" refers to a ±10% variation from the nominal value unless otherwise indicated or inferred.

[0574] It should be understood that the order of steps or order for performing certain actions is immaterial so long as the present invention remain operable. Moreover, two or more steps or actions may be conducted simultaneously.

[0575] The use of any and all examples, or exemplary language herein, for example, "such as" or "including," is intended merely to illustrate better the present invention and does not pose a limitation on the scope of the invention unless claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the present invention.

EXAMPLES

[0576] The following examples are merely illustrative and are not intended to limit the scope or content of the invention in any way.

Example 1. Kinetics and affinity of binding to different variants of CD33.

[0577] Kinetics and affinity of a series of Fab fragments of anti-CD33 antibodies with different CD33 variants (human CD33 ECD, cyno CD33 ECD, V-domain of human CD33, C-domain or human CD33 and selected CD33 SNPs) were assessed by surface plasmon resonance using Biacore 8K instrument (GE Healthcare). Anti-Fab antibody was immobilized on a CM5 chip using standard amine coupling chemistry. CD33 FABs were captured on the anti-Fab chip at a density of ~100 RU. Solutions containing different concentrations of soluble monomeric CD33 or its domains were injected over the captured FABs and control surfaces at 30 µl/min at 37 °C. Surfaces were regenerated between cycles by quick injection of 10 mM glycine, pH 1.8. To obtain kinetic rate constants double-referenced data were fit to a 1:1 interaction model using Biacore 8K Evaluation software (GE Healthcare). The equilibrium binding constant K_D was determined by the ratio of binding rate constants k_d/k_a.

Octet Platform-Based Kinetic and Affinity Analyis

[0578] ForteBio affinity measurements were performed on an Octet HTX generally as described in Estep *et al.*, High throughput solution-based measurement of antibody-antigen affinity and epitope binning. *Mabs* 5(2), 270-278 (2013). Briefly, ForteBio affinity measurements were performed by loading IgGs on-line onto AHC sensors. Sensors were equilibrated off-line in assay buffer for 30 min and then monitored on-line for 60 seconds for baseline establishment. Sensors with loaded IgGs were exposed to 100 nM antigen for 3 minutes, and afterwards were transferred to assay buffer for 3 min for off-rate measurement. All kinetics were analyzed using the 1:1 binding model. The results are shown in Table 11.

Table 11. Kinetic parameters of human CD33 binding to IgG antibodies measured by BLI.

IgG ADI Name	K_D (M)	k_{on} (1/M/s)	k_{off} (1/s)
ADI-10154	3.70E-09	2.46E+05	8.97E-04
ADI-10155	5.30E-09	2.29E+05	1.21E-03
ADI-10157	4.20E-09	7.99E+04	3.36E-04
ADI-10158	2.60E-09	5.86E+05	1.55E-03
ADI-10159	5.80E-10	3.48E+05	2.00E-04
ADI-10160	5.10E-09	6.38E+05	3.25E-03
ADI-10161	3.70E-09	5.87E+05	2.17E-03
ADI-10163	6.80E-09	6.65E+05	4.53E-03
ADI-10164	4.30E-09	3.44E+05	1.48E-03
ADI-10165	4.00E-09	7.79E+05	3.11E-03
ADI-10167	3.90E-09	1.00E+06	3.93E-03
ADI-10168	1.00E-08	4.76E+05	4.78E-03
ADI-10173	9.70E-09	3.24E+05	3.14E-03
ADI-10177	3.60E-09	6.01E+05	2.14E-03
ADI-11776	2.94E-10	6.79E+05	2.00E-04
ADI-11801	4.57E-10	4.38E+05	2.00E-04
ADI-11802	4.53E-10	4.41E+05	2.00E-04
ADI-11807	3.07E-10	6.51E+05	2.00E-04
ADI-11809	3.13E-10	6.38E+05	2.00E-04
ADI-11812	1.91E-09	1.66E+05	3.15E-04
ADI-11815	1.44E-09	1.59E+05	2.29E-04
ADI-11819	2.43E-10	8.24E+05	2.00E-04
ADI-11825	5.40E-10	6.96E+05	3.76E-04
ADI-11826	3.93E-10	6.19E+05	2.43E-04

IgG ADI Name	K_D (M)	k_{on} (1/M/s)	k_{off} (1/s)
ADI-11828	8.10E-10	6.58E+05	5.33E-04
ADI-11830	1.20E-09	7.70E+05	9.23E-04
ADI-11835	2.81E-10	8.44E+05	2.37E-04
ADI-11839	2.45E-09	7.04E+05	1.72E-03
Lintuzumab	2.21E-09	4.31E+05	9.52E-04

Example 2. CD33 antibodies bind to human CD33 with high affinity and cross-react with cyno CD33.

[0579] Despite rather high homology between human and cyno CD33 (87% in the ECD), most of commercially available anti-CD33 antibodies, *e.g.,* lintuzumab, mylotarg, etc. lack cross-reactivity with cyno CD33. Figure 2 shows alignment of full length human and cyno CD33 highlighting the differences in the primary sequence in the ECD domain.

[0580] Affinity of 29 Fab fragments binding to human and cyno CD33 ECD were assayed by Biacore analysis. Eight out of 29 antibodies show cross-reactivity with cyno CD33. Kinetic parameters of binding are given in Table 12. Data are compared to lintuzumab. Several antibodies show affinities >100 fold higher than lintuzumab.

[0581] Binding of the Fab fragments from CD33 monoclonal antibodies to the human CD33 extracellular domain (ECD) was measured by Biacore at 37 °C. The Biacore profile of ADI-10159 is shown in FIG. 3A; the Biacore profile of ADI-10177 is shown in FIG. 3B; the Biacore profile of ADI-11776 is shown in FIG. 3C; the Biacore profile of ADI-11801 in FIG. 3D; the Biacore profile of ADI-11807 is shown in FIG. 3E; the Biacore profile of ADI-11809 is shown in FIG. 3F; the Biacore profile of ADI-11815 is shown in FIG. 3G; the Biacore profile of ADI-11819 FIG. 3H; the Biacore profile of ADI-11830 is shown in FIG. 3I; the Biacore profile of ADI-11835 is shown in FIG. 3J; and the Biacore profile of the Fab fragment from Lintuzumab is shown in FIG. FIG. 3K.

[0582] Binding of the Fab fragments from CD33 monoclonal antibodies to the cyno CD33 ECD was measured by Biacore at 37 °C. The Biacore profile of ADI-10159 is shown in FIG. 4A; the Biacore profile of ADI-10177 in FIG. 4B; the Biacore profile of ADI-11776 is shown in FIG. 4C; the Biacore profile of ADI11807 is shown in FIG. 4D; the Biacore profile of ADI-11809 is shown in FIG. 4E; the Biacore profile of ADI-11819 is shown in FIG. 4F; the Biacore profile of ADI-11830 is shown in FIG. 4G; and the Biacore profile of ADI-11835 is shown in FIG. 4H.

[0583] Binding of the Fab fragments from CD33 monoclonal antibodies to V domain and C domain of human CD33 was measured by Biacore at 37 °C. FIGs. 5A-5J represent binding to the V-domain; panels K-T represent binding to the C domain. Both FIGs. 5A and 5K are Biacore profiles of ADI-10159; both FIGs. 5B and 5L are Biacore profiles of ADI-10177; both FIGs. 5C and 5M are Biacore profiles of ADI-11776; both FIGs. 5D and 5N are Biacore profiles of ADI-11801; both FIGs. 5E and 5O are Biacore profiles of ADI-11807; both FIGs. 5F and 5P are Biacore profiles of ADI-11809; both FIGs. 5G and 5Q are Biacore profiles of ADI-11815; both FIGs. 5H and 5R are Biacore profiles of ADI-11819; both FIGs. 5I and 5S are Biacore profiles of ADI-11830; and FIGs. 5J and 5T are Biacore profiles of ADI-11835.

Table 12. Kinetic parameters of human CD33 ECD and cyno CD33 ECD binding to Fabs measured by SPR at 37 °C. No binding is defined as absence of signal at highest concentration of 100 nM.

Antibody	Human CD33			Cyno CD33		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-10159	4.29e5	1.95e-3	4.53	5.28e5	4.36e-2	74.9
ADI-10177	5.58e5	6.36e-3	11.4	3.53e5	7.54e-3	21.4
ADI-11776	1.6e6	1.24e-3	0.78	2.62e6	4.72e-3	1.81
ADI-11807	1.14e6	3.32e-4	0.29	9.98e5	1.51e-4	0.15
ADI-11809	1.02e6	1.23e-6	0.0012	1.06e6	1.26e-4	0.118
ADI-11819	2.84e6	5.65e-5	0.02	3.82e6	1.90e-2	4.96
ADI-11830	1.99e6	5.47e-3	2.75	1.34e6	3.64e-2	27.8
ADI-11835	2.6e6	1.43e-3	0.53	2.76e6	1.89e-2	6.86
ADI-11815	3.39e5	7.91e-5	0.23	No binding		
ADI-11801	7.56e5	4.17e-4	0.55	No binding		
ADI-10152	2.46e5	9.14e-3	37.2	No binding		
ADI-10154	1.92e5	8.33e-3	43.4	No binding		
ADI-10155	1.70e5	6.85e-3	40.2	No binding		
ADI-10157	2.82e6	7.60e-3	2.69	No binding		
ADI-10158	4.75e5	1.49e-2	3.14	No binding		
ADI-10160	6.37e5	2.69e-2	42.2	No binding		
ADI-10161	5.74e5	1.18e-2	20.6	No binding		
ADI-10163	5.15e5	2.75e-2	53.5	No binding		

Antibody	Human CD33			Cyno CD33		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-10164	3.19e5	1.01e-2	31.5	No binding		
ADI-10165	5.91e5	1.88e-2	31.8	No binding		
ADI-10167	1.25e6	3.07e-2	24.4	No binding		
ADI-10168	3.75e5	1.75e-2	46.6	No binding		
ADI-10173	2.12e5	1.25e-2	58.8	No binding		
ADI-11802	4.9e5	1.54e-3	3.14	No binding		
ADI-11812	3.96e5	4.86e-4	1.23	No binding		
ADI-11825	2.13e6	3.8e-3	1.78	No binding		
ADI-11826	1.76e6	4.63e-3	2.63	No binding		
ADI-11828	1.32e6	3.51e-3	2.67	1.03e6	5.48e-2	53.5
ADI-11839	8.74e5	1.62e-2	18.6	No binding		
Lintuzumab	7.35e5	1.22e-2	16.7	No binding		

Mapping of binding interface to individual domains of CD33

[0584] The binding interface between the Fab fragment of each CD33 antibody to CD33 was mapped. FIGs. 5A-5T show binding of Fab fragments of different CD33 antibodies to individual domains of human CD33 (V domain and C domain). No binding to C domain was observed for any antibody tested. ADI-11815 did not bind to either V or C domain, suggesting that it requires a unique conformational epitope.

[0585] Table 13 shows a comparison between kinetics of binding to full ECD of human CD33 and a V domain. ADI-10159, ADI-11176, ADI-11807, ADI-11830, ADI-11835, ADI-11801, ADI-10155, ADI-11802, ADI-11825, ADI-11826, ADI-11828, and ADI-11839 show similar kinetics suggesting that the epitope for these antibodies are located entirely in the V domain. Reduced binding to V domain is observed for ADI-10177, ADI-11809 ADI-11819, ADI-10157, ADI-10158, and ADI-10164, suggesting that these antibodies bind to a conformational epitope, partially located in the V domain.

[0586] Kinetics of binding to the C domain of human CD33 was also measured with ADI-10152, ADI-10154, ADI-10155, ADI-10157, ADI-10158, ADI-10160, ADI-10161, ADI-10163, ADI-10164, ADI-10165, ADI-10167, ADI-10168, ADI-10173, ADI-11802, ADI-11812, ADI-11825, ADI-11826, ADI-11828, and ADI-11839. None of these antibodies bound the C domain of human CD33.

Table 13. Biacore analysis of FABs binding to recombinant full-length ECD and V domain of human CD33 performed at 37 °C. Asterisk indicates antibodies that bind to a conformational epitope partially located in V domain.

Antibody	Human CD33 V domain			Human CD33		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-10159	9.05e5	5.0e-3	5.56	4.29e5	1.95e-3	4.53
ADI-10177*	1.56e6	8.57e-2	54.8	5.58e5	6.36e-3	11.4
ADI-11776	4.52e6	1.43e-2	0.33	1.6e6	1.24e-3	0.78
ADI-11807	3.07e6	8.47e-4	0.28	1.14e6	3.32e-4	0.29
ADI-11809*	2.6e6	7.69e-4	0.3	1.02e6	1.23e-6	0.0012
ADI-11819	6.75e6	9.16e-4	0.14	2.84e6	5.65e-5	0.02
ADI-11830	6.67e6	2.99e-2	4.5	1.99e6	5.47e-3	2.75
ADI-11835	7.6e6	8.68e-3	1.14	2.6e6	1.43e-3	0.53
ADI-11815	No binding			3.39e5	7.91e-5	0.23
ADI-11801	1.8e6	1.25e-3	0.69	7.56e5	4.17e-4	0.55
ADI-10152	4.88e5	4.09e-2	100	2.46e5	9.14e-3	37.2
ADI-10154	1.52e6	3.35e-1	220	1.92e5	8.33e-3	43.4
ADI-10155	5.48e5	4.67e-2	85.2	1.70e5	6.85e-3	40.2
ADI-10157*	1.12e5	1.51e-2	134	2.82e6	7.60e-3	2.69
ADI-10158*	1.04e6	1.33e-1	127	4.75e5	1.49e-2	3.14
ADI-10160	1.59e6	3.27e-1	206	6.37e5	2.69e-2	42.2
ADI-10161	1.29e6	1.24e-1	95.8	5.74e5	1.18e-2	20.6
ADI-10163	No binding			5.15e5	2.75e-2	53.5
ADI-10164	1.29e6	3.7e-1	286	3.19e5	1.01e-2	31.5
ADI-10165	No binding			5.91e5	1.88e-2	31.8
ADI-10167	No binding			1.25e6	3.07e-2	24.4
ADI-10168	No binding			3.75e5	1.75e-2	46.6
ADI-10173	No binding			2.12e5	1.25e-2	58.8
ADI-11802	1.34e6	4.35e-3	3.2	4.9e5	1.54e-3	3.14
ADI-11812	No binding			3.96e5	4.86e-4	1.23
ADI-11825	4.93e6	1.95e-2	3.95	2.13e6	3.8e-3	1.78
ADI-11826	5.12e6	2.25e-3	4.38	1.76e6	4.63e-3	2.63

Antibody	Human CD33 V domain			Human CD33		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-11828	3.37e6	2.13e-2	6.3	1.32e6	3.51e-3	2.67
ADI-11839	9.19e6	4.1e-1	44.6	8.74e5	1.62e-2	18.6

Antibodies recognize CD33 independent of its glycosylation status.

[0587] The ability of anti-CD33 antibodies to recognize glycosylated CD33 was assayed. Table 14 shows that antibodies recognize V domain independent of its glycosylation status. Human CD33 is heavily glycosylated with 2 glycosylation sites located in the V domain. Differences in the glycosylation level of CD33 in different cells have been reported in the literature. Glycosylation can potentially disturb antibody binding to the target. In some samples, the V domain was deglycosylated by PNGase before testing. De-glycosylation status was confirmed by a shift on SDS-PAGE and MS. All antibodies tested in Table 14 bound to deglycosylated V CD33 similarly to the fully glycosylated version except for ADI-10163, ADI-10165, ADI-10167, and ADI-10173.

Table 14. Biacore analysis of FABs binding to fully glycosylated vs deglycosylated V domain performed at 37 °C.

Antibody	Deglycosylated V domain			V domain		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-10159	9.78e5	1.2e-2	12.3	9.05e5	5.0e-3	5.56
ADI-10177	1.88e6	7.01e-2	38.2	1.56e6	8.57e-2	54.8
ADI-11776	4.85e6	1.36e-3	0.28	4.52e6	1.43e-2	0.33
ADI-11807	3.9e6	7.45e-4	0.19	3.07e6	8.47e-4	0.28
ADI-11809	3.4e6	7.11e-4	0.21	2.6e6	7.69e-4	0.3
ADI-11819	9.15e6	1.03e-3	0.11	6.75e6	9.16e-4	0.14
ADI-11830	6.8e6	2.69e-2	3.95	6.67e6	2.99e-2	4.5
ADI-11835	7.94e6	7.79e-3	0.98	7.6e6	8.68e-3	1.14
ADI-11801	2.1e6	1.15e-3	0.55	1.8e6	1.25e-3	0.69
ADI-10152	1.05e5	7.7e-2	76.8	4.88e5	4.09e-2	100
ADI-10154	3.13e5	6.55e-2	209	1.52e6	3.35e-1	220
ADI-10155	1.25e6	1.32e-1	105	5.48e5	4.67e-2	85.2

Antibody	Deglycosylated V domain			V domain		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-10157	4.11e5	2.61e-2	63.8	1.12e5	1.51e-2	134
ADI-10158	2.63e6	2.31e-1	88.1	1.04e6	1.33e-1	127
ADI-10160	1.7e6	2.25e-1	133	1.59e6	3.27e-1	206
ADI-10161	2.29e6	1.96e-1	85.6	1.29e6	1.24e-1	95.8
ADI-10163	1.68e6	2.56e-1	152	No binding		
ADI-10164	8.11e5	1.16e-1	143	1.29e6	3.7e-1	286
ADI-10165	1.3e6	2.03e-1	156	No binding		
ADI-10167	1.66e6	1.28e-1	77.8	No binding		
ADI-10168	No binding			No binding		
ADI-10173	6.74e5	1.31e-1	200	No binding		
ADI-11802	1.57e6	4.17e-3	2.65	1.34e6	4.35e-3	3.2
ADI-11812	No binding			No binding		
ADI-11825	5.78e6	1.8e-2	3.11	4.93e6	1.95e-2	3.95
ADI-11826	5.37e6	1.98e-2	3.69	5.12e6	2.25e-3	4.38
ADI-11828	3.588e6	1.89e-2	4.87	3.37e6	2.13e-2	6.3
ADI-11839	1.65e6	1.16e-1	70.3	9.19e6	4.1e-1	44.6

CD33 antibodies bind to the R69G SNP of CD33.

[0588] The ability of anti-CD33 antibodies to recognize the R69G mutation in CD33 was assayed. Although several SNPs have been described for CD33, R69G is particularly prominent, occurring in 39-42% of the population. Table 15 shows antibodies binding to human CD33 containing the R69G mutation.

Table 15. Biacore analysis of FABs binding to CD33 R69G.

Antibody	Human CD33 R69G			Human CD33		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-10159	4.26e5	2.43e-3	5.68	4.29e5	1.95e-3	4.53
ADI-10177	2.3e5	2.01e-3	87.4	5.58e5	6.36e-3	11.4
ADI-11776	1.98e6	4.26e-4	0.22	1.6e6	1.24e-3	0.78
ADI-11807	5.97e5	2.59e-4	0.43	1.14e6	3.32e-4	0.29
ADI-11809	8.15e5	1.79e-4	0.22	1.02e6	1.23e-6	0.0012
ADI-11819	2.78e6	2.44e-4	0.09	2.84e6	5.65e-5	0.02

ADI-11830	2.27e6	6.63e-3	2.94	1.99e6	5.47e-3	2.75
ADI-11835	3.07e6	2.05e-3	0.67	2.6e6	1.43e-3	0.53
ADI-11815	3.00e5	1.3e-3	4.34	3.39e5	7.91e-5	0.23
ADI-11801	No binding			7.56e5	4.17e-4	0.55
ADI-10152	2.88e5	2.18e-2	75.8	2.46e5	9.14e-3	37.2
ADI-10154	1.53e5	2.83e-2	186	1.92e5	8.33e-3	43.4
ADI-10155	2.33e5	1.05e-2	45.0	1.70e5	6.85e-3	40.2
ADI-10157	1.56e6	2.87e-2	17.8	2.82e6	7.60e-3	2.69
ADI-10158	5.30e5	3.31e-2	62.3	4.75e5	1.49e-2	3.14
ADI-10160	8.36e5	5.33e-2	63.7	6.37e5	2.69e-2	42.2
ADI-10161	6.29e5	3.07e-2	48.9	5.74e5	1.18e-2	20.6
ADI-10163	5.59e5	5.9e-2	106	5.15e5	2.75e-2	53.5
ADI-10164	3.08e5	3.5e-2	113	3.19e5	1.01e-2	31.5
ADI-10165	6.9e5	5.02e-2	72.7	5.91e5	1.88e-2	31.8
ADI-10167	1.22e6	8.74e-2	71.6	1.25e6	3.07e-2	24.4
ADI-10168	4.85e5	3.07e-2	63.5	3.75e5	1.75e-2	46.6
ADI-10173	No binding			2.12e5	1.25e-2	58.8
ADI-11802	No binding			4.9e5	1.54e-3	3.14
ADI-11812	3.38e5	2.28e-3	6.74	3.96e5	4.86e-4	1.23
ADI-11825	1.86e6	6.95e-3	3.74	2.13e6	3.8e-3	1.78
ADI-11826	1.89e6	7.23e-3	3.83	1.76e6	4.63e-3	2.63
ADI-11828	1.16e6	7.00e-3	6.03	1.32e6	3.51e-3	2.67
ADI-11839	No binding			8.74e5	1.62e-2	18.6

CD33 antibodies bind to the S128N SNP of CD33

[0589] The ability of anti-CD33 antibodies to recognize the S128N mutation in CD33 was assayed. Table 16 shows antibodies binding to human CD33 containing the S128N mutation. The binding affinity of ADI-10152, ADI-10154, ADI-10157, ADI-10158, ADI-10163, ADI-10164, ADI-10165, ADI-10167, ADI-10168, and ADI-10173 to human CD33 was impaired by the S128N SNP.

Table 16. Biacore analysis of FABs binding to CD33 S128N.

Antibody	Human CD33 S128N			Human CD33		
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)
ADI-10152	2.74e5	3.39e-2	124	2.46e5	9.14e-3	37.2
ADI-10154	1.93e5	5.39e-2	279	1.92e5	8.33e-3	43.4
ADI-10155	1.87e5	1.59e-2	85	1.70e5	6.85e-3	40.2
ADI-10157	5.65e4	9.24e-3	163	2.82e6	7.60e-3	2.69
ADI-10158	5.73e5	4.17e-2	72.8	4.75e5	1.49e-2	3.14
ADI-10160	7.86e5	6.73e-2	85.7	6.37e5	2.69e-2	42.2
ADI-10161	6.05e5	3.85e-2	63.6	5.74e5	1.18e-2	20.6
ADI-10163	5.07e5	7.48e-2	147	5.15e5	2.75e-2	53.5
ADI-10164	1.93e5	5.39e-2	279	3.19e5	1.01e-2	31.5
ADI-10165	6.41e5	5.82e-2	90.7	5.91e5	1.88e-2	31.8
ADI-10167	1.28e6	1.27e-1	98.6	1.25e6	3.07e-2	24.4
ADI-10168	4.04e5	4.69e-2	116	3.75e5	1.75e-2	46.6
ADI-10173	1.83e5	3.42e-2	187	2.12e5	1.25e-2	58.8
ADI-11802	6.62e5	5.90e-4	0.809	4.9e5	1.54e-3	3.14
ADI-11812	5.56e5	1.12e-3	2.01	3.96e5	4.86e-4	1.23
ADI-11825	2.10e6	6.49e-3	3.09	2.13e6	3.8e-3	1.78
ADI-11826	2.17e6	5.74e-3	2.65	1.76e6	4.63e-3	2.63
ADI-11828	1.37e6	7.42e-3	5.41	1.32e6	3.51e-3	2.67
ADI-11839	9.63e5	2.84e-2	29.5	8.74e5	1.62e-2	18.6

ADI-11815 recognizes a unique conformational epitope.

[0590] The binding epitope of the CD33-binding domain of ADI-11815 was assayed. FIG. 6 and Table 17 demonstrate that ADI-11815 has a unique conformational epitope. This antibody binds to the full-length ECD of human CD33, but not to individual domains and does not cross-block with lintuzumab.

Table 17. Kinetic parameters of ADI-11815 Fab binding to different domains and SNP R69G of human CD33.

	hCD33			V domain			C domain			hCD33 R69G SNP			Cross-blocking with lintuzumab
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)	
ADI-11815	3.39e5	7.91e-5	0.23	No binding			No binding			3.00e5	1.3e-3	4.34	No

ADI-11801 binds to a unique epitope that includes R69.

[0591] The binding epitope of CD33-binding domain including ADI-11815 was assayed. FIG. 7 and Table 18 demonstrate the epitope on CD33 that ADI-11801 recognize. Its binding to the human CD33 ECD is abrogated by R69G mutation.

Table 18. Kinetics of ADI-11801 Fab binding to different domains of CD33 and SNP R69G.

	hCD33			V domain			C domain			hCD33 R69G SNP			Cross-blocking with lintuzumab
	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)	k_a (1/Ms)	k_d (1/s)	K_D (nM)	
ADI-11801	7.56e5	4.17e-4	0.55	1.80e6	1.25e-3	0.69	No binding			No binding			No

Example 3: Assessment of TriNKET binding to cell expressing human NKG2D

[0592] The ability of TriNKETs that include an NKG2D-binding domain and a CD33-binding domain to bind to NKG2D was assayed. EL4 cells transduced with human NKG2D and human KHYG-1 cells were used to test binding to cell-expressed human NKG2D. TriNKETs were diluted to the top concentration, and then diluted serially. The mAb or TriNKET dilutions were used to stain cells, and binding of the TriNKET or mAb was detected using a fluorophore-conjugated anti-human IgG secondary antibody. Cells were analyzed by flow cytometry, binding MFI was normalized to secondary antibody controls to obtain fold over background values.

[0593] FIGs. 10A-10B show binding of CD33-targeting TriNKETs to human NKG2D expressed on EL4 (top) or KHYG-1 (bottom) cells. FOB binding signal was similar on both EL4-hNKG2D cells and KHYG-1 cells, the ranking of binding between clones was also maintain on the two cell lines. FIG. 10A shows binding of CD33-targeting TriNKETs to human NKG2D expressed on EL4 cells. FIG. 10B shows binding of CD33-targeting TriNKETs to human NKG2D expressed on KHYG-1 cells. FOB binding signal was similar

on both EL4-hNKG2D cells and KHYG-1 cells, the ranking of binding between clones was also maintain on the two cell lines.

Example 4: Assessment of TriNKET or mAb binding to cell expressed human cancer antigens

[0594] The ability of TriNKETs that include an NKG2D-binding domain and a CD33-binding domain to bind to CD33 was assayed. The Molm-13, human AML cell line, was used to assess binding of monoclonal antibodies to CD33 expressed on the cell surface. mAbs were diluted to 2 μg/mL, and mAb dilutions were used to stain cells. Bound antibody was detected using a fluorophore conjugated anti-human IgG secondary antibody. Cells were analyzed by flow cytometry, binding to cell-expressed CD33 was compared to isotype stained and unstained cell populations.

[0595] Human cancer cell lines expressing CD33 were used to assess tumor antigen binding of TriNKETs derived from different NKG2D-targeting clones. The human AML cell line Molm-13 was used to assess binding of TriNKETs to cell expressed CD33. TriNKETs were diluted, and were incubated with the respective cells. Binding of the TriNKET was detected using a fluorophore conjugated anti-human IgG secondary antibody. Cells were analyzed by flow cytometry, binding MFI to cell expressed CD33 was normalized to secondary antibody controls to obtain fold over background values.

[0596] The ability of CD33 TriNKETs to bind CD33 expressed on Molm-13 cells was tested. FIG. 8 shows binding of TriNKETs targeting CD33 to Molm- shows binding MFI of six anti-CD33 antibodies to CD33 expressed on Molm-13 cells. All six antibodies bound to cell-expressed CD33. Five of the six antibodies show higher MFI binding signal compared to Lintuzumab.

[0597] The ability of CD33 TriNKETs to induce rested NK cell-mediated killing of Molm-13 AML cells was tested. Four different CD33-targeting domains were used with five NKG2D-targeting domains to make a total of 20 different TriNKETs. Regardless of the NKG2D-targeting domain used in the TriNKET, binding to CD33 was conserved for a single CD33-targeting domain.

Example 5: Assessment of TriNKET or mAb internalization

[0598] Internalization of TriNKETs after binding to CD33 on cell surface was assayed. The Molm-13, human AML cell line, was used to assess internalization of monoclonal antibodies bound to CD33 expressed on the cell surface. Monoclonal antibodies were diluted

to 2 μg/mL, and mAb dilutions were used to stain cells. Following surface staining of CD33 samples were split, half the sample was placed at 37 °C overnight to facilitate internalization, with the other half of the sample bound antibody was detected using a fluorophore conjugated anti-human IgG secondary antibody. Cells were fixed after staining with the secondary antibody, and were stored at 4 °C overnight for analysis on the following day. After 24 hours at 37 °C samples were removed from the incubator, and bound antibody on the surface of the cells was detected using a fluorophore conjugated anti-human IgG secondary antibody. Samples were fixed and all samples were analyzed on the same day. Internalization of antibodies was calculated as follows: % internalization = (1-(sample MFI 24hours/baseline MFI)) * 100%.

[0599] FIG. 9 shows internalization of anti-CD33 antibodies bound to the surface of Molm-13 cells after 24 hours. All the anti-CD33 antibodies showed similar internalization after 24 hours. Lintuzumab showed slightly higher internalization compare to other anti-CD33 antibodies.

Example 6: Activation of primary NK cells by TriNKETs

[0600] The ability of TriNKETs that include an NKG2D-binding domain and a CD33-binding domain to activate primary NK cells was assayed. 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 was typically >90% CD3-CD56+. Isolated NK cells were cultured in media containing 100 ng/mL IL-2 for activation or rested overnight without cytokine. IL-2-activated NK cells were used either 24-48 hours later; rested NK cells were always used the day after purification.

[0601] Human cancer cell lines expressing a cancer target of interest were harvested from culture, and cells were adjusted to $2x10^6$/mL. Monoclonal antibodies or TriNKETs targeting the cancer target of interest were diluted in culture media. Rested and/or activated NK cells were harvested from culture, cells were washed, and were resuspended at $2x10^6$/mL in culture media. IL-2, and fluorophore-conjugated anti-CD107a was added to the NK cells for the activation culture. Brefeldin-A and monensin were diluted into culture media to block protein transport out of the cell for intracellular cytokine staining. Into a 96-well plate 50 μl of tumor targets, mAbs/TriNKETs, BFA/monensin, and NK cells were added for a total

culture volume of 200 µl. Plate was cultured for 4 hours before samples were prepared for FACS analysis.

[0602] Following the 4 hour activation culture, cells were prepared for analysis by flow cytometry using fluorophore-conjugated antibodies against CD3, CD56 and IFNγ. CD107a and IFNγ staining was analyzed in CD3-CD56+ populations to assess NK cell activation.

[0603] FIG. 12 shows TriNKET-mediated activation of rested human NK cells in co-culture with CD33-expressing THP-1 AML cells. Human NK cell activation was assessed using IFNγ production and CD107a degranulation as markers for activation. All TriNKETs and monoclonal antibodies activated human NK cells above the isotype control. Similar activity was observed for four different anti-CD33 antibodies. TriNKET activity was dependent upon the NKG2D-targeting clone, some clones provided better TriNKET mediated activation than others. NKG2D clones provided similar activity with each of the anti-CD33 targeting domains.

Example 7: Primary human NK cell cytotoxicity assay

[0604] The ability of TriNKETs that include an NKG2D-binding domain and a CD33-binding domain to induce cytotoxicity of NK cells against CD33-expressing cells was assayed. 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 was typically >90% CD3-CD56+. Isolated NK cells were cultured in media containing 100 ng/mL IL-2 or were rested overnight without cytokine. IL-2-activated or rested NK cells were used the following day in cytotoxicity assays.

[0605] KHYG-1 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 cells were harvest 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.

DELFIA cytotoxicity assay:

[0606] Human cancer cell lines expressing a target of interest were harvested from culture, cells were washed with HBS, and were resuspended in growth media at 10^6/mL for labeling with BATDA reagent (Perkin Elmer AD0116). Manufacturer instructions were followed for labeling of the target cells. After labeling cells were washed 3x with HBS, and

were resuspended at 0.5-1.0x10^5/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 wells were prepared for max 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 and/or activated NK cells were harvested from culture, cells were washed, and were resuspended at 10^5-2.0x10^6/mL in culture media depending on the desired E:T ratio. 50 µl of NK cells was added to each well of the plate to make a total of 200 µl culture volume. The plate was incubated at 37 °C with 5% CO2 for 2-3 hours before developing the assay.

[0607] After culturing for 2-3 hours, the plate was removed from the incubator and the cells were pelleted by centrifugation at 200g 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 the light and incubated on a plate shaker at 250 rpm for 15 minutes. Plate was read using either Victor 3 or SpectraMax i3X instruments. % Specific lysis was calculated as follows: % Specific lysis = ((Experimental release – Spontaneous release) / (Maximum release – Spontaneous release)) * 100%.

[0608] FIG. 13 and FIG. 14 show human NK cell killing of Molm-13 (FIG. 13) and THP-1 (FIG. 14) AML target cells mediated by CD33-targeting TriNKETs. Human NK cell killing of Molm-13 AML target cells mediated by CD33-targeting TriNKETs was assayed (FIG. 13). Rested NK effector cells were used with Molm-13 target cells. Activated human NK effector cells gave higher background killing, compared to rested human NK effector cells. With NK effector cells, TriNKETs were able to increase lysis against Molm-13 AML target cells. Similar activity of each TriNKET was observed with rested and activated human NK cells, as well as with Molm-13 target cells.

[0609] Human NK cell killing of THP-1 AML target cells, mediated by CD33-targeting TriNKETs was assayed. Activated human NK effector cells were used with THP-1 cells (FIG. 14), which resulted in higher background killing, compared to rested human NK effector cells. With NK effector cells, TriNKETs were able to increase lysis against THP-1 AML target cells. Similar activity of each TriNKET was observed with rested and activated human NK cells, as well as with THP-1 target cells.

[0610] Thus, with NK effector cells TriNKETs were able to increase lysis against Molm-13 (FIG. 13) and THP-1 (FIG. 14) AML target cells. Similar activity of each TriNKET was observed with rested and activated human NK cells, as well as with Molm-13 (FIG. 13) and THP-1 (FIG. 14) target cells.

[0611] FIG. 15A, FIG. 16, and FIG. 17A show KHYG-1 effector cell killing of Molm-13 (FIG. 15A), EOL-1 (FIG. 16), and THP-1 (FIG. 17A) human AML target cells respectively. KHYG-1 cells were demonstrated to express surface NKG2D, but do not express CD16. Therefore, TriNKET mediated killing here is dependent upon NKG2D mediated activation of the KHYG-1 effector cells. TriNKETs were able to mediate KHYG-1 effector cell killing of all three human AML target cell lines. Similar, TriNKET activity was demonstrated on all three target cell lines.

[0612] TriNKET mediated cytotoxicity of rested human NK cells was also tested. FIG. 15B and FIG. 17B show that TriNKETs also mediated cytotoxicity of rested human NK cells against Molm-13 (FIG. 15B) and THP-1 (FIG. 17B) human AML cells. FIG. 15B shows that TriNKETs mediated rested human NK cell killing of Molm-13 human AML cells. In FIG. 15B the rested human NK effector cell (E) to target cancer cell (T) ratio (E:T) was 10:1. The E:T ratio may reflect differences in the maximal % lysis.

[0613] TriNKETs also mediated rested human NK cell killing of THP-1 target cells, which express the high-affinity FcγRI. FIG. 17B shows that TriNKETs mediated rested human NK cell killing of THP-1 human AML cells, in which the E:T was 5:1.

Example 8: Assessment of TriNKET binding to cells expressing human NKG2D

[0614] I07 mAb was identified as a monoclonal antibody with high binding affinity to CD33. The heavy and light chain amino acid sequences of I07-F405L, an Fc variant of I07, are provided below. The I07-F405L mAb included a substitution of Leu for Phe at position 405 (under EU numbering) in the Fc CH3 domain. A Lys may be optionally included at the C-terminus of the heavy chain.

I07-F405L mAb heavy chain

EVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPGKGLEWVATIKQDG
SEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ
GTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFLLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

[SEQ ID NO:199]

I07-F405L mAb light chain

DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYEASSLESGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSQSYPPITFGGGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY
SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

[SEQ ID NO:200]

[0615] A49-F3'-TriNKET-I07, a TriNKET derivative of I07 mAb, is described in Section II – Multi-specific Binding Proteins. The amino acid sequences of this TriNKET are provided in SEQ ID NOs: 187, 189, and 190.

[0616] The ability of A49-F3'-TriNKET-I07 to bind to NKG2D was assessed using EL4 cells transduced with human NKG2D (EL4-hNKG2D). Briefly, A49-F3'-TriNKET-I07 and I07-F405L mAb were serially diluted. EL4-hNKG2D cells were incubated with the diluted TriNKET or mAb solutions. Binding of the TriNKET or mAb to the EL4 cells was detected using a fluorophore-conjugated anti-human IgG secondary antibody. The cells were analyzed by flow cytometry, and fold over background values were calculated by normalizing binding MFI to the MFI of a control group in which the cells were incubated with the secondary antibody only.

[0617] As shown in FIG. 35, I07-F405L mAb showed no binding to EL4-hNKG2D cells. A49-F3'-TriNKET-I07 demonstrated weak binding to EL4-hNKG2D cells, without reaching saturation even at the high concentrations of 100 μg/mL.

Example 9: Assessment of TriNKET binding to cells expressing human CD33

[0618] The ability of A49-F3'-TriNKET-I07 to bind to CD33 was assessed using human cancer cell lines expressing CD33. Briefly, human AML cell lines Mv4-11 and Molm-13, which expressed CD33, were incubated with serially diluted A49-F3'-TriNKET-I07 and I07-F405L mAb solutions. Binding of A49-F3'-TriNKET-I07 or I07-F405L mAb to the AML cells was detected using a fluorophore-conjugated anti-human IgG secondary antibody. The cells were analyzed by flow cytometry, and fold over background values were calculated by normalizing binding MFI to the MFI of a control group in which the cells were incubated with the secondary antibody only.

[0619] As shown in FIGs. 36A and 36B, A49-F3'-TriNKET-I07 exhibited a decrease in binding potency by three to four fold compared to I07-F405L mAb on both Molm-13 and

Mv4-11 cells. A49-F3'-TriNKET-I07 was also found to bind to the cells with a higher maximum fold over background compared to I07-F405L mAb.

Example 10: Assessment of TriNKET internalization

[0620] Internalization of A49-F3'-TriNKET-I07 and I07-F405L mAb upon binding to CD33 was assessed using human AML cell lines EOL-1 and Molm-13, which expressed CD33 on the cell surface. Briefly, the cells were incubated with 2 μg/mL A49-F3'-TriNKET-I07 or I07-F405L mAb for 20 minutes at room temperature. The cell samples were then split into three portions. The first and second portions were placed at 37 °C for 2 hours and 24 hours, respectively, to allow antibody internalization. Then the cells were incubated with a fluorophore-conjugated anti-human IgG secondary antibody, and were fixed for flow cytometry analysis. The third portion of the cell samples, used to set the baseline level, was incubated with the fluorophore-conjugated anti-human IgG secondary antibody without incubation at 37 °C. The cells were fixed after staining with the secondary antibody, and were stored at 4 °C for analysis on the following day (when the first half of the samples were ready). The amount of A49-F3'-TriNKET-I07 and I07-F405L mAb bound to the cell surface was analyzed by flow cytometry on the same day. Internalization of antibodies was calculated as: % internalization = (1-(MFI of 24-hour sample / MFI of baseline sample)) × 100%.

[0621] As shown in FIGs. 37A and 37B, internalization of A49-F3'-TriNKET-I07 and I07-F405L mAb after engagement of CD33 increased overtime on EOL-1 and Molm-13 cells. In both cells, I07-F405L mAb was internalized more rapidly and to a greater extent than A49-F3'-TriNKET-I07.

Example 11: Activation of primary NK cells by TriNKET

[0622] The ability of A49-F3'-TriNKET-I07 to elicit cytotoxicity of primary NK cells against human AML cells was assessed using the DELFIA cytotoxicity assay. Briefly, PBMCs were isolated from human peripheral blood buffy coats using density gradient centrifugation. The isolated PBMCs were washed, and NK cells were isolated using a negative selection technique with magnetic beads. The purity of the isolated NK cells was typically >90% $CD3^-CD56^+$. The isolated NK cells were rested without cytokine overnight.

[0623] On the following day, human AML cell lines Molm-13, THP-1, and EOL-1 were harvested from culture. The AML cells were washed with HBS, and were resuspended in growth media at 10^6 cells/mL for labeling with BATDA reagent (Perkin Elmer AD0116)

following the manufacturer instructions. After labeling, the AML cells were washed three times with HBS, and were resuspended at 0.5-1.0×10^5 cells/mL in culture media. 100 µl of BATDA labeled cells were added to each well of a 96-well plate.

[0624] The tested TriNKET or mAb was diluted in culture media, and 50 µl of diluted TriNKET or mAb was added to each well. Rested NK cells were harvested from culture, washed, and resuspended at 10^5-2.0×10^6 cells/mL in culture media to attain a desired E:T ratio of 5:1. 50 µl of NK cells were added to each well of the plate to make a total of 200 µl culture volume in each well. The plate was incubated at 37C with 5%CO_2 for 2-3 hours.

[0625] After the culturing, the plate was removed from the incubator, and the cells were pelleted by centrifugation at 200×g for 5 minutes. 20 µl of culture supernatant was transferred to a clean microplate provided from the manufacturer. Supernatant from the labeled cells incubated alone was used to measure spontaneous release of TDA. Supernatant from labeled cells incubated with 1% Triton-X was used to measure maximum lysis of the target cells. Supernatant from the labeled cells prior to the 2-3 hours of incubation was used to measure the background and for quality control purposes.

[0626] 200 µl of room temperature europium solution was added to each well containing culture supernatant. The plate was protected from light and incubated on a plate shaker at 250 rpm for 15 minutes. Fluorescence was measured using a Victor 3 or SpectraMax i3X instrument.

[0627] The fluorescent levels represented lysis of the target cells. The values of % specific lysis were calculated as: % specific lysis = ((Experimental release – Spontaneous release) / (Maximum release – Spontaneous release)) × 100%.

[0628] A49-F3'-TriNKET-I07 and several monoclonal antibodies were tested in this assay. The monoclonal antibodies include I07-F405L mAb, I07-DE mAb, lintuzumab-GA, and 280-31-01(mut)-DE. I07-DE mAb is a variant of I07 mAb, with S239D and I332E substitutions in the Fc to enhance ADCC activity (bold-underlined in the sequence below). The amino acid sequence of I07-DE heavy chain is shown below, optionally with a Lys at the C-terminus.

I07-DE mAb heavy chain

EVQLVESGGGLVQPGGSLRLSCAASGFTFGSYWMSWVRQAPGKGLEWVATIKQDG
SEKSYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPLNAGELDVWGQ
GTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPELLGGP**D**VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP**E**EKTI

SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
[SEQ ID NO:201]

[0629] The light chain of I07-DE mAb is identical to that of I07-F405L mAb [SEQ ID NO:200].

[0630] 280-31-01(mut)-DE is a variant of antibody clone 280-31-01 (mut) disclosed in WO2012045752, with S239D and I332E substitutions in the Fc to enhance ADCC activity (bold-underlined in the sequence below). The amino acid sequences of 280-31-01(mut)-DE heavy chain and light chain are shown below, optionally with a Lys at the C-terminus of the heavy chain.

280-31-01(mut)-DE heavy chain
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSDYAISWVRQAPGQGLEWMGRIIPILGV
ADYAQKFQGRVTITADKSTRTAYMELSSLRSEDTAVYYCARNWADAFDIWGQGTM
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF
PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPP
CPAPELLGGP**D**VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP**E**EKTISKAKG
QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
(SEQ ID NO:202)

280-31-01(mut)-DE light chain
DIQLTQSPSSLSASVGDRVTITCRASQGISSVLAWYQQKPGKAPKLLIYDASSLESGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQFDSSITFGQGTKLEIKRTVAAPSVFIFPPS
DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSS
TLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO:203)

[0631] An SNP in the CD16 gene can result in V158 or F158 variants of the human CD16 protein. CD16 with F158 is known to have reduced binding affinity of CD16 to Fc than CD16 with V158, thereby decreasing antibody-dependent cell-mediated cytotoxicity (ADCC). NK cells having CD16-F158 are therefore less responsive to CD16 stimulation than NK cells expressing CD16-V158. Indeed, as shown in FIG. 38A, I07-F405L mAb only led to a low level of killing of Molm-13 cells by NK cells that only expressed the low affinity CD16 variant ($CD16^{F/F}$). In comparison, A49-F3'-TriNKET-I07 mediated more potent NK cell killing with a higher specific lysis of Molm-13 cells, likely due to its additional ability to engage NK cells by NKG2D binding. Similarly, when incubated with NK cells that had this SNP in one allele ($CD16^{V/F}$), A49-F3'-TriNKET-I07 exhibited stronger activity in killing EOL-1 cells than I07-F405L mAb (FIG. 38B).

[0632] THP-1 cells express FcγRI, which can bind to IgG1 Fc at high affinity. The competition for Fc binding by target cells can further reduce NK cell killing. Therefore, as shown in FIGs. 38C and 38D, when THP-1 cells were incubated with $CD16^{F/F}$ NK cells in the presence of I07-F405L or lintuzumab-GA mAb, no specific lysis of THP-1 cells was observed. Even I07-DE, an ADCC-enhancing variant of I07, failed to elicit NK cell cytotoxicity. Among the monoclonal antibodies tested, only 280-31-01(mut)-DE, an ADCC-enhancing variant of antibody clone 280-31-01 (mut) disclosed in WO2012045752, exhibited cell killing activity at high concentrations. Remarkably, A49-F3'-TriNKET-I07 mediated more potent NK cell killing with a higher specific lysis of THP-1 cells, likely due to its additional ability to engage NK cells by NKG2D binding.

Example 12: Activation of primary $CD8^+$ T cells by TriNKET

[0633] NKG2D is expressed on NK cells and many T cells, including $CD8^+$ T cells. The ability of A49-F3'-TriNKET-I07 to elicit cytotoxicity of primary $CD8^+$ T cells against human AML cells was assessed using the DELFIA cytotoxicity assay.

[0634] Briefly, human peripheral blood mononuclear cells (PBMCs) were isolated from human peripheral blood buffy coats using density gradient centrifugation. The isolated PBMCs were stimulated with 1 μg/mL Concanavalin A (ConA) at 37 °C for 18 hours. Then ConA was removed, and the PBMCs were cultured with 25 unit/mL IL-2 at 37 °C for 4 days. $CD8^+$ T cells were purified using a negative selection technique with magnetic beads, then cultured in media containing 10 ng/mL IL-15 at 37 °C for 7-13 days.

[0635] The primary human effector $CD8^+$ T cells generated above were characterized for cell markers. The cells were stained with fluorophore-conjugated antibodies against CD3, CD8, NKG2D, and CD16, and analyzed by flow cytometry. As shown in FIG. 39, the isolated $CD8^+$ T cells had high purity, as more than 99% of them were positive of CD3, CD8, and NKG2D expression, and were negative of CD16 expression.

[0636] To assess the ability of A49-F3'-TriNKET-I07 to elicit cytotoxicity of primary $CD8^+$ T cells, Molm-13 cells were harvested from culture, washed, and resuspended in growth media at 10^6 cells/mL. The cells were labeled with BATDA reagent (Perkin Elmer AD0116) following manufacturer instructions. After labeling, the cells were washed three times with HBS, and were resuspended at 0.5×10^5 cells/mL in culture media. 100 μl of BATDA labeled cells were added to each well of a 96-well plate. 50 μl of serially diluted monoclonal antibody or TriNKET was added to each well.

[0637] $CD8^+$ effector T cells were harvested from culture, washed, and resuspended at 5×10^6 cells/mL in culture media. 50 µl of $CD8^+$ T cells were added to each well of the plate to reach an E:T ratio of 50:1 and a total of culture volume of 200 µl. The plate was incubated at 37°C with 5% CO_2 for 3.5 hours. After incubation, the cells were pelleted by centrifugation at 500×g for 5 minutes. 20 µl of culture supernatant was transferred to a clean microplate provided from the manufacturer. Supernatant from the labeled cells incubated alone was used to measure spontaneous release of TDA. Supernatant from labeled cells incubated with 1% Triton-X was used to measure maximum lysis of the target cells.

[0638] 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 250rpm for 15 minutes. Fluorescence was measured using a SpectraMax i3X instrument.

[0639] The fluorescent levels represented lysis of the target cells. The values of % specific lysis were calculated as: % specific lysis = ((Experimental release – Spontaneous release) / (Maximum release – Spontaneous release)) × 100%.

[0640] As shown in FIGs. 40A and 40B, A49-F3'-TriNKET-I07 enhanced the cytotoxic activity of human primary $CD8^+$ T cells in a dose-dependent manner. A49-F3'-TriNKET-H76, a protein described in Section II – Multi-specific Binding Proteins (having polypeptides comprising the sequences of SEQ ID NOs: 197, 189, and 190), was also active under the conditions but exhibited less potency than A49-F3'-TriNKET-I07. Monoclonal antibody I07-F405L and a non-target TriNKET did not show this activity.

Example 13: Binding of TriNKET to monocytes

[0641] The expression of CD33 on blood cells is assessed by flow cytometry using the method described in Example 9. Briefly, human whole blood was incubated with A49-F3'-TriNKET-I07 or human IgG1 isotype control antibody conjugated to a fluorophore. Binding of A49-F3'-TriNKET-I07 or the isotype control antibody was detected by flow cytometry. To assess the binding levels on specific types of cells, fluorophore-conjugated antibodies that bind to surface markers of NK cells, $CD8^+$ T cells, $CD4^+$ T cells, B cells, and monocytes were added to the incubation, and the presence or absence of binding of these antibodies were used for gating when analyzing the flow cytometry data.

[0642] As shown in FIGs. 41A-41E, the binding of A49-F3'-TriNKET-I07 to NK cells was weak compared to a non-target human IgG1 isotype antibody control, whereas strong binding of the TriNKET to $CD33^+$ monocytes was observed.

Example 14: Long-term NK cell cytotoxicity mediated by TriNKET

[0643] NK cells have a natural ability to sense transformed or stressed cells and kill them, but do not kill healthy cells. We tested the ability of A49-F3'-TriNKET-I07 to preserve the natural selective NK cell cytotoxicity using Molm-13 AML cells and human primary monocytes as target cells. The Molm-13 cells were obtained from DSMZ cell bank. The human primary monocytes were isolated from human peripheral blood. Briefly, PBMCs were isolated from human peripheral blood buffy coats using density gradient centrifugation. Monocytes were isolated by negative selection. CD33 expression on human primary monocytes and Molm-13 AML cells were confirmed by flow cytometry analysis (FIGs. 42A-42B).

[0644] Human primary NK cells were isolated from human peripheral blood. Briefly, PBMCs were isolated from human peripheral blood buffy coats using density gradient centrifugation. NK cells were isolated by negative selection. To distinguish target cells from NK cells in the co-culture, the target cells were fluorescently labeled. Specifically, the isolated monocytes were labeled with IncuCyte CytoLight Rapid live-cell labeling reagent according manufacturer's recommendations. The Molm-13 cells were infected with lentivirus encoding nuclear GFP, and cells with stable expression were selected with puromycin.

[0645] Isolated NK cells and target cells were mixed at an E:T ratio of 10:1 in the presence of 20 nM A49-F3'-TriNKET-I07. Non-specific activation of NK cells in the co-cultures was conducted in parallel as a positive control group for AML cell killing. The mixture was added to an Ibidi μ-slide. Time-lapse images for the phase and green channels were collected every hour, with 3 images per sample, using an IncuCyte S3 instrument. The images were analyzed using the IncuCyte S3 software. Live target cells were detected by green fluorescence, and the number of green cells at each time point was normalized to the number of green cells at time 0 from the same sample.

[0646] As shown in FIGs. 43A and 43B, Molm-13 AML cells were able to proliferation in the presence of the NK cells alone, but target cell outgrowth was substantially inhibited by A49-F3'-TriNKET-I07. By contrast, A49-F3'-TriNKET-I07 did not mediate human NK cell killing of normal monocytes in the long-term co-culture. The activity of A49-F3'-TriNKET-I07 was similar to that of PMA+ionomycin, which also preserves the natural selectivity of NK cells. These results suggest that A49-F3'-TriNKET-I07 selectively compromised cancer cells, and potentially had a wide therapeutic window.

INCORPORATION BY REFERENCE

[0647] The entire disclosure of each of the patent documents and scientific articles referred to herein is incorporated by reference for all purposes.

EQUIVALENTS

[0648] 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 on 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 the range of equivalency of the claims are intended to be embraced therein.

WHAT IS CLAIMED IS:

1. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:9.

2. The antibody heavy chain variable domain according to claim 1, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:45; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:46; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:47.

3. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1.

4. The antibody heavy chain variable domain according to claim 3, wherein the amino acid sequence comprises: a complementarity-determining region 1 (CDR1) sequence represented by the amino acid sequence of SEQ ID NO:21; a complementarity-determining region 2 (CDR2) sequence represented by the amino acid sequence of SEQ ID NO:22; and a complementarity-determining region 3 (CDR3) sequence represented by the amino acid sequence of SEQ ID NO:23.

5. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:3.

6. The antibody heavy chain variable domain according to claim 5, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:27; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:28; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:29.

7. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:5.

8. The antibody heavy chain variable domain according to claim 7, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:33; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:34; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:35.

9. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:7.

10. The antibody heavy chain variable domain according to claim 9, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:39; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:40; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:41.

11. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:11.

12. The antibody heavy chain variable domain according to claim 11, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:51; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:52; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:53.

13. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:13.

14. The antibody heavy chain variable domain according to claim 13, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:57; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:58; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:59.

15. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:15.

16. The antibody heavy chain variable domain according to claim 15, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:63; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:64; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:65.

17. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:17.

18. The antibody heavy chain variable domain according to claim 17, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:69; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:70; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:71.

19. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:19.

20. The antibody heavy chain variable domain according to claim 19, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:75; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:76; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:77.

21. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:266.

22. The antibody heavy chain variable domain according to claim 21, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:528; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:305; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:529.

23. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:268.

24. The antibody heavy chain variable domain according to claim 23, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:530; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:311; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:531.

25. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:270.

26. The antibody heavy chain variable domain according to claim 25, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:532; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:317; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:533.

27. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:272.

28. The antibody heavy chain variable domain according to claim 27, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ

ID NO:534; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:323; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:535.

29. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:274.

30. The antibody heavy chain variable domain according to claim 29, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:536; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:329; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:537.

31. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:276.

32. The antibody heavy chain variable domain according to claim 31, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:538; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:335; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:539.

33. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:278.

34. The antibody heavy chain variable domain according to claim 33, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:540; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:341; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:541.

35. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:280.

36. The antibody heavy chain variable domain according to claim 35, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:542; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:347; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:543.

37. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:282.

38. The antibody heavy chain variable domain according to claim 37, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:544; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:353; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:545.

39. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:284.

40. The antibody heavy chain variable domain according to claim 39, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:546; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:359; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:547.

41. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:286.

42. The antibody heavy chain variable domain according to claim 41, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:548; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:365; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:549.

43. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:288.

44. The antibody heavy chain variable domain according to claim 43, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:550; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:371; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:551.

45. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:290.

46. The antibody heavy chain variable domain according to claim 45, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:552; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:377; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:553.

47. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:292.

48. The antibody heavy chain variable domain according to claim 47, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:554; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:383; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:555.

49. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:294.

50. The antibody heavy chain variable domain according to claim 49, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:556; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:389; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:557.

51. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:296.

52. The antibody heavy chain variable domain according to claim 51, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:558; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:395; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:559.

53. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:298.

54. The antibody heavy chain variable domain according to claim 53, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:560; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:401; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:561.

55. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:300.

56. The antibody heavy chain variable domain according to claim 55, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ

ID NO:562; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:407; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:563.

57. An antibody heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:302.

58. The antibody heavy chain variable domain according to claim 57, wherein the amino acid sequence comprises: a CDR1 sequence represented by the amino acid sequence of SEQ ID NO:564; a CDR2 sequence represented by the amino acid sequence of SEQ ID NO:413; and a CDR3 sequence represented by the amino acid sequence of SEQ ID NO:565.

59. An antibody heavy chain comprising an antibody heavy chain variable domain according to any one of claims 1-58 and an amino acid sequence at least 90% identical to an antibody constant region.

60. The antibody heavy chain of claim 59, wherein the antibody constant region is a human IgG constant region comprising hinge, CH2, and CH3 domains.

61. The antibody heavy chain of claim 60, wherein the antibody constant region is a human IgG constant region further comprising a CH1 domain.

62. The antibody heavy chain according to any one of claims 59-61, wherein the antibody constant region is an IgG1 constant region.

63. The antibody heavy chain according to claim 62, wherein the amino acid sequence at least 90% identical to an 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, L351, S354, E356, E357, K360, Q362, S364, T366, L368, K370, N390, K392, T394, D399, S400, D401, F405, Y407, K409, T411, and K439.

64. The antibody heavy chain of claim 63, wherein the amino acid sequence at least 90% identical to an antibody constant region differs from the amino acid sequence of an IgG1 constant region by one or more substitutions selected from the group consisting of Q347E, Q347R, Y349S, Y349K, Y349T, Y349D, Y349E, Y349C, 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, D399R, D399K,

D399V, S400K, S400R, D401K, F405A, F405T, Y407A, Y407I, Y407V, K409F, K409W, K409D, T411D, T411E, K439D, and K439E.

65. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 1 or 2, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:10.

66. The antigen-binding site according to claim 65, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:48, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:49, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:50.

67. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 3 or 4, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:2.

68. The antigen-binding site according to claim 67, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:24, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:25, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:26.

69. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 5 or 6, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:4.

70. The antigen-binding site according to claim 69, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:30, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:31, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:32.

71. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 7 or 8, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:6.

72. The antigen-binding site according to claim 71, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:36, a

CDR2 sequence identical to the amino acid sequence of SEQ ID NO:37, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:38.

73. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 9 or 10, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:8.

74. The antigen-binding site according to claim 73, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:42, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:43, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:44.

75. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 11 or 12, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:12.

76. The antigen-binding site according to claim 75, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:54, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:55, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:56.

77. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 13 or 14, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:14.

78. The antigen-binding site according to claim 77, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:60, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:61, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:62.

79. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 15 or 16, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:16.

80. The antigen-binding site according to claim 79, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:66, a

CDR2 sequence identical to the amino acid sequence of SEQ ID NO:67, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:68.

81. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 17 or 18, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:18.

82. The antigen-binding site according to claim 81, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:72, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:73, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:74.

83. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 19 or 20, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:20.

84. The antigen-binding site according to claim 83, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:78, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:79, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:80.

85. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 21 or 22, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:267.

86. The antigen-binding site according to claim 85, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:307, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:308, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:309.

87. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 23 or 24, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:269.

88. The antigen-binding site according to claim 87, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:313,

a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:314, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:315.

89. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 25 or 26, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:271.

90. The antigen-binding site according to claim 89, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:319, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:320, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:321.

91. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 27 or 28, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:273.

92. The antigen-binding site according to claim 91, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:325, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:326, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:327.

93. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 29 or 30, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:275.

94. The antigen-binding site according to claim 93, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:331, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:332, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:333.

95. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 31 or 32, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:277.

96. The antigen-binding site according to claim 95, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:337,

a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:338, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:339.

97. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 33 or 34, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:279.

98. The antigen-binding site according to claim 97, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:343, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:344, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:345.

99. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 35 or 36, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:281.

100. The antigen-binding site according to claim 99, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:349, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:350, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:351.

101. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 37 or 38, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:283.

102. The antigen-binding site according to claim 101, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:355, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:356, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:357.

103. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 39 or 40, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:285.

104. The antigen-binding site according to claim 103, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:361,

a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:362, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:363.

105. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 41 or 42, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:287.

106. The antigen-binding site according to claim 105, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:367, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:368, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:369.

107. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 43 or 44, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:289.

108. The antigen-binding site according to claim 107, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:373, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:374, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:375.

109. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 45 or 46, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:291.

110. The antigen-binding site according to claim 109, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:379, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:380, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:381.

111. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 47 or 48, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:293.

112. The antigen-binding site according to claim 111, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:385,

a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:386, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:387.

113. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 49 or 50, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:295.

114. The antigen-binding site according to claim 113, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:391, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:392, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:393.

115. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 51 or 52, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:297.

116. The antigen-binding site according to claim 115, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:397, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:398, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:399.

117. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 53 or 54, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:299.

118. The antigen-binding site according to claim 117, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:403, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:404, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:405.

119. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 55 or 56, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:301.

120. The antigen-binding site according to claim 119, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:409,

a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:410, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:411.

121. An antigen-binding site comprising the antibody heavy chain variable domain according to claim 57 or 58, and an antibody light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO:303.

122. The antigen-binding site according to claim 121, wherein the light chain variable domain includes a CDR1 sequence identical to the amino acid sequence of SEQ ID NO:415, a CDR2 sequence identical to the amino acid sequence of SEQ ID NO:416, and a CDR3 sequence identical to the amino acid sequence of SEQ ID NO:417.

123. A protein comprising the antigen-binding site according to any one of claims 65–122, wherein the antigen-binding site binds to human CD33.

124. The protein of claim 123, wherein the protein further comprises a second antigen binding site same or different from the antigen-binding site that binds to human CD33.

125. The protein of claim 123 or 124, further comprising an antibody constant region.

126. The protein of claims 125, wherein the antibody constant region is capable of binding to CD16 and comprises two polypeptide chains, each of which comprises a hinge, CH2 and CH3 domain.

127. The protein of claim 125 or 126, wherein each of the two polypeptide chains of the antibody constant region comprises amino acid sequence at least 90% identical to human IgG1 constant region.

128. The protein of claim 127, 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, L351, S354, E356, E357, K360, Q362, S364, T366, L368, K370, K392, T394, D399, S400, D401, F405, Y407, K409, T411 and K439; and 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, Y349, L351, S354, E356, E357, S364, T366, L368, K370, N390, K392, T394, D399, D401, F405, Y407, K409, T411 and K439.

129. The protein of claim 127, wherein 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.

130. The protein of claim 127, wherein 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.

131. The protein of claim 127, wherein 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.

132. The protein of claim 127, wherein 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.

133. The protein of claim 127, wherein 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.

134. The protein of claim 127, wherein 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.

135. The protein of claim 127, wherein 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.

136. The protein of claim 127, wherein 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.

137. The protein of claim 127, wherein 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.

138. The protein of claim 127, wherein 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.

139. The protein of claim 127, wherein 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.

140. The protein of claim 127, wherein 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.

141. The protein of claim 127, wherein 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.

142. The protein of claim 127, wherein 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.

143. The protein of claim 127, wherein 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.

144. The protein of claim 127, wherein 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.

145. The protein of claim 127, wherein 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.

146. The protein of claim 127, wherein 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.

147. The protein of claim 127, wherein 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.

148. The protein of claim 127, wherein 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.

149. A protein comprising an antigen-binding site that competes for binding to human and cynomolgus CD33 with an antibody comprising an antibody heavy chain variable domain and an antibody light chain variable domain having the amino acid sequences of SEQ ID NOs: 1 and 2; 3 and 4; 5 and 6; 7 and 8; 9 and 10; 11 and 12; 13 and 14; 15 and 16; 17 and 18; 19 and 20; 266 and 267; 268 and 269; 270 and 271; 272 and 273; 274 and 275; 276 and 277; 278 and 279; 280 and 281; 282 and 283; 284 and 285; 286 and 287; 288 and 289; 290

and 291; 292 and 293; 294 and 295; 296 and 297; 298 and 299; 300 and 301; or 302 and 303, respectively.

150. A formulation comprising a protein of any one of claims 123-149, and a pharmaceutically acceptable carrier.

151. An isolated nucleic acid encoding a chimeric antigen receptor (CAR), wherein the nucleic acid comprises a nucleic acid sequence that encodes a CD33-binding scFv comprising a sequence at least 90% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484; a nucleic acid sequence encoding a transmembrane domain; and a nucleic acid sequence encoding an intracellular signaling domain.

152. An isolated nucleic acid encoding a chimeric antigen receptor (CAR), wherein the nucleic acid comprises a nucleic acid sequence that encodes a CD33-binding scFv comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484; a nucleic acid sequence encoding a transmembrane domain; and a nucleic acid sequence encoding an intracellular signaling domain.

153. An isolated nucleic acid encoding a chimeric antigen receptor (CAR), wherein the nucleic acid comprises a nucleic acid sequence that encodes a CD33-binding scFv comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484; a nucleic acid sequence encoding a transmembrane domain; and a nucleic acid sequence encoding an intracellular signaling domain.

154. The isolated nucleic acid sequence of any one of claims 151-153, wherein the transmembrane domain is selected from the transmembrane regions of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD152, and CD154.

155. The isolated nucleic acid of any one of claims 151-154, wherein the CD33-binding scFv is connected to the transmembrane domain by a hinge region.

156. The isolated nucleic acid of any one of claims 151-155, wherein the intracellular signaling domain comprises a primary signaling domain comprising a functional signaling domain of CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12.

157. The isolated nucleic acid of any one of claims 151-156, wherein the intracellular signaling domain further comprises a costimulatory signaling domain comprising a functional signaling domain of a costimulatory receptor.

158. The isolated nucleic acid of claim 157, wherein the costimulatory receptor is selected from the group consisting of OX40, CD27, CD28, CD30, CD40, PD-1, CD2, CD7, CD258, NKG2C, B7-H3, a ligand that binds to CD83, ICAM-1, LFA-1 (CD11a/CD18), ICOS and 4-1BB (CD137), or any combination thereof.

159. An expression vector comprising the isolated nucleic acid of any one of claims 111-118.

160. A chimeric antigen receptor (CAR), wherein the CAR comprises a CD33-binding scFv comprising amino acid sequence at least 90% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484; a transmembrane domain; and an intracellular signaling domain.

161. The CAR of claim 160, wherein the transmembrane domain is selected from the transmembrane regions of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD152, and CD154.

162. The CAR of claim 160 or 161, wherein the CD33-binding scFv is connected to the transmembrane domain by a hinge region.

163. The CAR of any one of claims 160-162, wherein the intracellular signaling domain comprises a primary signaling domain comprising a functional signaling domain of CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12.

164. The CAR of any one of claims 160-163, wherein the intracellular signaling domain further comprises a costimulatory signaling domain comprising a functional signaling domain of a costimulatory receptor.

165. The CAR of claim 164, wherein the costimulatory receptor is selected from the group consisting of OX40, CD27, CD28, CD30, CD40, PD-1, CD2, CD7, CD258, NKG2C, B7-H3,

a ligand that binds to CD83, ICAM-1, LFA-1 (CD11a/CD18), ICOS and 4-1BB (CD137), or any combination thereof.

166. An immune effector cell comprising the nucleic acid of any one of claims 151-158.

167. An immune effector cell comprising the vector of claim 159.

168. An immune effector cell expressing the CAR of any one of claims 160-165.

169. The immune effector cell of any one of claims 166-168, wherein the immune effector cell is a T cell.

170. The immune effector cell of claim 169, wherein the T cell is a $CD8^+$ T cell, a $CD4^+$ T cell, or an NKT cell.

171. The immune effector cell of any one of claims 166-168, wherein the immune effector cell is an NK cell.

172. A CD33/CD3-directed bispecific T-cell engager comprising a protein comprising a sequence at least 90% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484.

173. A CD33/CD3-directed bispecific T-cell engager comprising a protein comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484.

174. A CD33/CD3-directed bispecific T-cell engager comprising a protein comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484.

175. An isolated nucleic acid encoding the CD33/CD3-directed bispecific T-cell engager of any one of claims 172-174.

176. An antibody-drug conjugate comprising a protein comprising a sequence at least 90% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484.

177. An antibody-drug conjugate comprising a protein comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484.

178. An antibody-drug conjugate comprising a protein comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484.

179. The antibody-drug conjugate of any one of claims 176-178, further comprising a drug moiety selected from auristatin, N-acetyl-γ calicheamicin, maytansinoid, pyrrolobenzodiazepine, and SN-38.

180. An immunocytokine comprising a sequence at least 90% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484, connected to a cytokine.

181. An immunocytokine comprising a sequence at least 95% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484, connected to a cytokine.

182. An immunocytokine comprising a sequence at least 99% identical to an amino acid sequence selected from SEQ ID NOs:188, 198, 206-223, and 447-484, connected to a cytokine.

183. The immunocytokine of any one of claims 170-172, wherein the cytokine is selected from IL-2, IL-4, IL-10, IL-12, IL-15, TNF, and IFNα.

184. An isolated nucleic acid encoding an immunocytokine of any one of claims 170-173.

185. A method of treating a CD33-expressing cancer, the method comprising administering an effective amount of the protein according to any one of claims 123-149, the formulation according to claim 150, the immune effector cell according to any one of claims 166-171, the CD33/CD3-directed bispecific T-cell engager according to any one of claims 172-174, the antibody-drug conjugate according to any one of claims 176-179, or the immunocytokine according to any one of claims 180-183 to a subject in need thereof.

186. The method of claim 185, wherein the cancer is selected from the group consisting of acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), chronic lymphocytic leukemia (CML), myeloid blast crisis of CML, acute lymphoblastic leukemia (ALL), acute lymphoblastic lymphoma, myeloproliferative neoplasms (MPNs), lymphoma, non-Hodgkin lymphomas, and classical Hodgkin lymphoma.

187. The method of claim 186, wherein the AML is selected from undifferentiated acute myeloblastic leukemia, acute myeloblastic leukemia with minimal maturation, acute myeloblastic leukemia with maturation, acute promyelocytic leukemia (APL), acute myelomonocytic leukemia, acute myelomonocytic leukemia with eosinophilia, acute monocytic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia (AMKL), acute basophilic leukemia, acute panmyelosis with fibrosis, and blastic plasmacytoid dendritic cell neoplasm (BPDCN).

188. The method of claim 186 or 187, wherein the AML is characterized by expression of CLL-1 on the AML leukemia stem cells (LSCs).

189. The method of claim 188, wherein the LSCs further express a membrane marker selected from CD34, CD38, CD123, TIM3, CD25, CD32, and CD96.

190. The method of any one of claims 186-189, wherein the AML is a minimal residual disease (MRD).

191. The method of claim 190, wherein the MRD is characterized by the presence or absence of a mutation selected from *FLT3-ITD* ((Fms-like tyrosine kinase 3)-internal tandem duplications (ITD)), *NPM1* (Nucleophosmin 1), *DNMT3A* (DNA methyltransferase gene *DNMT3A)*, and *IDH* (Isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2)).

192. The method of claim 186, wherein the MDS is selected from MDS with multilineage dysplasia (MDS-MLD), MDS with single lineage dysplasia (MDS-SLD), MDS with ring sideroblasts (MDS-RS), MDS with excess blasts (MDS-EB), MDS with isolated del(5q), and MDS, unclassified (MDS-U).

193. The method of claim 186 or 192, wherein the MDS is a primary MDS or a secondary MDS.

194. The method of claim 186, wherein the ALL is selected from B-cell acute lymphoblastic leukemia (B-ALL) and T-cell acute lymphoblastic leukemia (T-ALL).

195. The method of claim 186, wherein the MPN is selected from polycythaemia vera, essential thrombocythemia (ET), and myelofibrosis.

196. The method of claim 186, wherein the non-Hodgkin lymphoma is selected from B-cell lymphoma and T-cell lymphoma.

197. The method of claim 186, wherein the lymphoma is selected from chronic lymphocytic leukemia (CLL), lymphoblastic lymphoma (LPL), diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), primary mediastinal large B-cell lymphoma (PMBL), follicular lymphoma, mantle cell lymphoma, hairy cell leukemia, plasma cell myeloma (PCM) or multiple myeloma (MM), mature T/NK neoplasms, and histiocytic neoplasms.

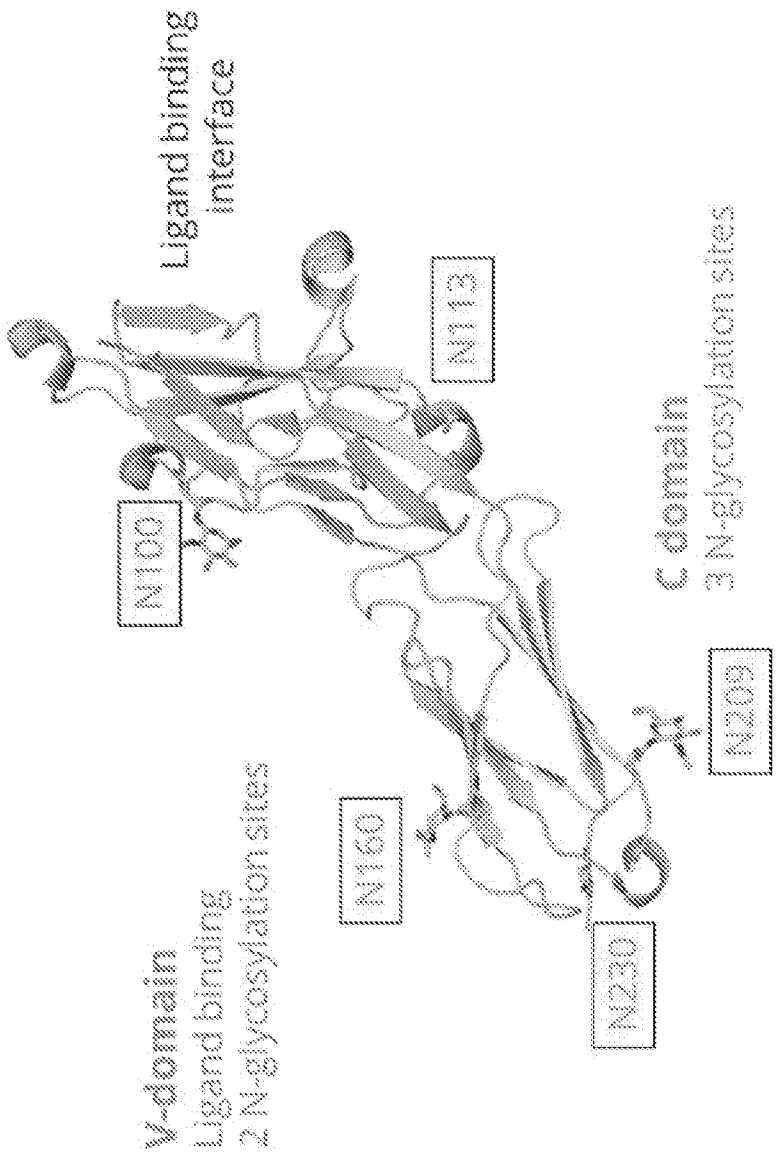

V-domain
Ligand binding
2 N-glycosylation sites
N100
Ligand binding
interface
N160
N113
N220
C domain
3 N-glycosylation sites
N209

FIG. 1

Features:
Query 1 70
Sbjct 1 89
Query 71 130
Sbjct 90 149
Query 131 190
Sbjct 150 209
Query 191 250
Sbjct 210 269
Query 251 310
Sbjct 270 325
Query 311 (SEQ ID NO:598)
Sbjct 326 (SEQ ID NO:599)

FIG. 2

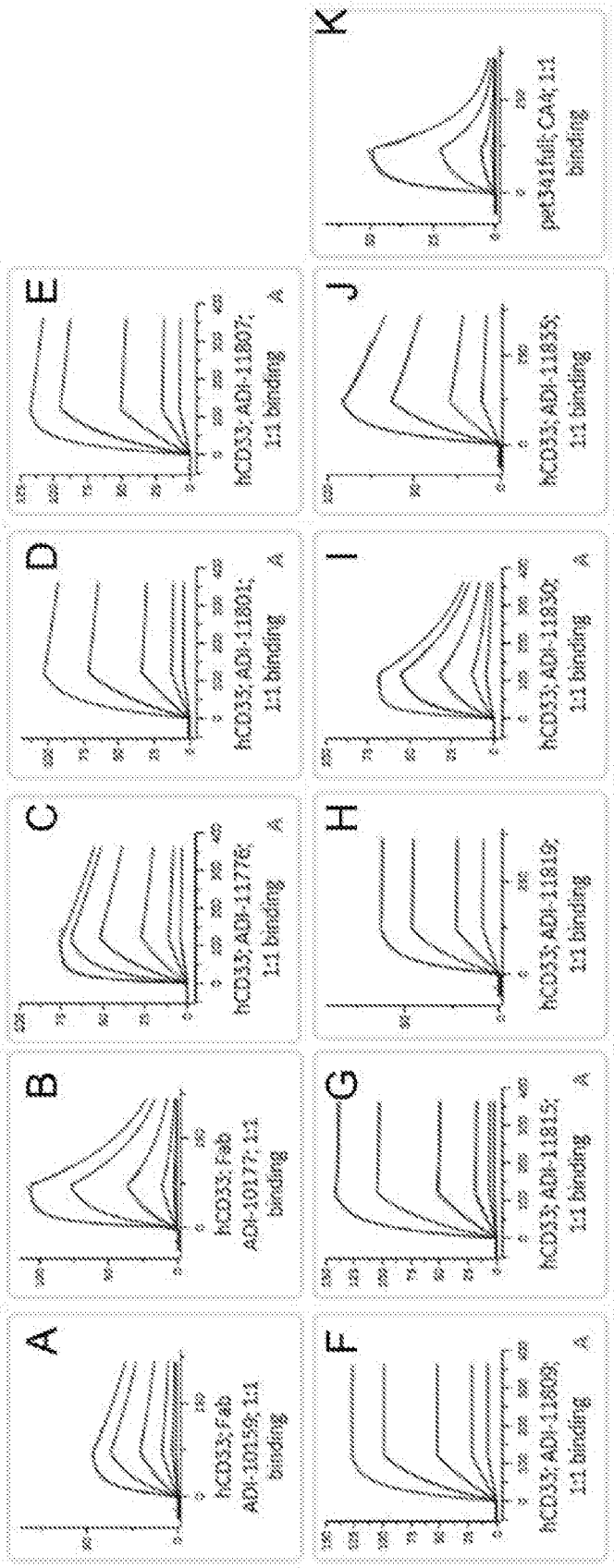

A
hCD33; Fab
ADI-10159; 1:1 binding
B
hCD33; Fab
ADI-10177; 1:1 binding
C
hCD33; ADI-11776; 1:1 binding
D
hCD33; ADI-11801; 1:1 binding
E
hCD33; ADI-11807; 1:1 binding
F
hCD33; ADI-11809; 1:1 binding
G
hCD33; ADI-11815; 1:1 binding
H
hCD33; ADI-11819; 1:1 binding
I
hCD33; ADI-11830; 1:1 binding
J
hCD33; ADI-11839; 1:1 binding
K
pet341fdll; CA4; 1:1 binding

FIG. 3

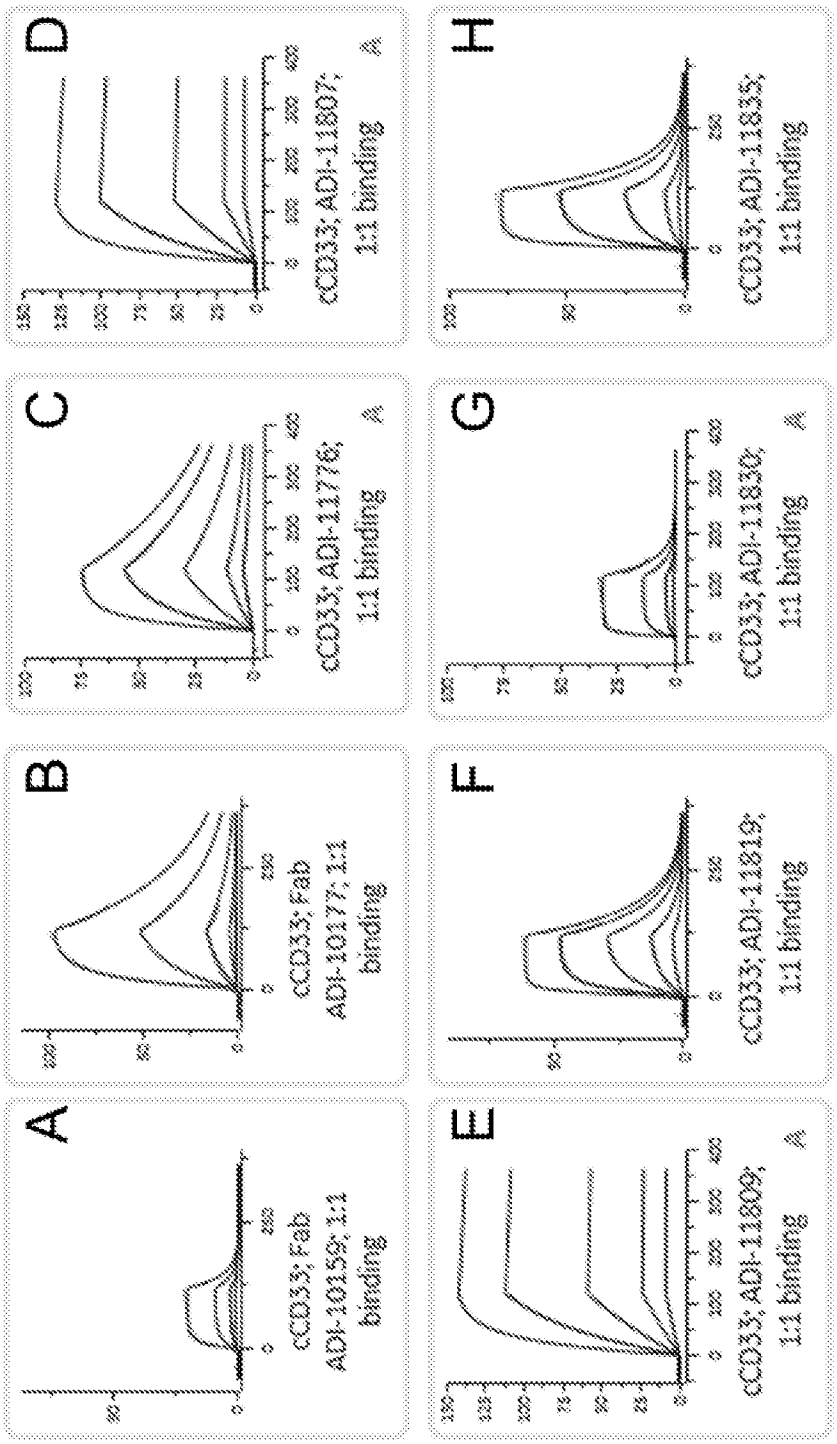

A
cCD33; Fab
ADI-10159; 1:1
binding
B
cCD33; Fab
ADI-10177; 1:1
binding
C
cCD33; ADI-11776;
1:1 binding
D
cCD33; ADI-11807;
1:1 binding
E
cCD33; ADI-11809;
1:1 binding
F
cCD33; ADI-11819;
1:1 binding
G
cCD33; ADI-11830;
1:1 binding
H
cCD33; ADI-11835;
1:1 binding

FIG. 4

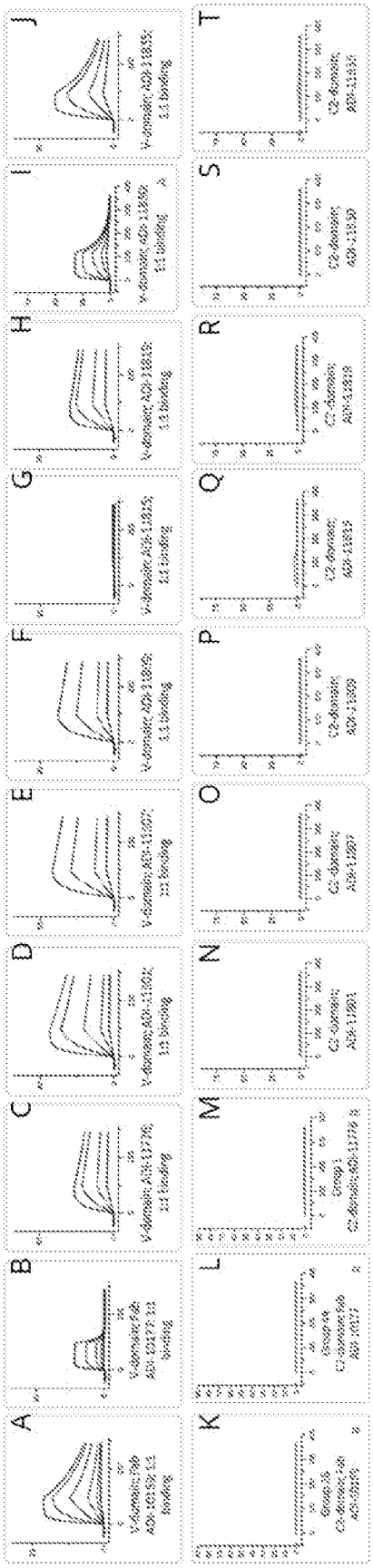


FIG. 5

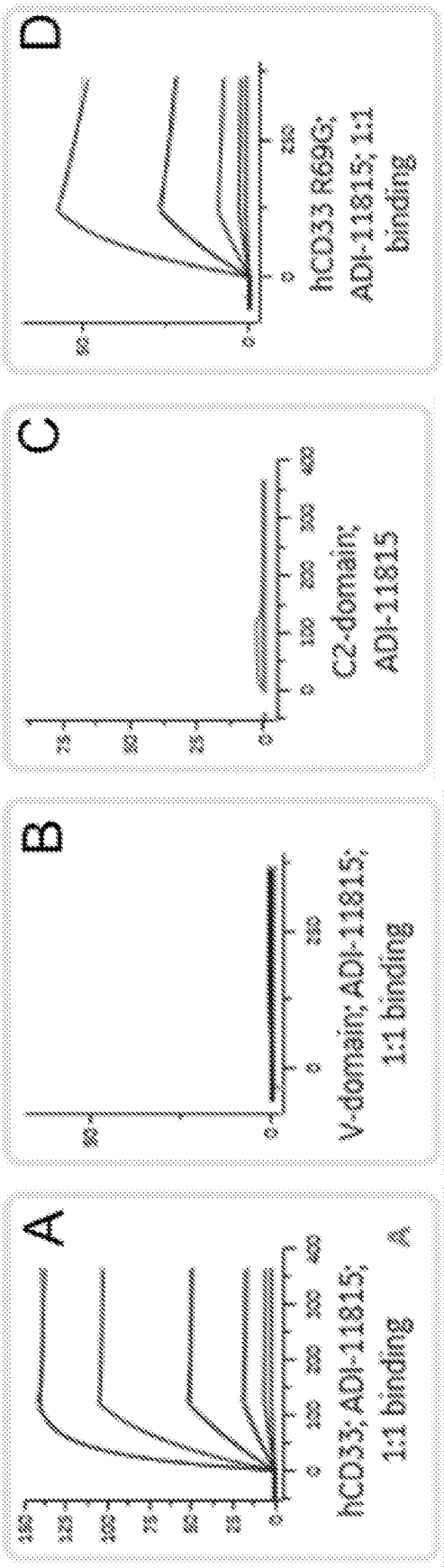

A
hCD33; ADI-11815;
1:1 binding
B
V-domain; ADI-11815;
1:1 binding
C
C2-domain;
ADI-11815
D
hCD33 R69G;
ADI-11815; 1:1
binding

FIG. 6

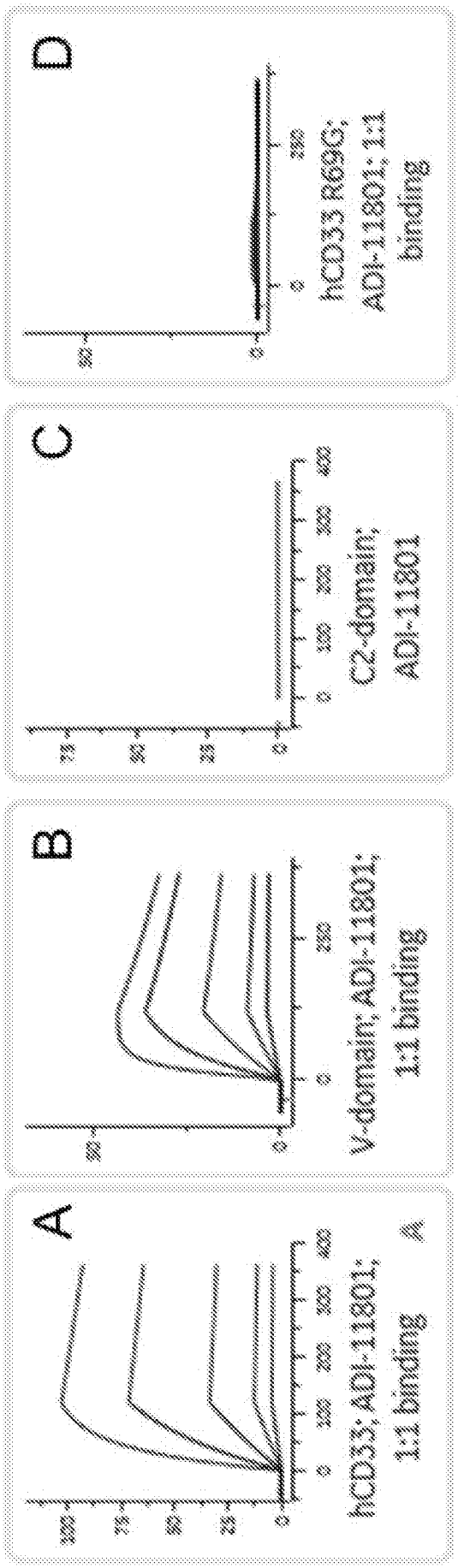

A
hCD33; ADI-11801;
1:1 binding
B
V-domain; ADI-11801;
1:1 binding
C
C2-domain;
ADI-11801
D
hCD33 R69G;
ADI-11801; 1:1
binding

FIG. 7

FIG. 8

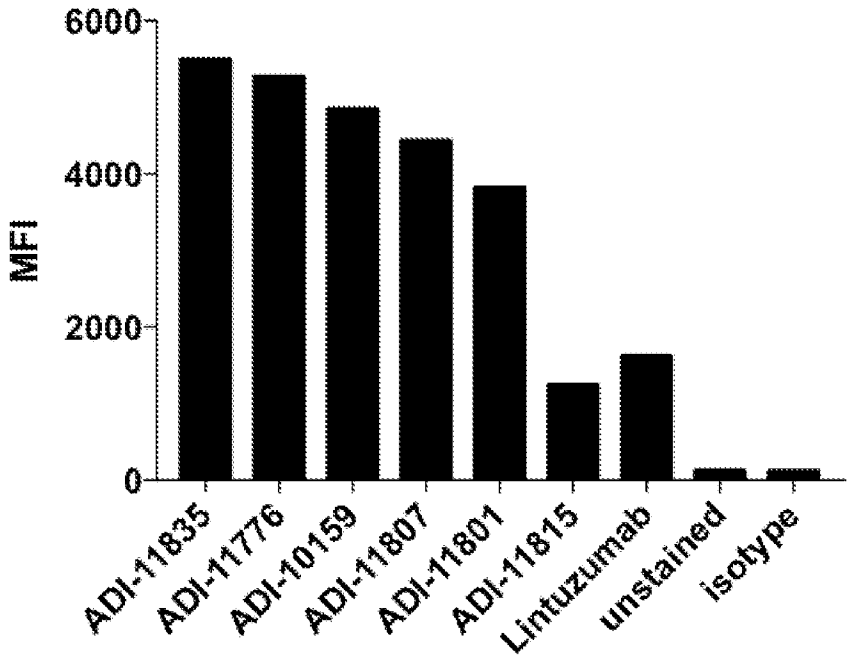

6000
4000
2000
0
MFI
ADI-11835
ADI-11776
ADI-10159
ADI-11807
ADI-11801
ADI-11815
Lintuzumab
unstained
isotype

FIG. 9

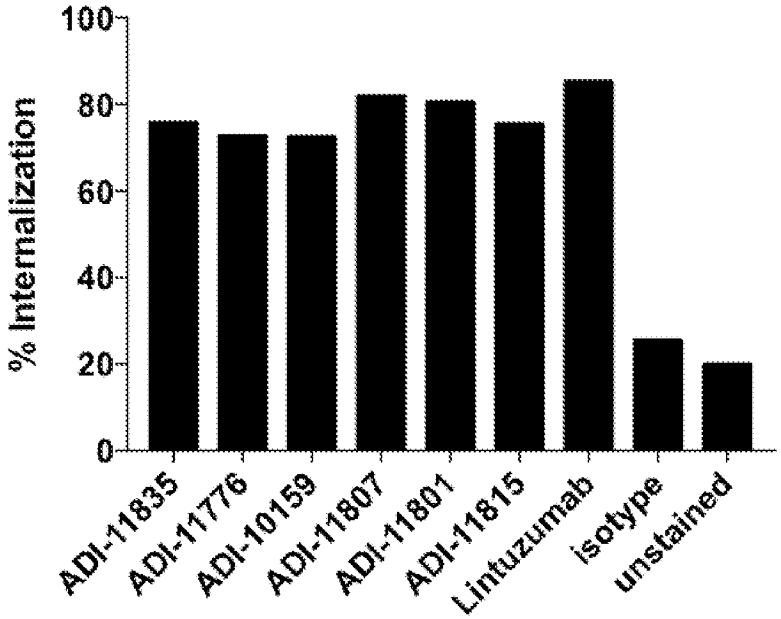

100
80
60
40
20
0
% Internalization
ADI-11835
ADI-11776
ADI-10159
ADI-11807
ADI-11801
ADI-11815
Lintuzumab
isotype
unstained

FIG. 10A

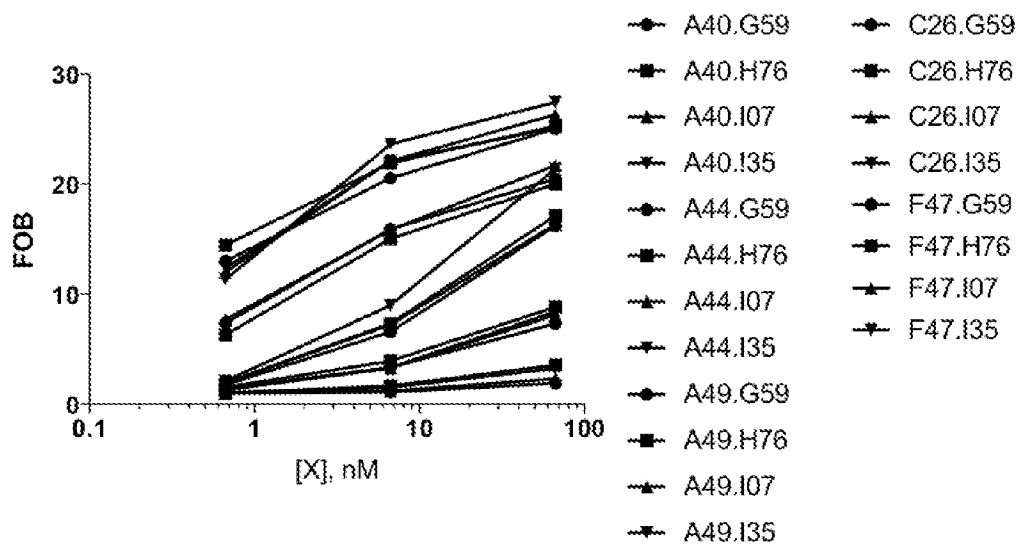


FIG. 10B

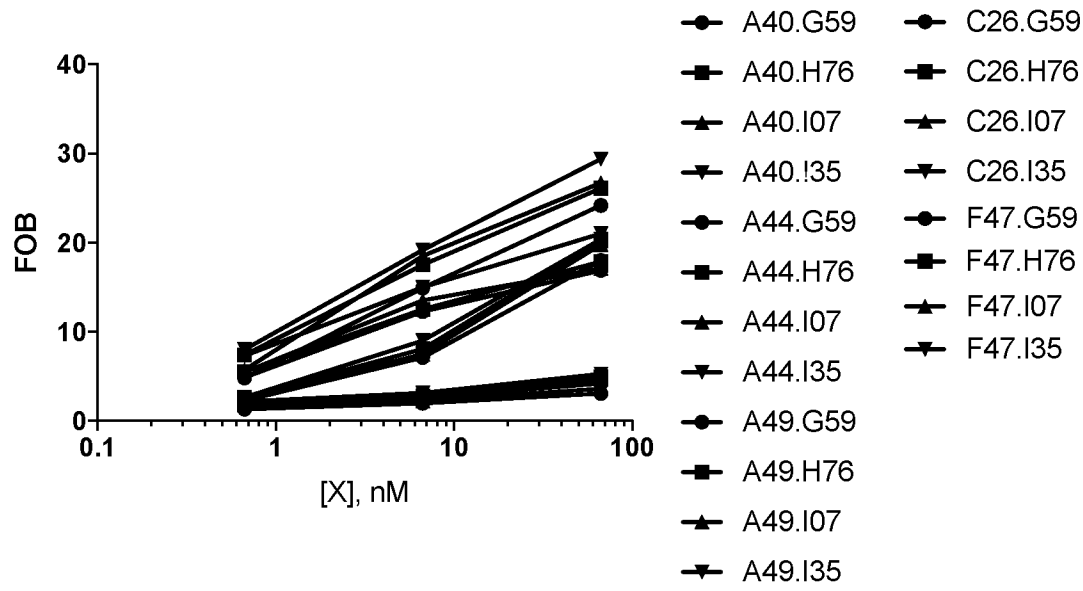


FIG. 11

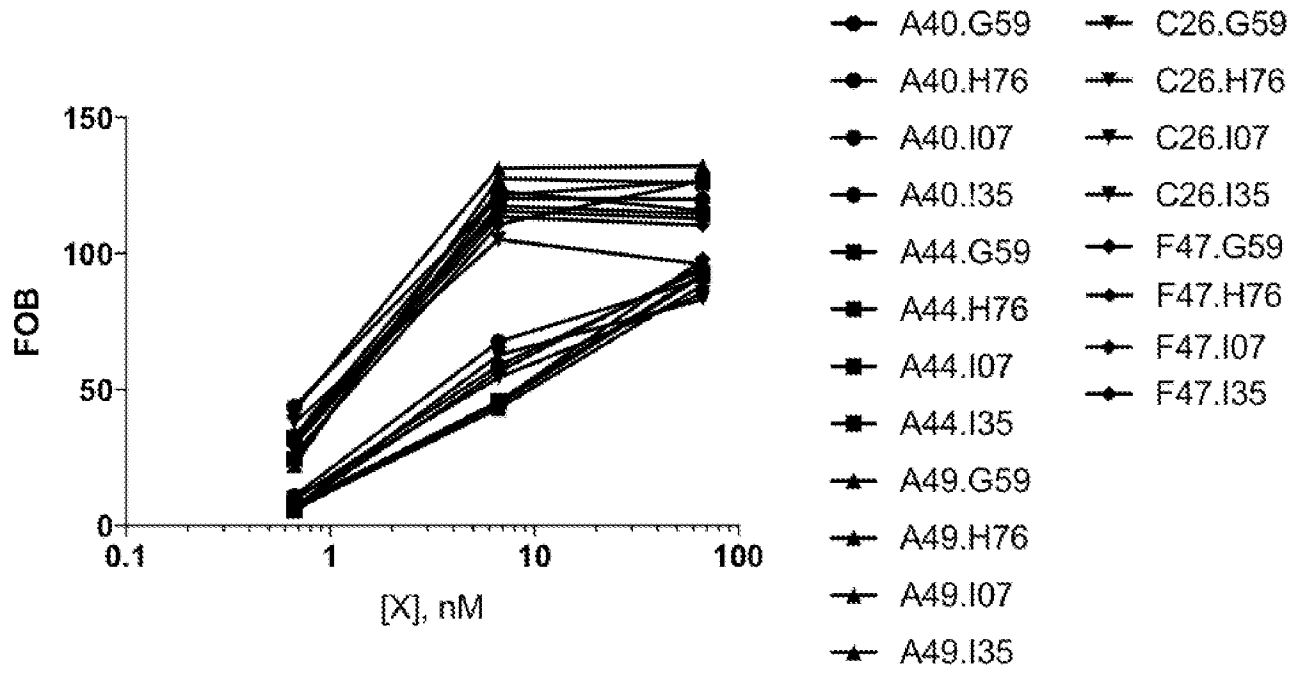

150
100
50
0
FOB
0.1
1
10
100
[X], nM
A40.G59
A40.H76
A40.I07
A40.I35
A44.G59
A44.H76
A44.I07
A44.I35
A49.G59
A49.H76
A49.I07
A49.I35
C26.G59
C26.H76
C26.I07
C26.I35
F47.G59
F47.H76
F47.I07
F47.I35

Fig. 12

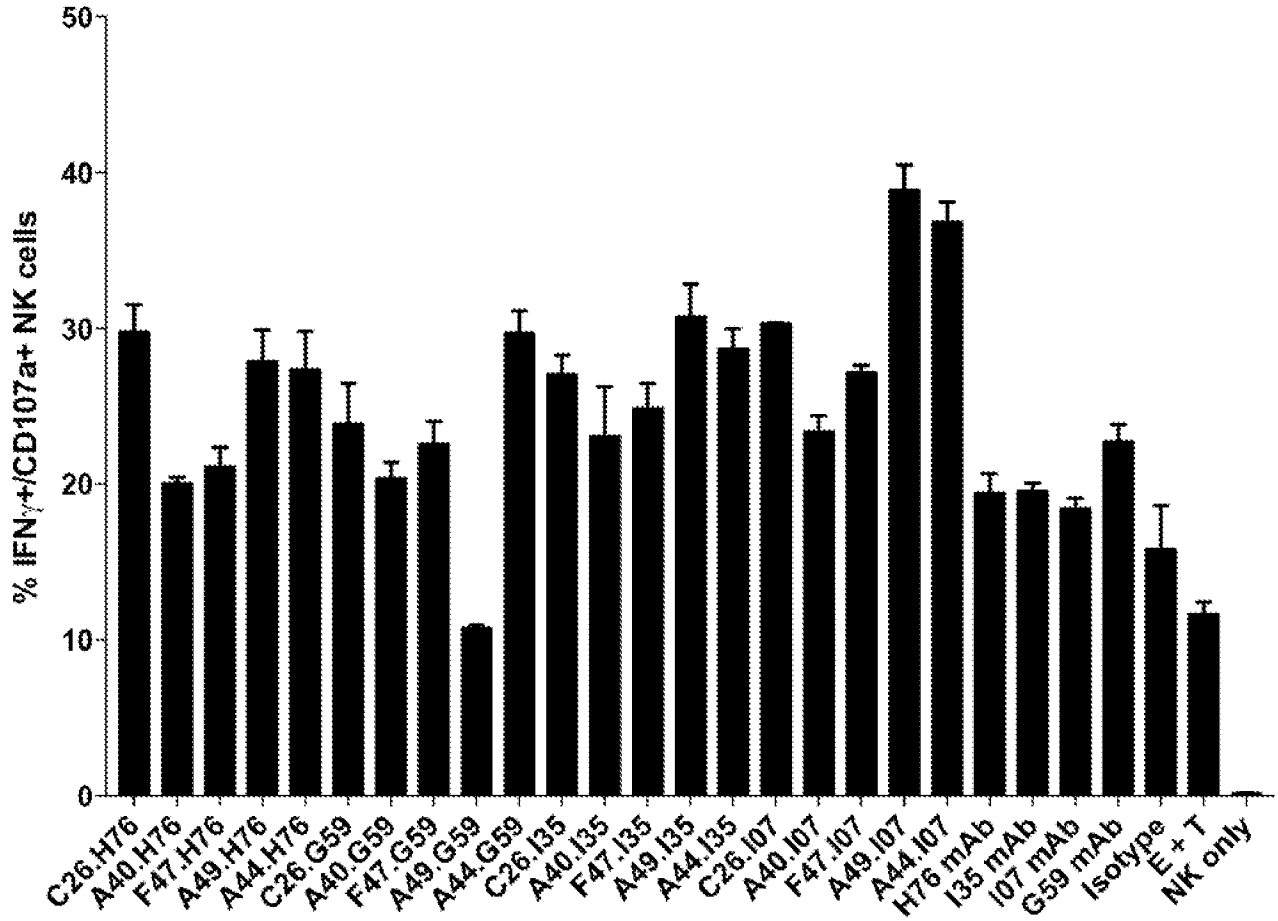

% IFNγ+/CD107a+ NK cells
50
40
30
20
10
0
C26.H76
A40.H76
F47.H76
A49.H76
A44.H76
C26.G59
A40.G59
F47.G59
A49.G59
A44.G59
C26.I35
A40.I35
F47.I35
A49.I35
A44.I35
C26.I07
A40.I07
F47.I07
A49.I07
A44.I07
H76 mAb
I35 mAb
I07 mAb
G59 mAb
Isotype
E + T
NK only

FIG. 13

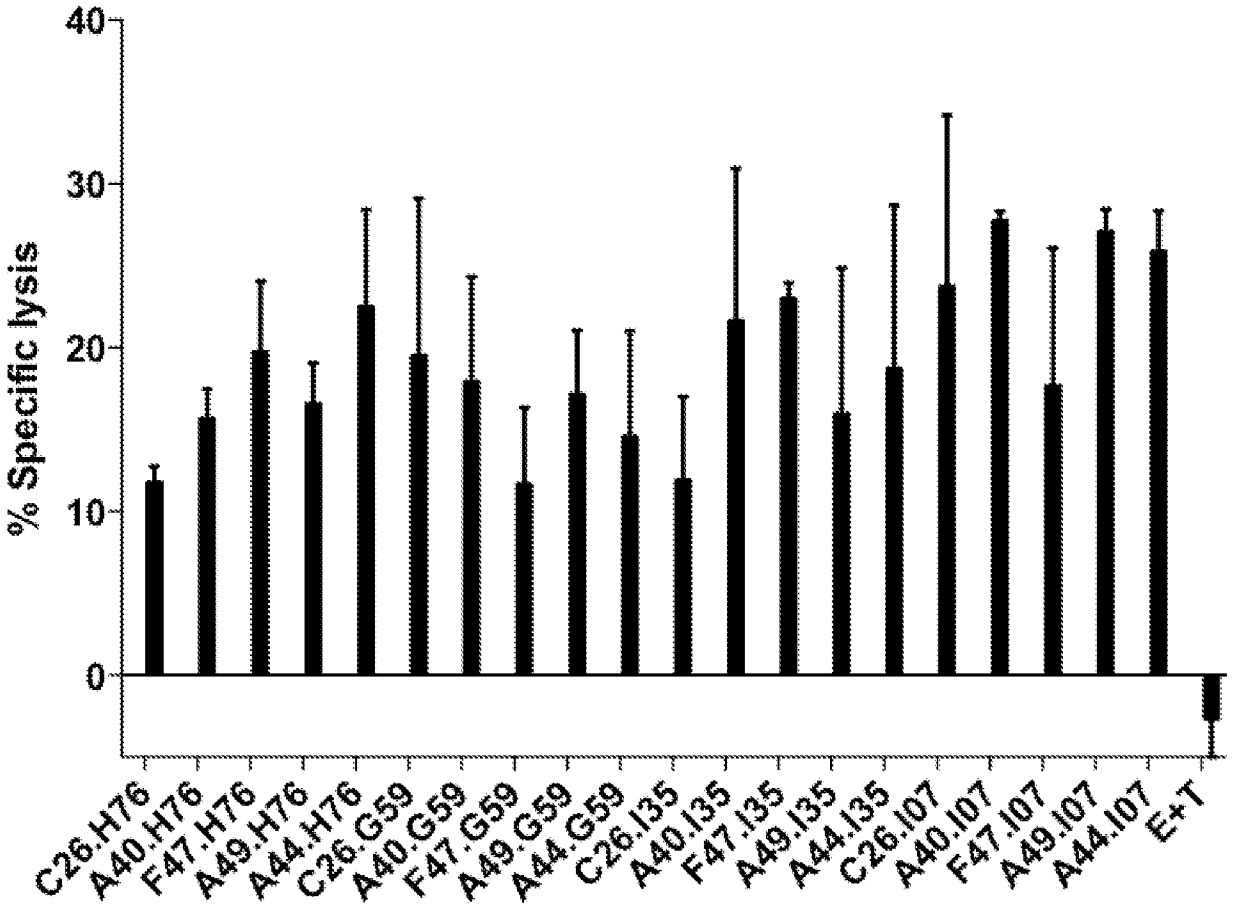

% Specific lysis
40
30
20
10
0
C26.H76
A40.H76
F47.H76
A49.H76
A44.H76
C26.G59
A40.G59
F47.G59
A49.G59
A44.G59
C26.I35
A40.I35
F47.I35
A49.I35
A44.I35
C26.I07
A40.I07
F47.I07
A49.I07
A44.I07
E+T

FIG. 14

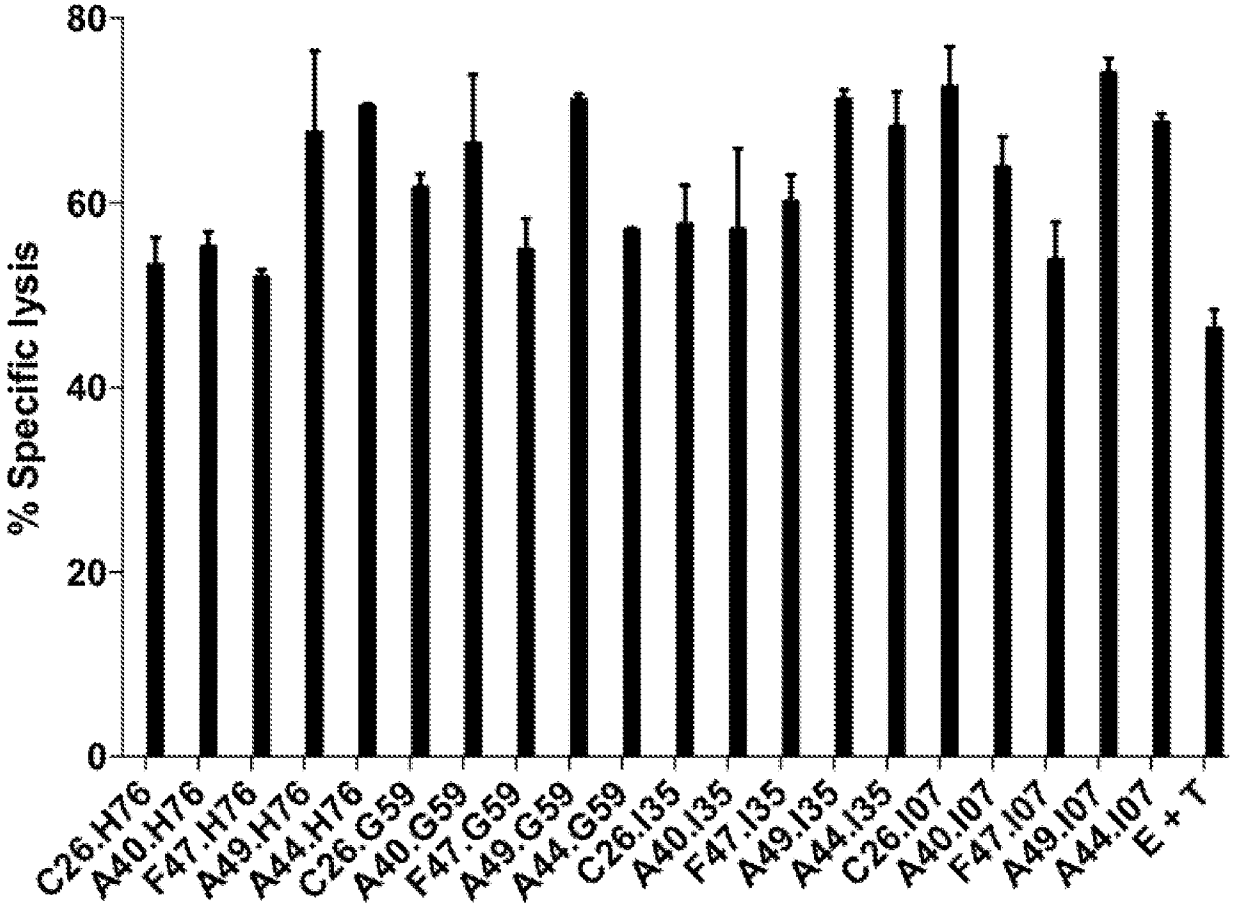

% Specific lysis
0
20
40
60
80
C26.H76
A40.H76
F47.H76
A49.H76
A44.H76
C26.G59
A40.G59
F47.G59
A49.G59
A44.G59
C26.I35
A40.I35
F47.I35
A49.I35
A44.I35
C26.I07
A40.I07
F47.I07
A49.I07
A44.I07
E + T

FIG. 15A

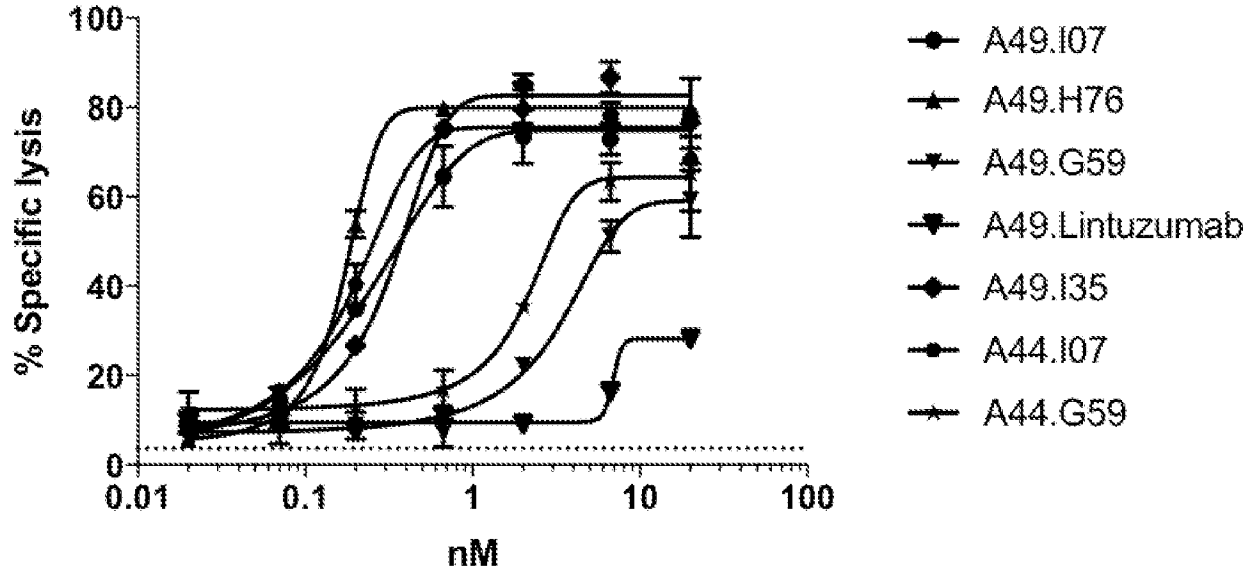


FIG. 15B

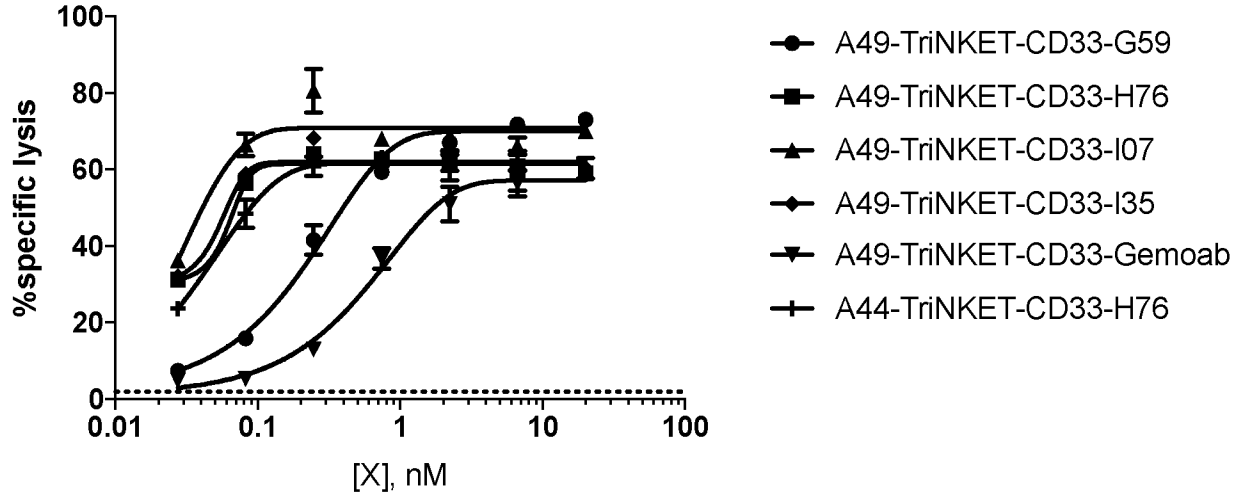


FIG. 16

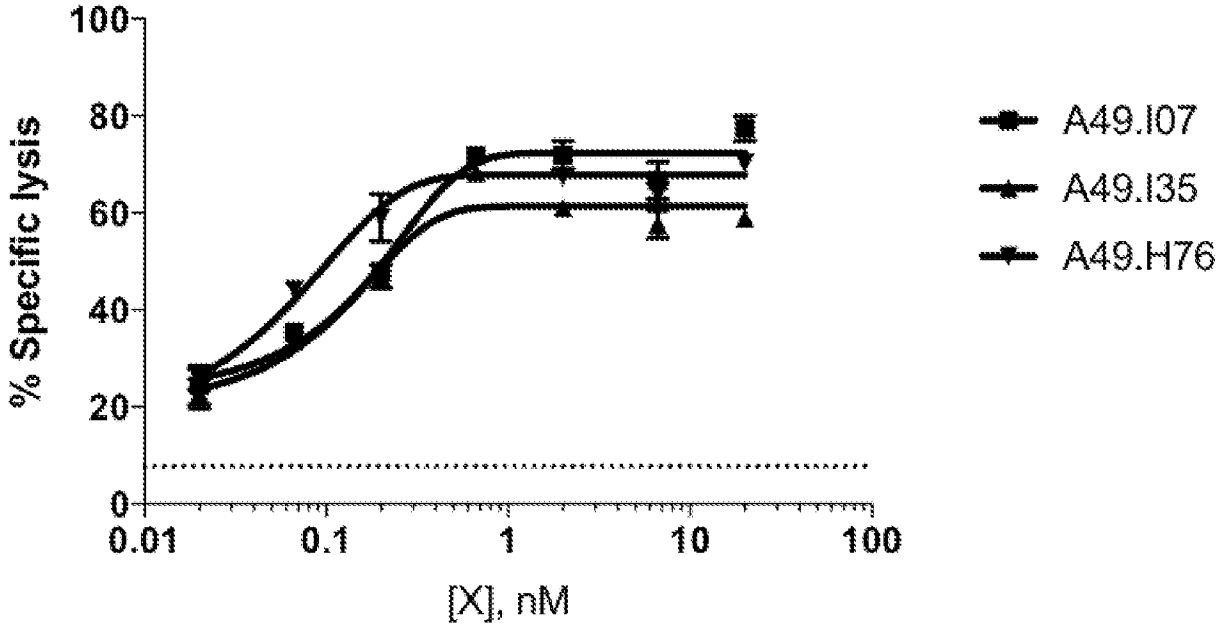

100
80
60
40
20
0
% Specific lysis
0.01
0.1
1
10
100
[X], nM
A49.I07
A49.I35
A49.H76

FIG. 17A

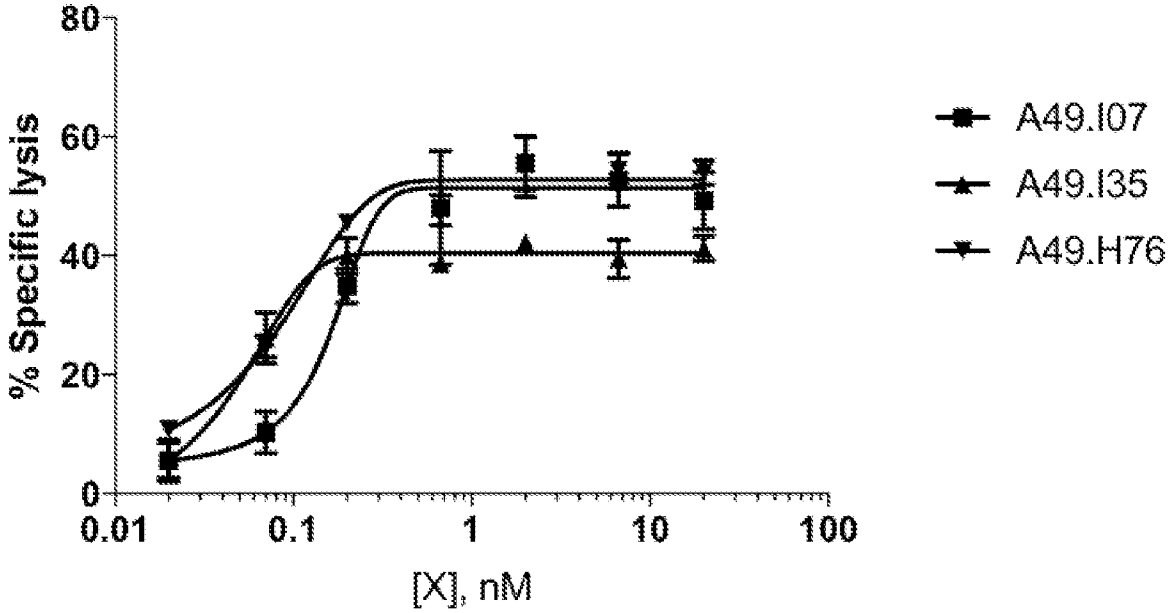


FIG. 17B

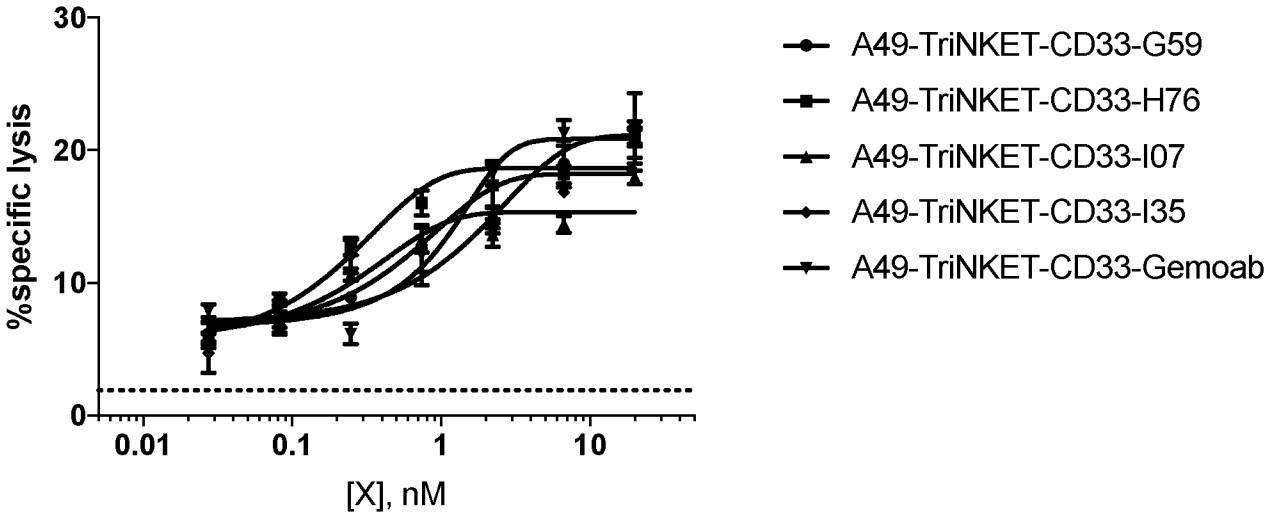


FIG. 18

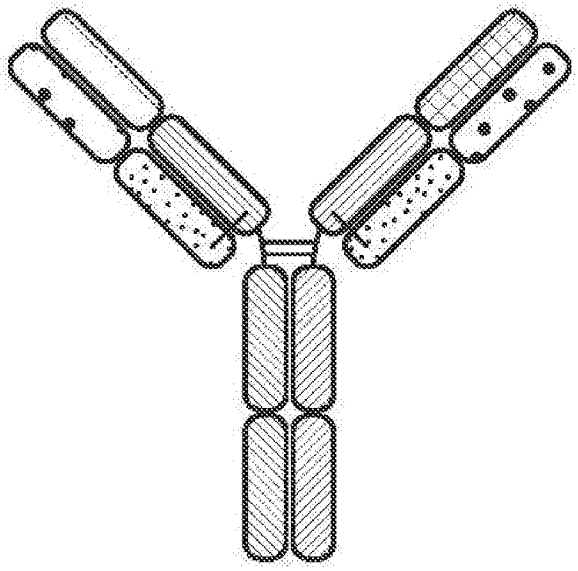


FIG. 19

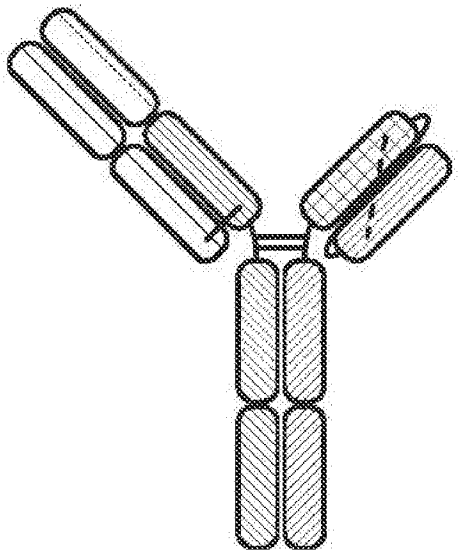


FIG. 20

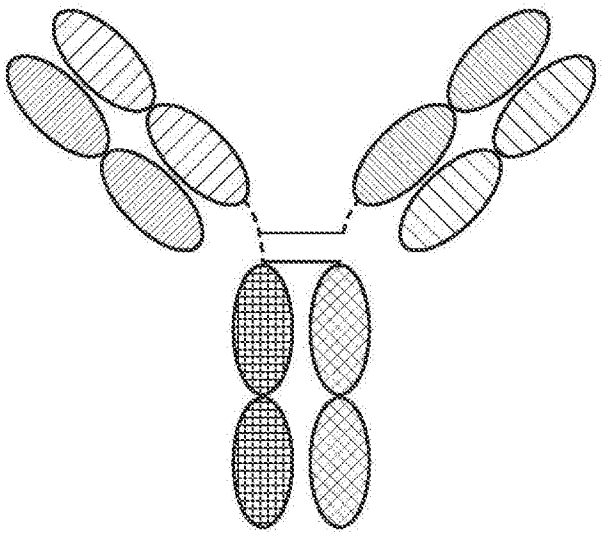


FIG. 21

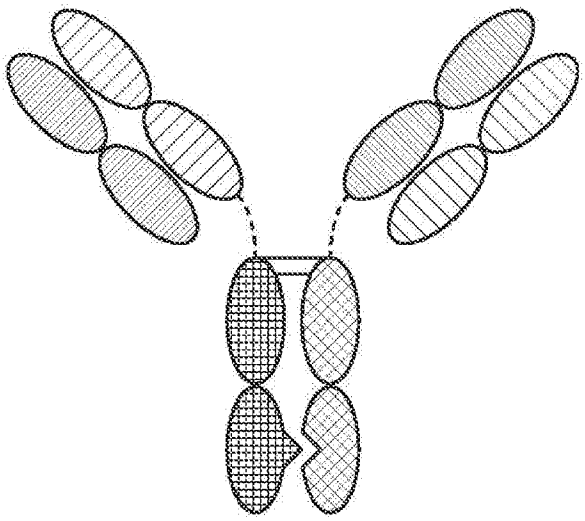


FIG. 22

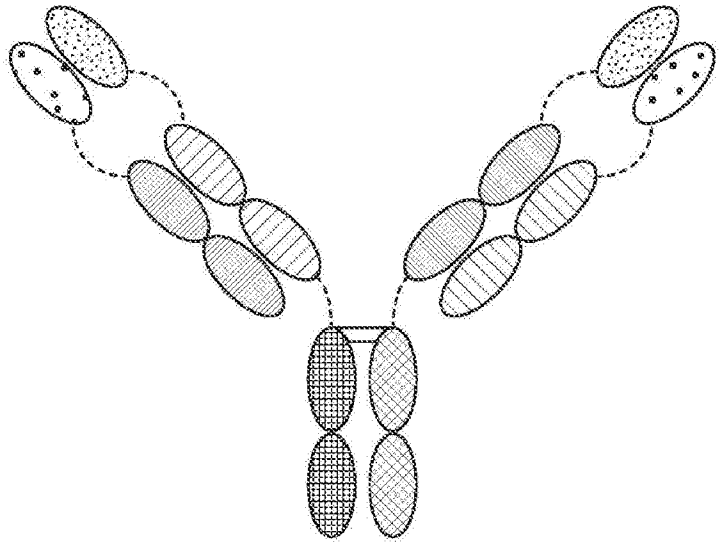


FIG. 23

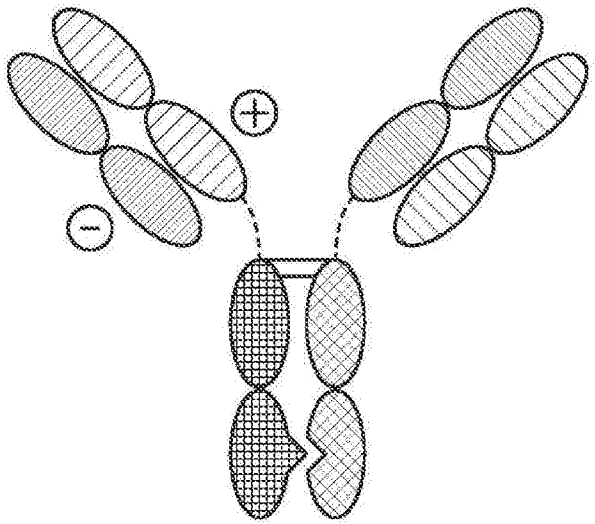


FIG. 24

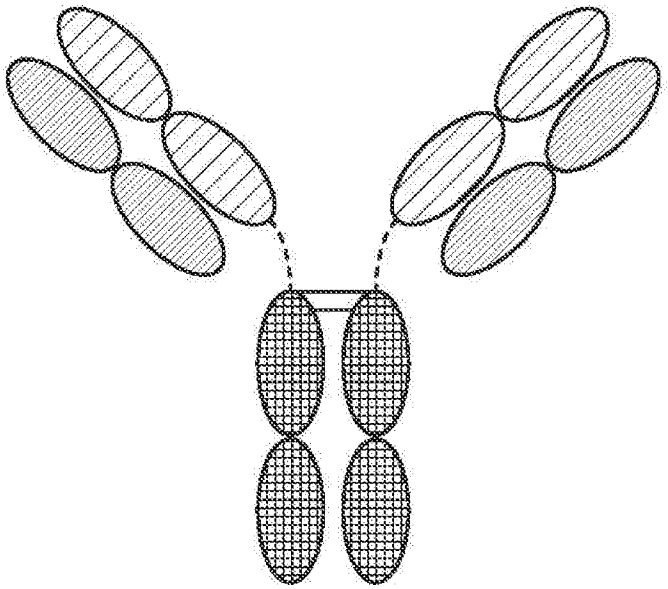


FIG. 25

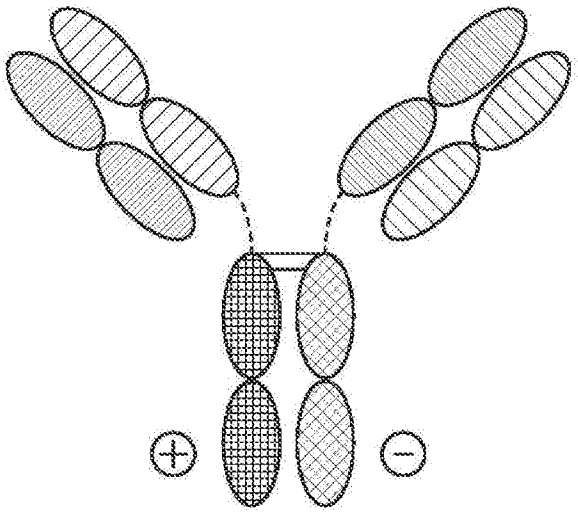


FIG. 26

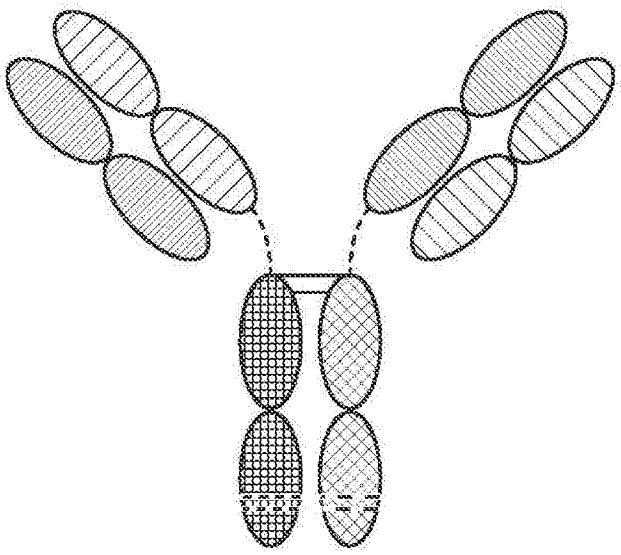


FIG. 27

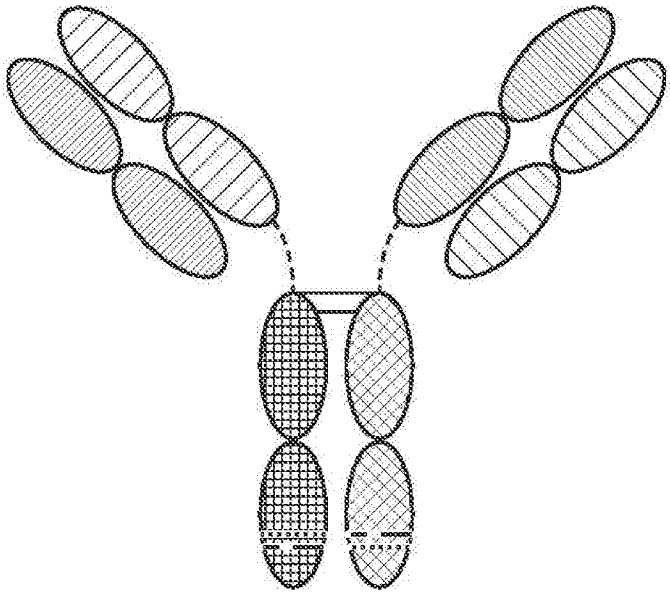


FIG. 28

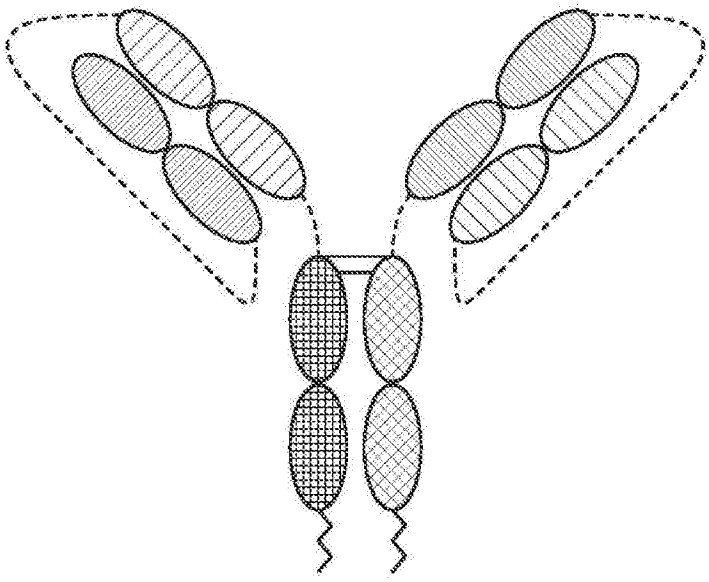


FIG. 29

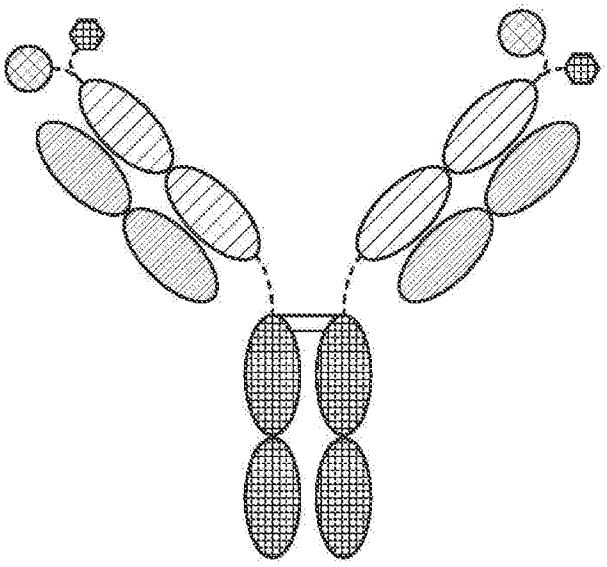


FIG. 30A

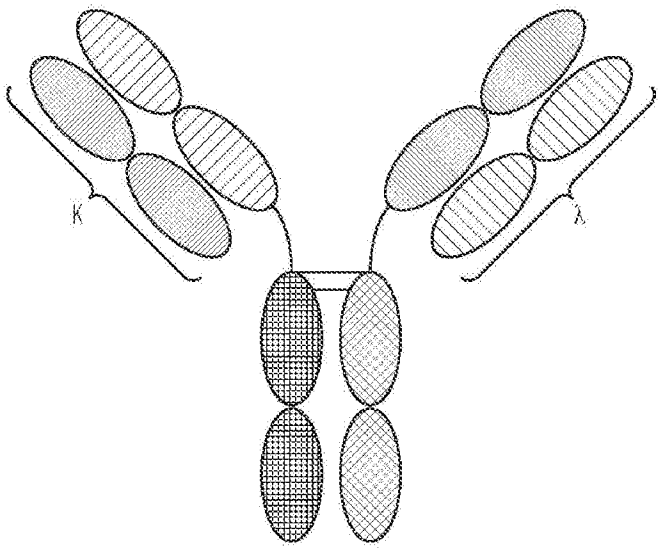


FIG. 30B

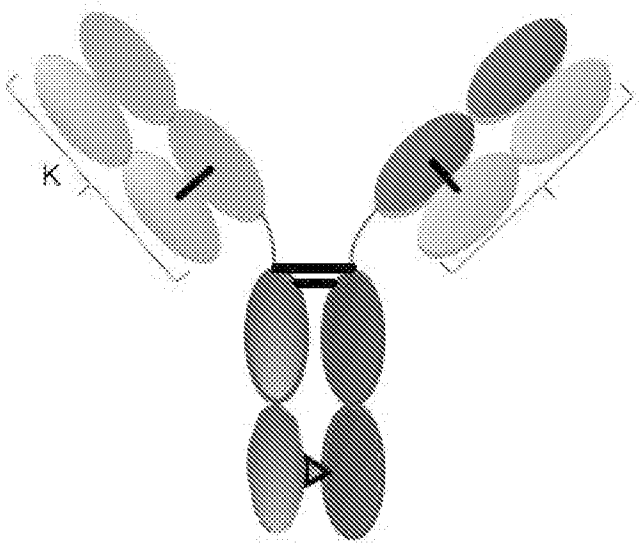


FIG. 31

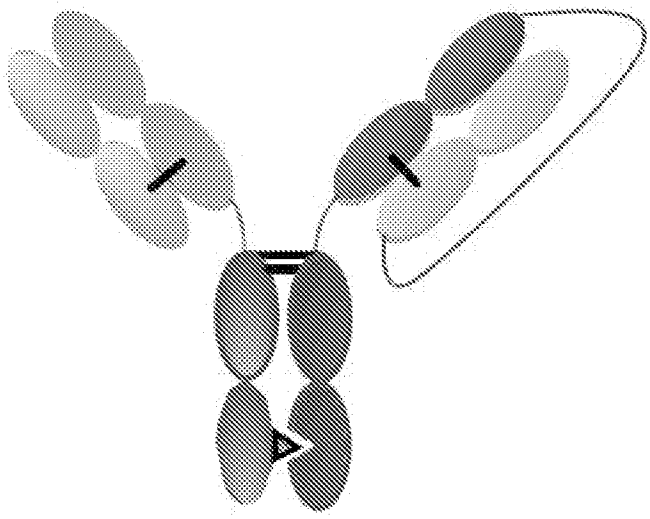


FIG. 32

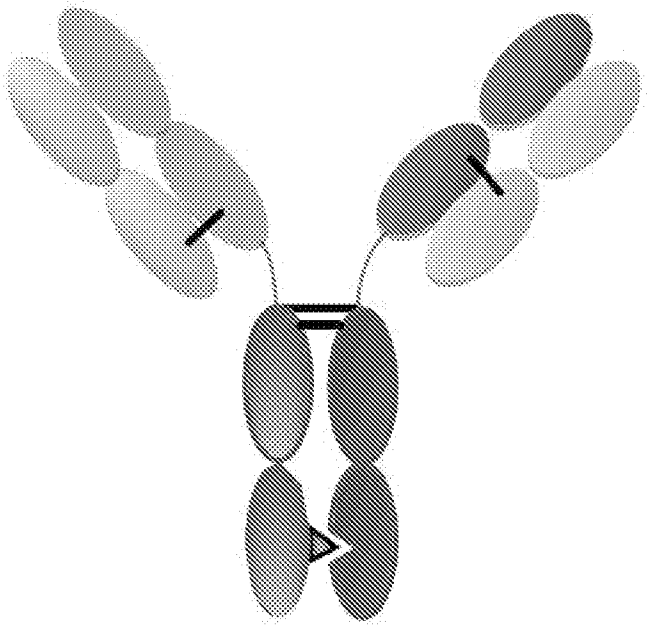


FIG. 33

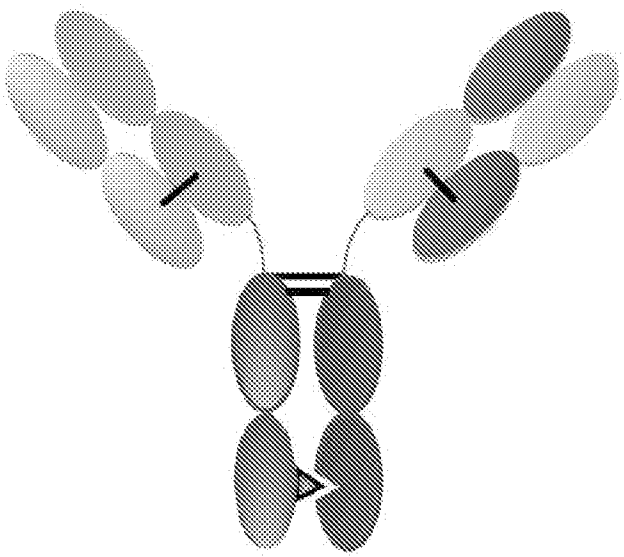


FIG. 34

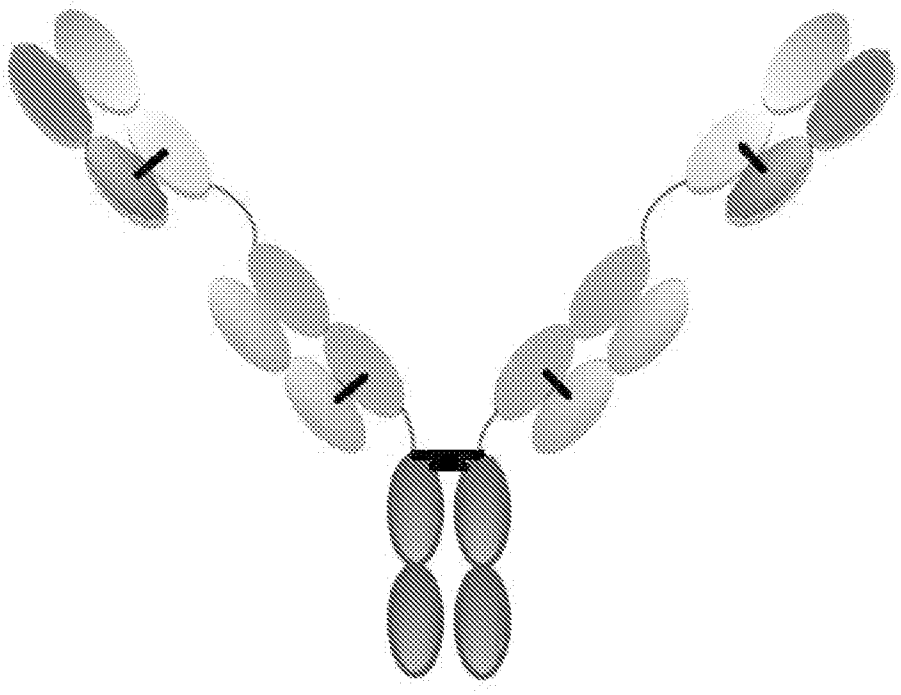


FIG. 35

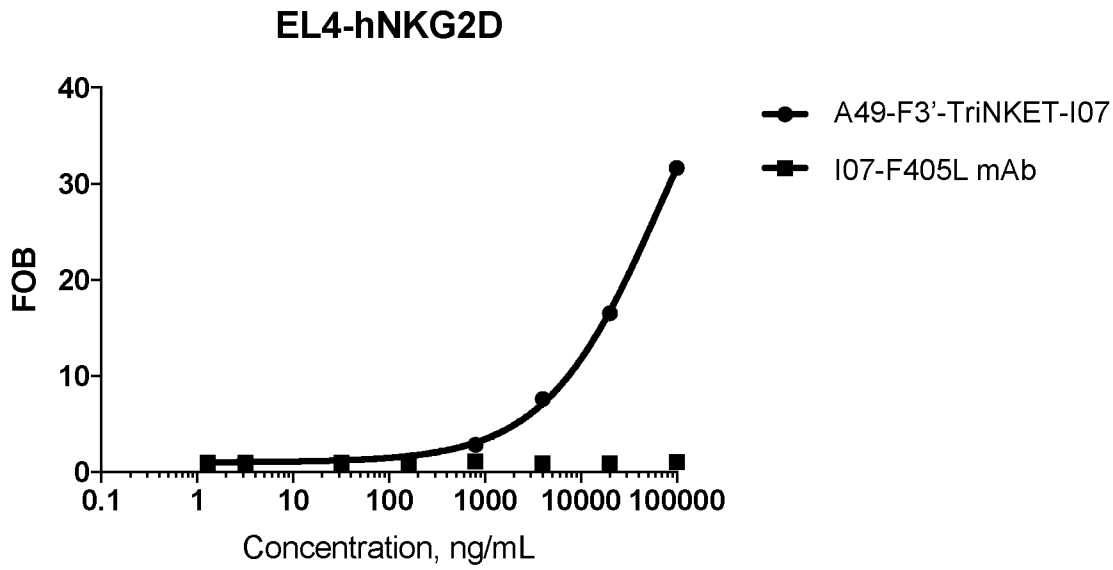

EL4-hNKG2D
FOB
40
30
20
10
0
0.1
1
10
100
1000
10000
100000
Concentration, ng/mL
A49-F3'-TriNKET-I07
I07-F405L mAb

FIG. 36A

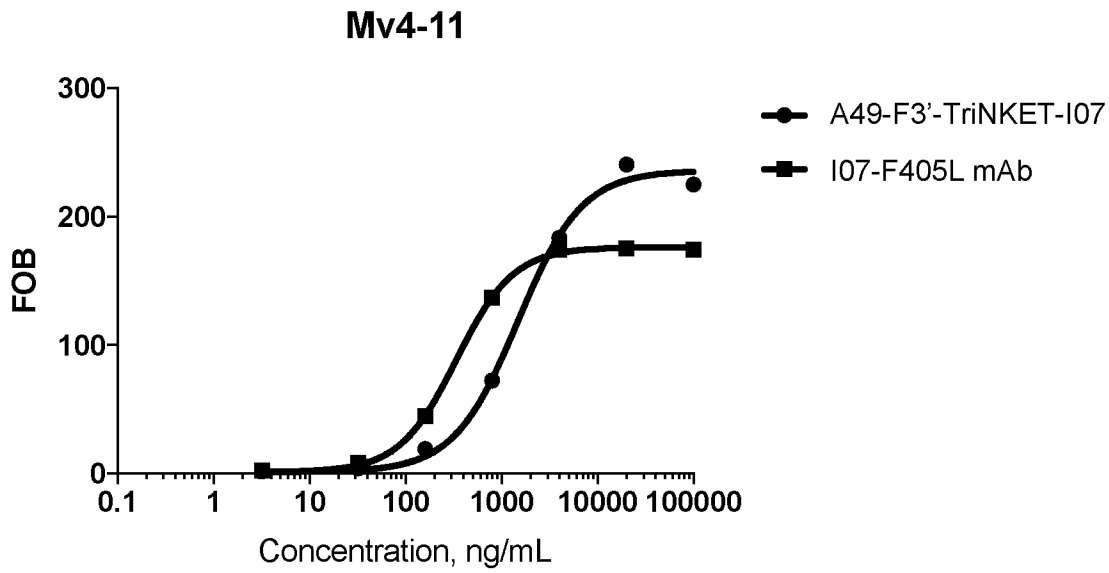


FIG. 36B

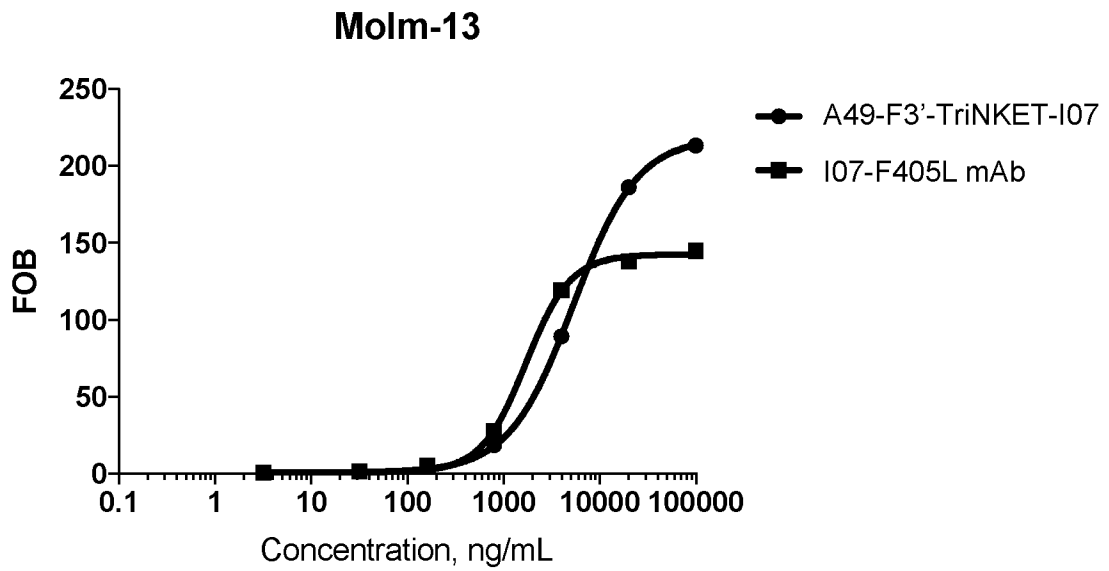


FIG. 37A

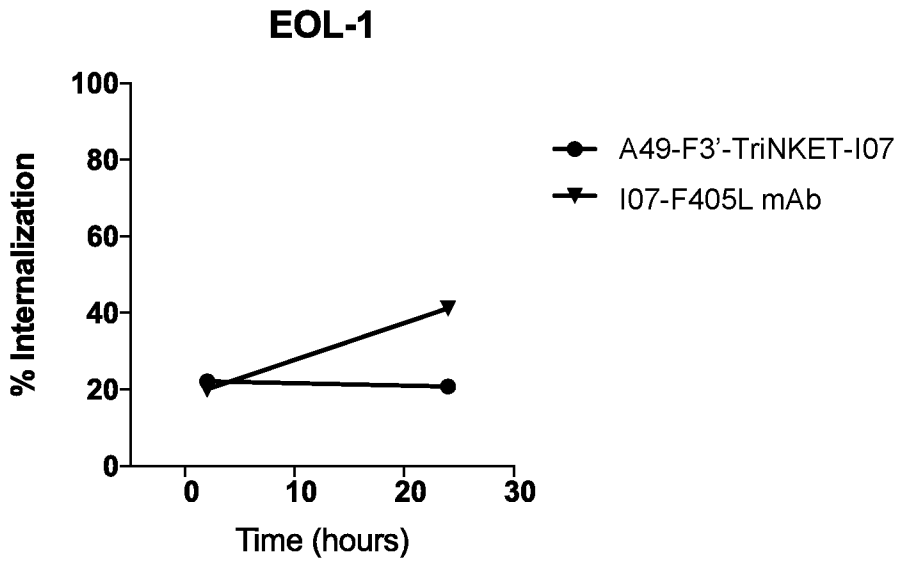


FIG. 37B

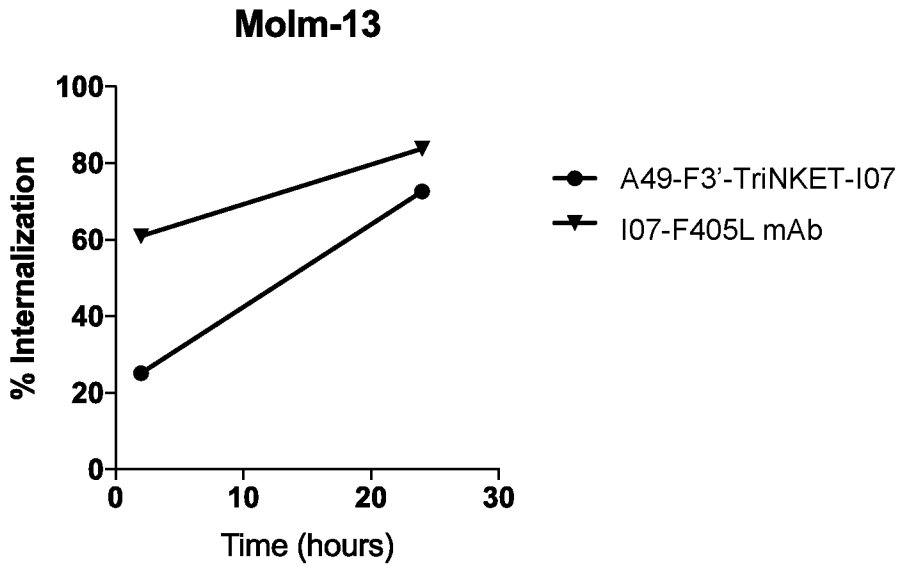


FIG. 38A

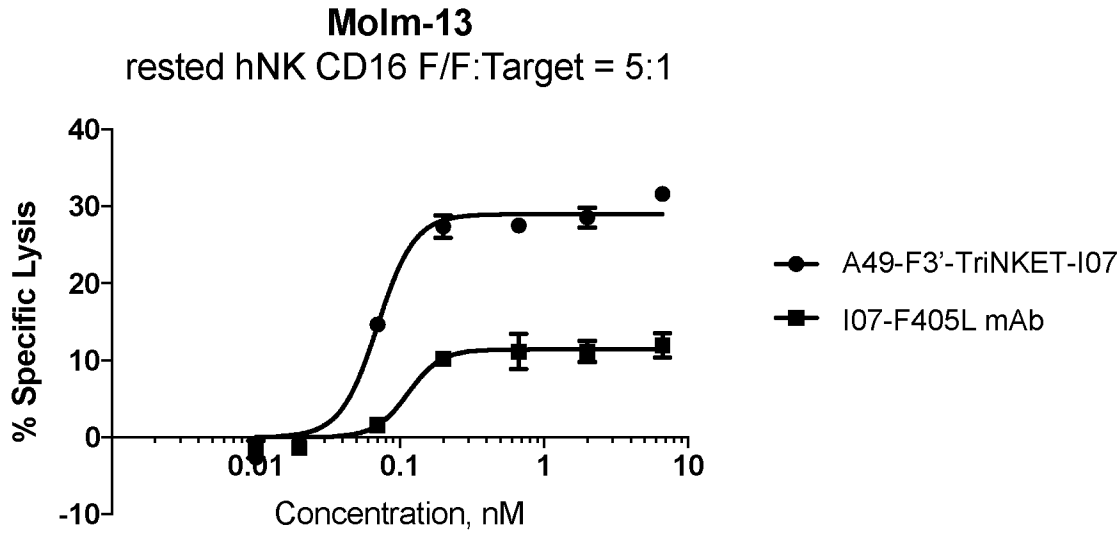


FIG. 38B

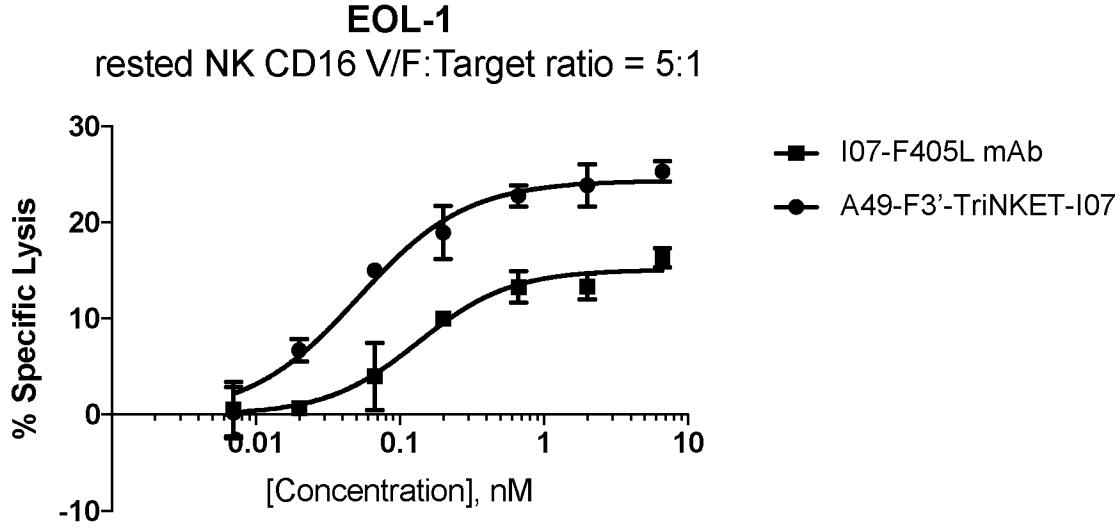


FIG. 38C

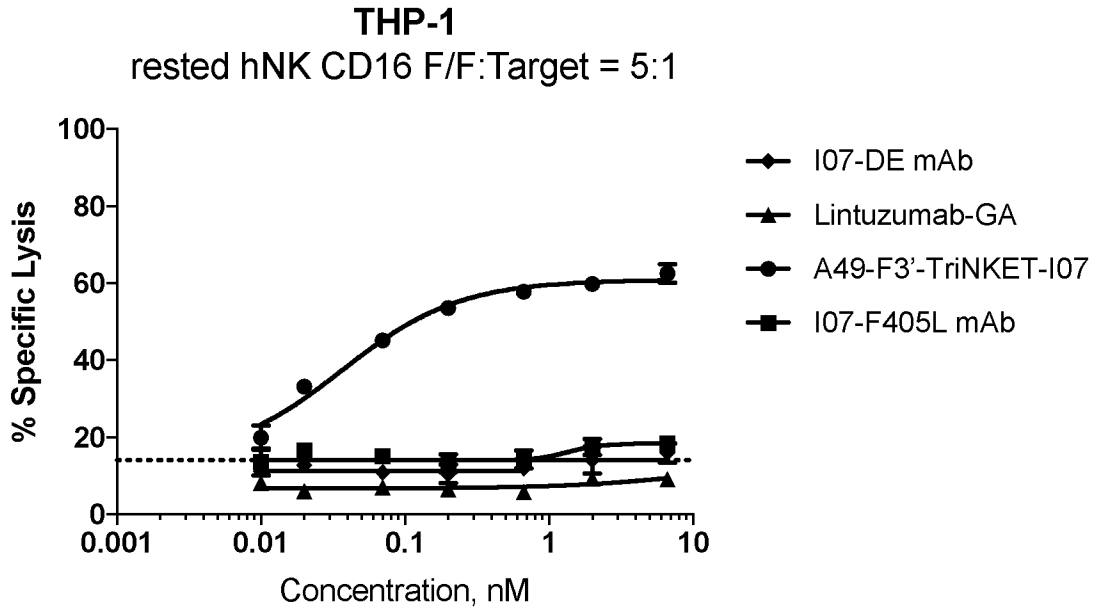


FIG. 38D

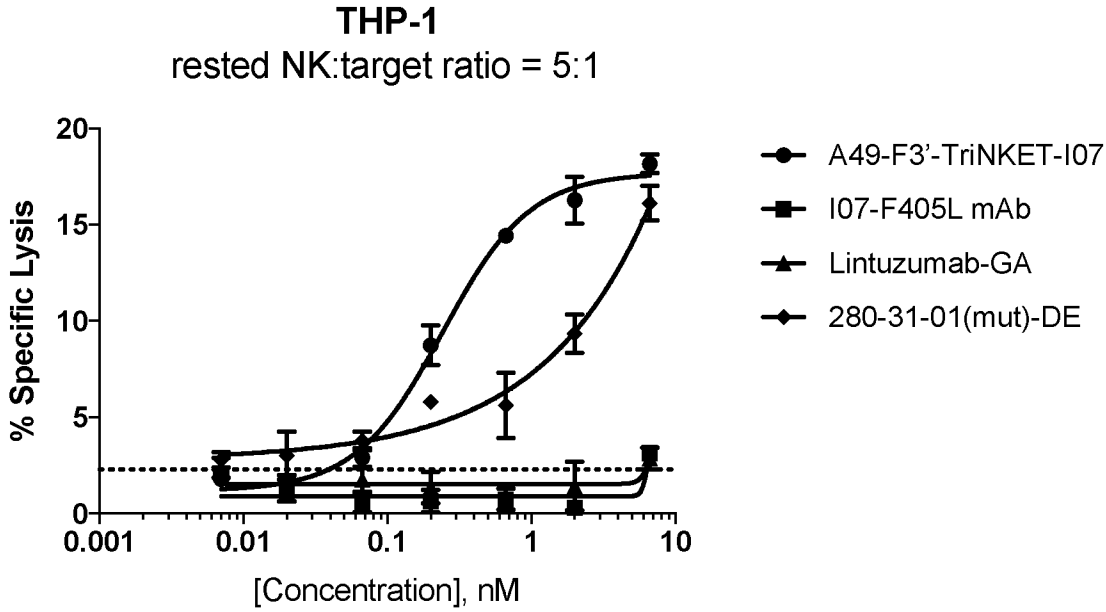


FIG. 39

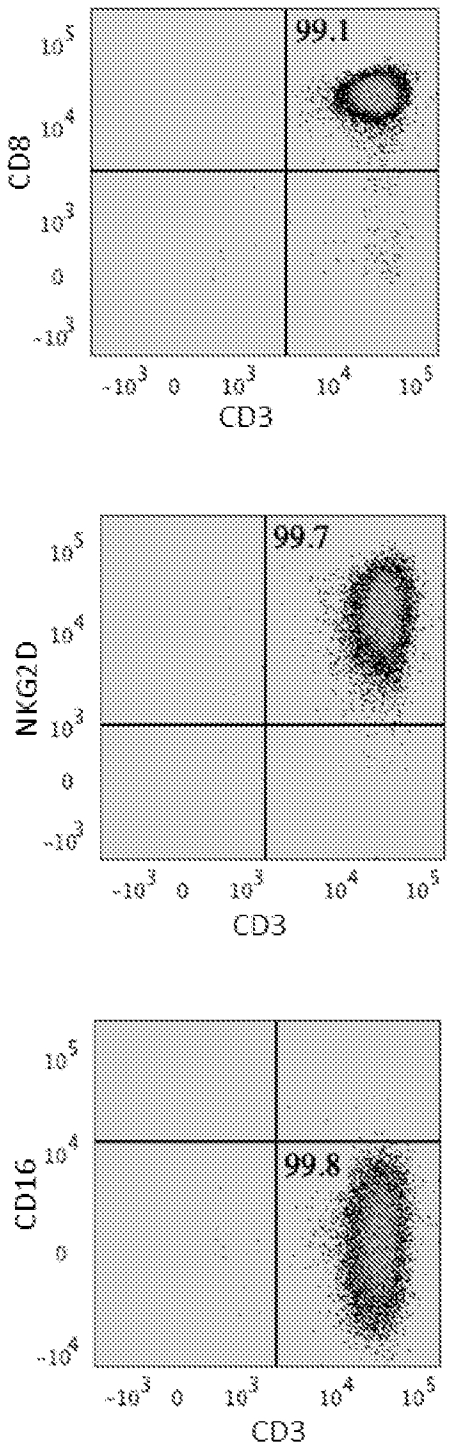


FIG. 40A

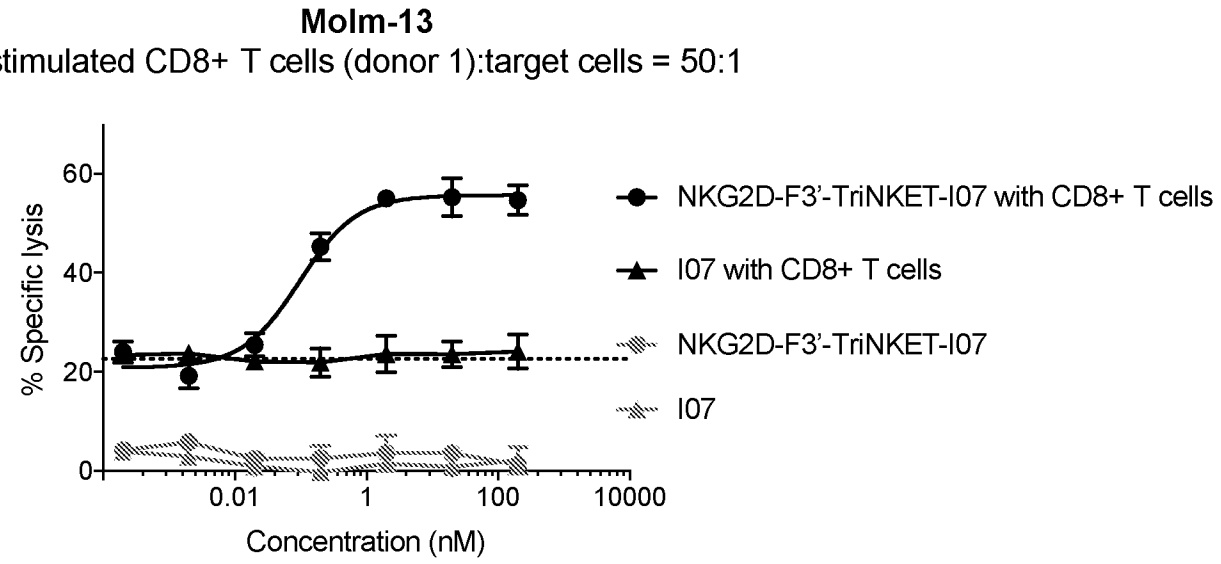


FIG. 40B

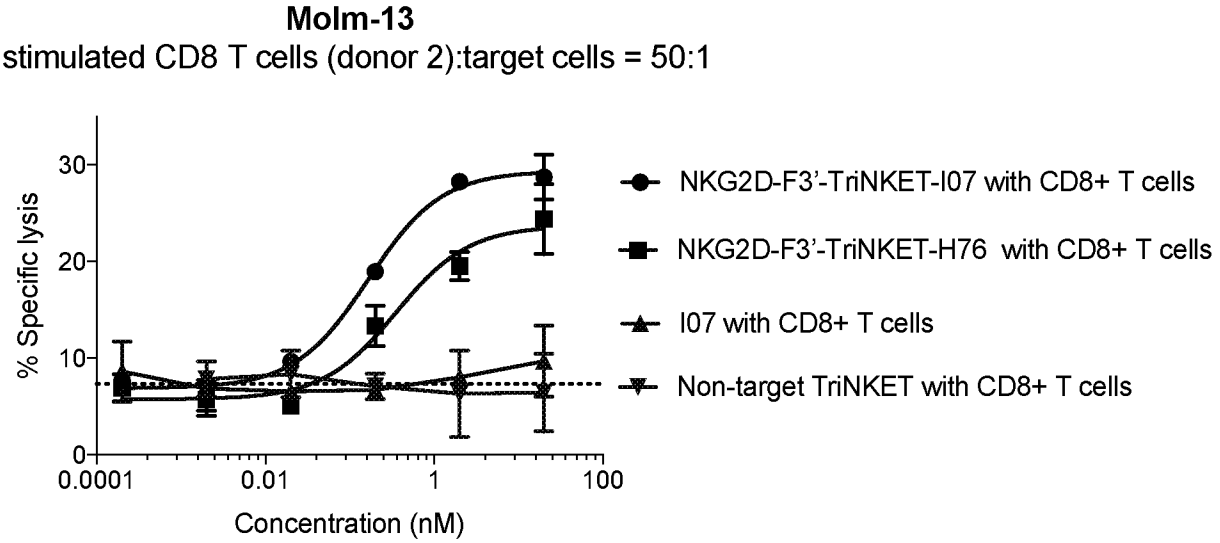
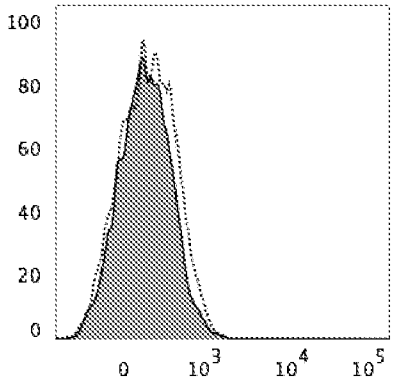
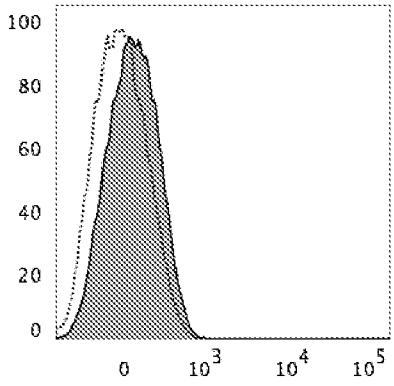


FIG. 41A



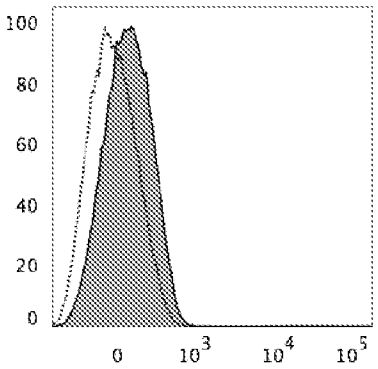
NK cells

FIG. 41B



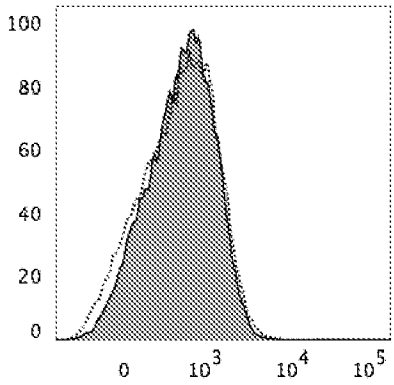
$CD8^+$ T cells

FIG. 41C



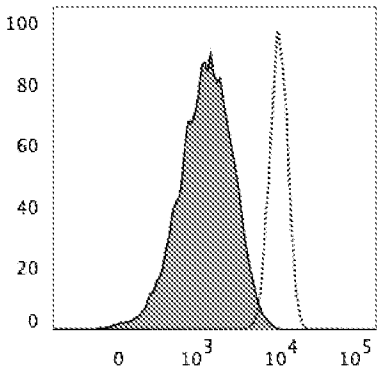
$CD4^+$ T cells

FIG. 41D



B cells

FIG. 41E



Monocytes

FIG. 42A

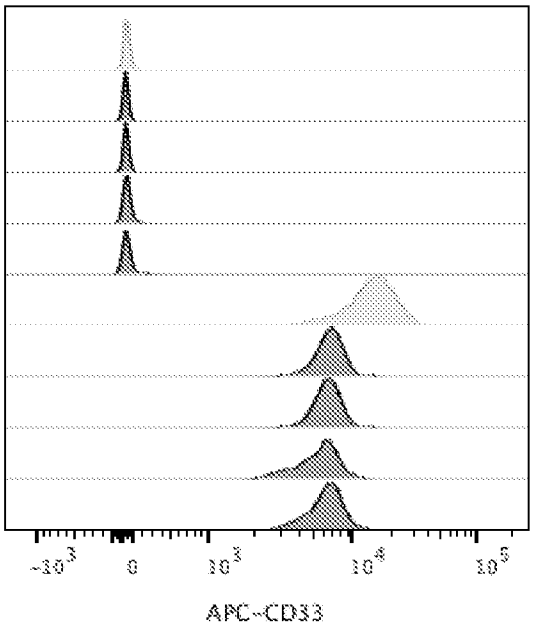


FIG. 42B

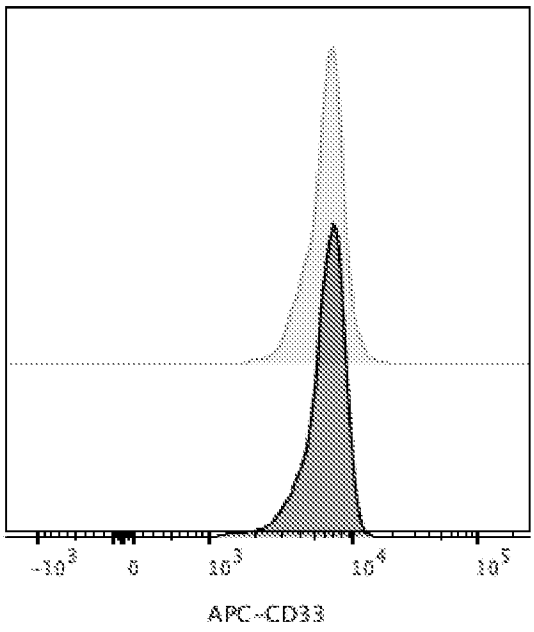


FIG. 43A

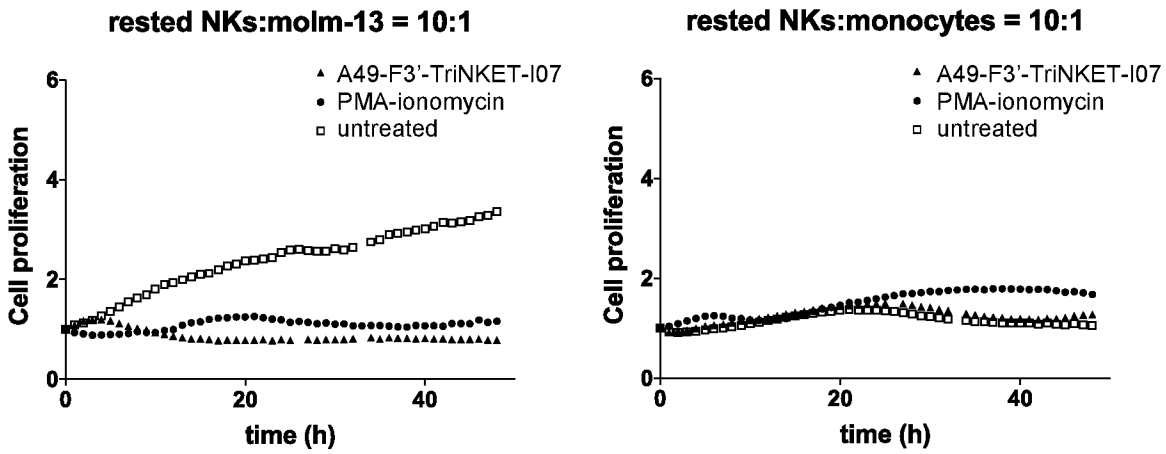


FIG. 43B

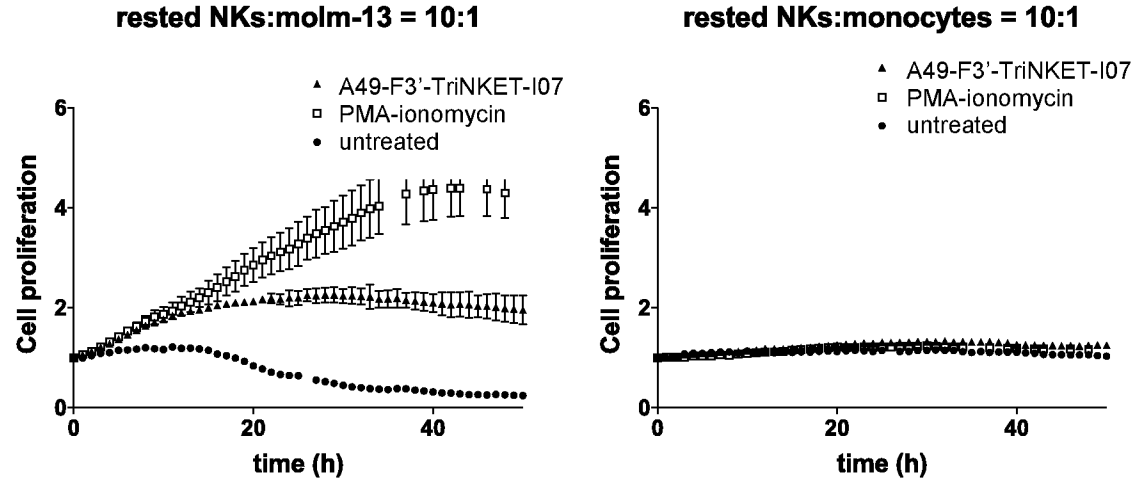
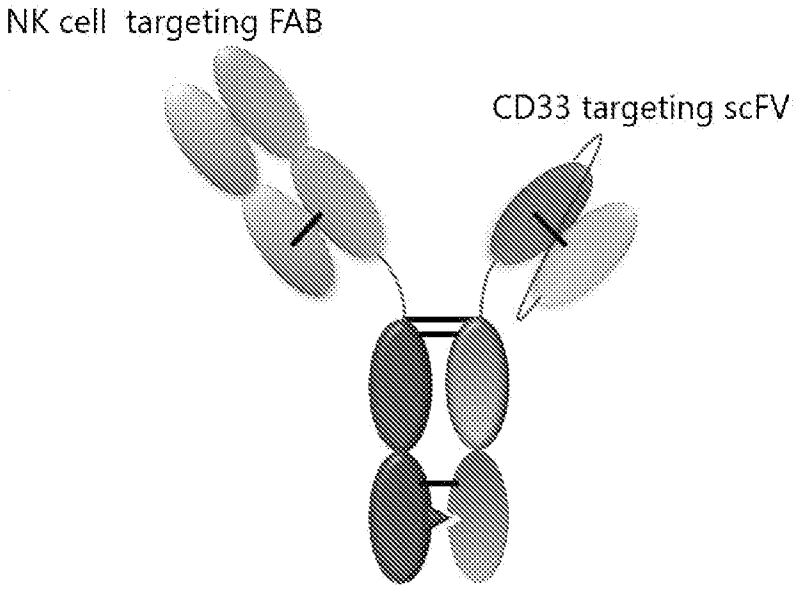


FIG. 44



F3' format

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<120> ANTIBODY VARIABLE DOMAINS TARGETING CD33, AND USE THEREOF

<130> DFY-050WO

<150> 62/632,756
<151> 2018-02-20

<160> 599

<170> PatentIn version 3.5

<210> 1
<211> 128
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<213> Artificial Sequence

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

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


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


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


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
            100                 105                 110
```

```
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210>  2
<211>  106
<212>  PRT
<213>  Artificial Sequence

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

<400>  2

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 Asp 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 Phe Pro Thr
                85                  90                  95


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


<210>  3
<211>  118
<212>  PRT
<213>  Artificial Sequence

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

<400>  3
```

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


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


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


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser
        115


<210>  4
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  4

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 Glu 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 Leu Glu Ser Tyr Pro Leu
                85                  90                  95

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

<210> 5
<211> 128
<212> PRT
<213> Artificial Sequence

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

<400> 5

```
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 Lys Tyr
            20                  25                  30

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

Ser Ala Ile Val Gly Ser Gly Glu Ser Thr Tyr Phe 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 Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
            100                 105                 110


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


<210>  6
<211>  106
<212>  PRT
<213>  Artificial Sequence

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

<400>  6

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 Asp Leu Pro Thr
                85                  90                  95


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


<210>  7
<211>  123
<212>  PRT
<213>  Artificial Sequence
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<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 7

```
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 Ser Asp Tyr
            20                  25                  30


Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Met Ile Asn Pro Ser Trp 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 Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
            100                 105                 110


Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 8
<211> 112
<212> PRT
<213> Artificial Sequence

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

<400> 8

```
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 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 Leu Leu Ile Tyr 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 Asp
                85                  90                  95

Val Ala Leu Pro Ile Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
```

<210> 9
<211> 118
<212> PRT
<213> Artificial Sequence

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

<400> 9

```
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 Gly Ser Tyr
            20                  25                  30

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

Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser
        115


<210>  10
<211>  108
<212>  PRT
<213>  Artificial Sequence

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

<400>  10

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 Glu 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 Gln Ser Tyr Pro Pro
                85                  90                  95


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


<210>  11
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<211> 118
<212> PRT
<213> Artificial Sequence

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

<400> 11

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 Pro Ser Tyr
20 25 30

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

Ala Thr Ile Lys Arg Asp Gly Ser Glu Lys Gly 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

<210> 12
<211> 108
<212> PRT
<213> Artificial Sequence

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

<400> 12

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 Glu 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 Gln Ser Tyr Pro Pro
                85                  90                  95

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


<210>  13
<211>  120
<212>  PRT
<213>  Artificial Sequence

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

<400>  13

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 Gly Thr 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 Arg Gly Ser Thr Val 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 Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210>  14
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  14

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 Ala His Ser Tyr Pro Leu
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
```

100 105

<210> 15
<211> 128
<212> PRT
<213> Artificial Sequence

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

<400> 15

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

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

Ser Ser Ile Ser Ser Ser Ser Glu Gly Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
100 105 110

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

<210> 16
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 16

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 Asn 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 Glu Ala Ser Ser Thr Lys 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 Asp Leu Pro Thr
85 90 95

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

<210> 17
<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 17

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

```
Ala Asn Ile Asn Thr Asp Gly Ser Glu Val 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 Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  18
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  18

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 Val Ile Tyr Ser Tyr
            20                  25                  30


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


Tyr Ala Ala Ser Ser Leu Lys 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 Val Tyr Asp Thr Pro Leu
```

85 90 95

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

<210> 19
<211> 120
<212> PRT
<213> Artificial Sequence

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

<400> 19

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 Thr
20 25 30

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

Trp Ile Gly Ser Ile Gly Tyr Ser Gly Thr Tyr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 20
<211> 106
<212> PRT

<213> Artificial Sequence

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

<400> 20

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 His Ser Val Tyr 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 Tyr Asp Asn Leu Pro Thr
85 90 95

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

<210> 21
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 21

Phe Thr Phe Ser Ser Tyr Gly Met Ser
1 5

<210> 22
<211> 17
<212> PRT

<213> Artificial Sequence

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

<400> 22

Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 23
<211> 21
<212> PRT
<213> Artificial Sequence

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

<400> 23

Ala Arg Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
1 5 10 15

Tyr Gly Met Asp Val
20

<210> 24
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 24

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
1 5 10

<210> 25
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 25

Asp Ala Ser Ser Leu Glu Ser
1   5

<210> 26
<211> 8
<212> PRT
<213> Artificial Sequence

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

<400> 26

Gln Gln Tyr Glu Ser Phe Pro Thr
1   5

<210> 27
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 27

Phe Thr Phe Ser Ser Tyr Trp Met Ser
1   5

<210> 28
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 28

Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
1   5   10   15

Gly

<210> 29
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 29

Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val
1   5   10

<210> 30
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 30

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
1   5   10

<210> 31
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 31

Glu Ala Ser Ser Leu Glu Ser
1   5

<210> 32
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 32

Gln Gln Leu Glu Ser Tyr Pro Leu Thr
1 5

<210> 33
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 33

Phe Thr Phe Ser Lys Tyr Thr Met Ser
1 5

<210> 34
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 34

Ala Ile Val Gly Ser Gly Glu Ser Thr Tyr Phe Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 35
<211> 21
<212> PRT
<213> Artificial Sequence

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

<400> 35

Ala Arg Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
1 5 10 15

Tyr Gly Met Asp Val
            20

<210> 36
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 36

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
1   5   10

<210> 37
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 37

Lys Ala Ser Ser Leu Glu Ser
1   5

<210> 38
<211> 8
<212> PRT
<213> Artificial Sequence

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

<400> 38

Gln Gln Tyr Asp Asp Leu Pro Thr
1   5

<210> 39
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 39

Tyr Thr Phe Ser Asp Tyr Tyr Met His
1   5

<210> 40
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 40

Met Ile Asn Pro Ser Trp Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1   5   10   15

Gly

<210> 41
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 41

Ala Arg Glu Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
1   5   10   15

<210> 42
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 42

Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr Leu Asp

1 5 10 15

<210> 43
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 43

Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 44
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 44

Met Gln Asp Val Ala Leu Pro Ile Thr
1 5

<210> 45
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 45

Phe Thr Phe Gly Ser Tyr Trp Met Ser
1 5

<210> 46
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 46

Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 47
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 47

Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val
1 5 10

<210> 48
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 48

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
1 5 10

<210> 49
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 49

Glu Ala Ser Ser Leu Glu Ser
1 5

<210> 50
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 50

Gln Gln Ser Gln Ser Tyr Pro Pro Ile Thr
1 5 10

<210> 51
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 51

Phe Thr Phe Pro Ser Tyr Trp Met Ser
1 5

<210> 52
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 52

Thr Ile Lys Arg Asp Gly Ser Glu Lys Gly Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 53
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 53

Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val
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 Ile Ser Ser Trp Leu Ala
1   5   10

<210> 55
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 55

Glu Ala Ser Ser Leu Glu Ser
1   5

<210> 56
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 56

Gln Gln Ser Gln Ser Tyr Pro Pro Ile Thr
1   5   10

<210> 57

<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 57

Tyr Thr Phe Gly Thr Tyr Tyr Met His
1 5

<210> 58
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 58

Ile Ile Asn Pro Ser Arg Gly Ser Thr Val Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 59
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 59

Ala Arg Gly Ala Gly Tyr Asp Asp Glu Asp Met Asp Val
1 5 10

<210> 60
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 60

Arg Ala Ser Gln Gly Ile Asp Ser Trp Leu Ala
1 5 10

<210> 61
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 61

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 62
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 62

Gln Gln Ala His Ser Tyr Pro Leu Thr
1 5

<210> 63
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 63

Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5

<210> 64
<211> 17
<212> PRT

<213> Artificial Sequence

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

<400> 64

Ser Ile Ser Ser Ser Ser Glu Gly Ile Tyr Tyr Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 65
<211> 21
<212> PRT
<213> Artificial Sequence

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

<400> 65

Ala Arg Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
1   5   10   15

Tyr Gly Met Asp Val
            20

<210> 66
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 66

Arg Ala Ser Asn Ser Ile Ser Ser Trp Leu Ala
1   5   10

<210> 67
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 67

Glu Ala Ser Ser Thr Lys Ser
1 5

<210> 68
<211> 8
<212> PRT
<213> Artificial Sequence

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

<400> 68

Gln Gln Tyr Asp Asp Leu Pro Thr
1 5

<210> 69
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 69

Phe Thr Phe Ser Ser Tyr Trp Met Ser
1 5

<210> 70
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 70

Asn Ile Asn Thr Asp Gly Ser Glu Val Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 71
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 71

Ala Arg Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
1   5   10   15

<210> 72
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 72

Arg Ala Ser Gln Val Ile Tyr Ser Tyr Leu Asn
1   5   10

<210> 73
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 73

Ala Ala Ser Ser Leu Lys Ser
1   5

<210> 74
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 74

Gln Gln Val Tyr Asp Thr Pro Leu Thr
1 5

<210> 75
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 75

Gly Ser Ile Ser Ser Thr Asp Tyr Tyr Trp Gly
1 5 10

<210> 76
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 76

Ser Ile Gly Tyr Ser Gly Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 77
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 77

Ala Arg Glu Thr Ala His Asp Val His Gly Met Asp Val
1 5 10

<210> 78
<211> 11
<212> PRT

<213> Artificial Sequence

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

<400> 78

Arg Ala Ser His Ser Val Tyr Ser Tyr Leu Ala
1   5   10

<210> 79
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 79

Asp Ala Ser Asn Arg Ala Thr
1   5

<210> 80
<211> 8
<212> PRT
<213> Artificial Sequence

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

<400> 80

Gln Gln Tyr Asp Asn Leu Pro Thr
1   5

<210> 81
<211> 126
<212> PRT
<213> Artificial Sequence

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

<400> 81

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>  82
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  82

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> 83
<211> 124
<212> PRT
<213> Artificial Sequence

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

<400> 83

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> 84
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 84

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> 85
<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 85

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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>  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 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> 87
<211> 122
<212> PRT
<213> Artificial Sequence

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

<400> 87

```
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> 88
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 88

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> 89
<211> 125
<212> PRT
<213> Artificial Sequence

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

<400> 89

```
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> 90
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 90

```
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> 91
<211> 122
<212> PRT
<213> Artificial Sequence

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

<220>
<221> VARIANT
<222> (102)..(102)
<223> Met, Leu, Ile, Val, Gln, or Phe

<400> 91

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

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

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

Ser Ser Ile Ser Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Pro Xaa 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> 92
<211> 15
<212> PRT
<213> Artificial Sequence

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

<220>
<221> VARIANT
<222> (6)..(6)
<223> Met, Leu, Ile, Val, Gln, or Phe

<400> 92

Ala Arg Gly Ala Pro Xaa Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10 15

<210> 93
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 93

Tyr Thr Phe Thr Ser Tyr Tyr Met His
1 5

<210> 94
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 94

Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 95
<211> 19
<212> PRT
<213> Artificial Sequence

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

<400> 95

Ala Arg Gly Ala Pro Asn Tyr Gly Asp Thr Thr His Asp Tyr Tyr Tyr
1 5 10 15

Met Asp Val

<210> 96
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 96

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 97

<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 97

Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 98
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 98

Gln Gln Tyr Asp Asp Trp Pro Phe Thr
1 5

<210> 99
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 99

Tyr Thr Phe Thr Gly Tyr Tyr Met His
1 5

<210> 100
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 100

Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln

1 5 10 15

Gly

<210> 101
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 101

Ala Arg Asp Thr Gly Glu Tyr Tyr Asp Thr Asp Asp His Gly Met Asp
1 5 10 15

Val

<210> 102
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 102

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 103
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 103

Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 104
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 104

Gln Gln Asp Asp Tyr Trp Pro Pro Thr
1 5

<210> 105
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 105

Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5

<210> 106
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 106

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 107
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 107

Ala Lys Asp Gly Gly Tyr Tyr Asp Ser Gly Ala Gly Asp Tyr
1 5 10

<210> 108
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 108

Arg Ala Ser Gln Gly Ile Asp Ser Trp Leu Ala
1 5 10

<210> 109
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 109

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 110
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 110

Gln Gln Gly Val Ser Tyr Pro Arg Thr
1 5

<210> 111

<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 111

Phe Thr Phe Ser Ser Tyr Ser Met Asn
1 5

<210> 112
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 112

Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 113
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 113

Ala Arg Gly Ala Pro Met Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10 15

<210> 114
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 114

Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
1 5 10

<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 Gly Val Ser Phe Pro Arg Thr
1 5

<210> 117
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 117

Tyr Thr Phe Thr Ser Tyr Tyr Met His
1 5

<210> 118
<211> 17
<212> PRT

<213> Artificial Sequence

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

<400> 118

Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 119
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 119

Ala Arg Glu Gly Ala Gly Phe Ala Tyr Gly Met Asp Tyr Tyr Tyr Met
1 5 10 15

Asp Val

<210> 120
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 120

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 121
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 121

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 122
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 122

Gln Gln Ser Asp Asn Trp Pro Phe Thr
1 5

<210> 123
<211> 13
<212> PRT
<213> Artificial Sequence

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

<220>
<221> VARIANT
<222> (4)..(4)
<223> Met, Leu, Ile, Val, Gln, or Phe

<400> 123

Gly Ala Pro Xaa Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 124
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 124

```
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>  125
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  125

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

<210> 126
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 126

Gly Ser Phe Ser Gly Tyr Tyr Trp Ser
1 5

<210> 127
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 127

Glu Ile Asp His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 128
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 128

Ala Arg Ala Arg Gly Pro Trp Ser Phe Asp Pro
1 5 10

<210> 129
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 129

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> 130

<211> 108
<212> PRT
<213> Artificial Sequence

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

<400> 130

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

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

<210> 131
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 131

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> 132
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 132

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 Tyr Thr
                85                  90                  95


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


<210>  133
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  133

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> 134
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 134

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> 135
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 135

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> 136
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 136

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>  137
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  137

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

<210> 138
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 138

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> 139
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 139

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> 140
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 140

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


<210>  141
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  141

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> 142
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 142

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 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
100 105

<210> 143
<211> 117
<212> PRT

<213> Artificial Sequence

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

<400> 143

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> 144
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 144

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>  145
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  145

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> 146
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 146

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> 147
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 147

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> 148
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 148

```
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>  149
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  149

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> 150
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 150

```
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> 151
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 151

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> 152
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 152

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> 153
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 153

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> 154
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 154

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>  155
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  155

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>  156
```

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

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

<400> 156

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> 157
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 157

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> 158
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 158

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>  159
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  159

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> 160
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 160

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> 161
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 161

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> 162
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 162

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>  163
<211>  117
<212>  PRT
<213>  Artificial Sequence

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

<400>  163

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> 164
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 164

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> 165
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 165

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> 166
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 166

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>  167
<211>  125
<212>  PRT
<213>  Artificial Sequence

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

<400>  167

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> 168
<211> 113
<212> PRT
<213> Artificial Sequence

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

<400> 168

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> 169
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 169

Gly Thr Phe Ser Ser Tyr Ala Ile Ser
1 5

<210> 170
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 170

Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 171
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 171

Ala Arg Gly Asp Ser Ser Ile Arg His Ala Tyr Tyr Tyr Tyr Gly Met
1 5 10 15

Asp Val

<210> 172

<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 172

Lys Ser Ser Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 173
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 173

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 174
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 174

Gln Gln Tyr Tyr Ser Thr Pro Ile Thr
1 5

<210> 175
<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 175

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> 176
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 176

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>  177
<211>  11
<212>  PRT
<213>  Artificial Sequence

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

<400>  177

Gly Ser Ile Ser Ser Ser Ser Tyr Tyr Trp Gly
1               5                   10


<210>  178
<211>  16
<212>  PRT
<213>  Artificial Sequence

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

<400>  178

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1               5                   10                  15


<210>  179
<211>  13
<212>  PRT
```

<213> Artificial Sequence

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

<400> 179

Ala Arg Gly Ser Asp Arg Phe His Pro Tyr Phe Asp Tyr
1 5 10

<210> 180
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 180

Arg Ala Ser Gln Ser Val Ser Arg Tyr Leu Ala
1 5 10

<210> 181
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 181

Ser Tyr Trp Met Ser
1 5

<210> 182
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 182

Arg Pro Leu Asn Ala Gly Glu Leu Asp Val
1 5 10

<210> 183
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 183

Lys Tyr Thr Met Ser
1 5

<210> 184
<211> 19
<212> PRT
<213> Artificial Sequence

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

<400> 184

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
1 5 10 15

Met Asp Val

<210> 185
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 185

Lys Ala Ser Ser Leu Glu
1 5

<210> 186
<211> 20
<212> PRT
<213> Artificial Sequence

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

<400> 186

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 187
<211> 474
<212> PRT
<213> Artificial Sequence

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

<400> 187

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 Glu 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 Gln Ser Tyr Pro Pro
85 90 95

Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

```
        115                 120                 125

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
    130                 135                 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Ser Tyr
145                 150                 155                 160

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
                165                 170                 175

Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser Tyr Val Asp Ser Val
            180                 185                 190

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
        195                 200                 205

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240

Met Val Thr Val Ser Ser Ala Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
```

325 330 335

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
340 345 350

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
355 360 365

Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp
370 375 380

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
385 390 395 400

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
405 410 415

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
420 425 430

Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
435 440 445

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
450 455 460

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470

<210> 188
<211> 246
<212> PRT
<213> Artificial Sequence

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

<400> 188

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 Glu 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 Gln Ser Tyr Pro Pro
                85                  90                  95

Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
    130                 135                 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Ser Tyr
145                 150                 155                 160

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
                165                 170                 175

Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser Tyr Val Asp Ser Val
            180                 185                 190

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
        195                 200                 205

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220
```

```
Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240


Met Val Thr Val Ser Ser
                245


<210>  189
<211>  451
<212>  PRT
<213>  Artificial Sequence

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

<400>  189

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 Ala Ser Thr Lys Gly Pro
        115                 120                 125


Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
```

```
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
    210                 215                 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
    290                 295                 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
                325                 330                 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
```

```
            340                 345                 350

Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Glu Asn Gln Val
        355                 360                 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Trp Leu Thr
                405                 410                 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445

Ser Pro Gly
    450


<210>  190
<211>  214
<212>  PRT
<213>  Artificial Sequence

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

<400>  190

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 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> 191
<211> 122
<212> PRT
<213> Artificial Sequence

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

<400> 191

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 Ile 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> 192
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 192

Ser Tyr Ser Met Asn
1 5

<210> 193
<211> 13
<212> PRT

<213> Artificial Sequence

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

<400> 193

Gly Ala Pro Met Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 194
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 194

Ala Arg Gly Ala Pro Ile Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10 15

<210> 195
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 195

Gly Ala Pro Ile Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 196
<211> 451
<212> PRT
<213> Artificial Sequence

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

<400> 196

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 Ile Gly Ala Ala Ala Gly Trp Phe Asp Pro Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
    210                 215                 220
```

```
Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225                 230                 235                 240


Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255


Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270


His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285


Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
    290                 295                 300


Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320


Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
                325                 330                 335


Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350


Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Glu Asn Gln Val
        355                 360                 365


Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380


Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400


Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Trp Leu Thr
                405                 410                 415


Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
```

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435   440   445

Ser Pro Gly
    450

<210> 197
<211> 482
<212> PRT
<213> Artificial Sequence

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

<400> 197

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 Asp Leu Pro Thr
                85   90   95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
        115   120   125

Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu

```
    130                 135                 140

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr Thr Met
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ser Ala
                165                 170                 175

Ile Val Gly Ser Gly Glu Ser Thr Tyr Phe Ala Asp Ser Val Lys Gly
            180                 185                 190

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
        195                 200                 205

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
225                 230                 235                 240

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
                245                 250                 255

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            260                 265                 270

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        275                 280                 285

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    290                 295                 300

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
305                 310                 315                 320

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
                325                 330                 335

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
```

340 345 350

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
355 360 365

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val
370 375 380

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
385 390 395 400

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
405 410 415

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
420 425 430

Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val
435 440 445

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
450 455 460

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
465 470 475 480

Pro Gly

<210> 198
<211> 254
<212> PRT
<213> Artificial Sequence

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

<400> 198

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 Asp Leu Pro Thr
                85                  90                  95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
        115                 120                 125

Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
    130                 135                 140

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr Thr Met
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ser Ala
                165                 170                 175

Ile Val Gly Ser Gly Glu Ser Thr Tyr Phe Ala Asp Ser Val Lys Gly
            180                 185                 190

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
        195                 200                 205

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220
```

```
Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
225                 230                 235                 240


Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                245                 250


<210>  199
<211>  447
<212>  PRT
<213>  Artificial Sequence

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

<400>  199

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 Gly Ser Tyr
            20                  25                  30


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


Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125


Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
```

```
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Leu Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln 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 Pro Gly
        435                 440                 445


<210>  200
<211>  215
<212>  PRT
<213>  Artificial Sequence

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

<400>  200

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 Glu 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 Gln Ser Tyr Pro Pro
                85                  90                  95


Ile Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
            100                 105                 110


Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
        115                 120                 125


Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
    130                 135                 140


Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160


Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175


Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190


Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
        195                 200                 205


Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210>  201
<211>  447
<212>  PRT
<213>  Artificial Sequence

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

<400>  201

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 Gly Ser Tyr
            20                  25                  30

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

Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110

Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
```

```
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Asp
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 His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro Glu 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln 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 Pro Gly
435 440 445

<210> 202
<211> 446
<212> PRT
<213> Artificial Sequence

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

<400> 202

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 Asp Tyr
20 25 30

Ala Ile Ser 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 Ala Asp Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg 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 Asn Trp Ala Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
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 Leu Leu Gly Gly Pro Asp 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 Glu 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
        435                 440                 445


<210>  203
<211>  213
<212>  PRT
<213>  Artificial Sequence

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

<400>  203

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 Arg Ala Ser Gln Gly Ile Ser Ser Val
            20                  25                  30


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


Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


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

65 70 75 80

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

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 204
<211> 474
<212> PRT
<213> Artificial Sequence

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

<400> 204

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 Glu 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 Gln Ser Tyr Pro Pro
                85                  90                  95

Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
    130                 135                 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Ser Tyr
145                 150                 155                 160

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
                165                 170                 175

Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser Tyr Val Asp Ser Val
            180                 185                 190

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
        195                 200                 205

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220
```

```
Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240


Met Val Thr Val Ser Ser Ala Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255


Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270


Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285


Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300


Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320


Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                325                 330                 335


Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
            340                 345                 350


Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
        355                 360                 365


Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp
    370                 375                 380


Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
385                 390                 395                 400


Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
                405                 410                 415


Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
            420                 425                 430
```

```
Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
        435                 440                 445


Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
    450                 455                 460


Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465                 470


<210>  205
<211>  451
<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 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 Ala Ser Thr Lys Gly Pro
```

```
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
    210                 215                 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
    290                 295                 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro
```

325 330 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
340 345 350

Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Glu Asn Gln Val
355 360 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
370 375 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Trp Leu Thr
405 410 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Gly
450

<210> 206
<211> 254
<212> PRT
<213> Artificial Sequence

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

<400> 206

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 Asp 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 Phe Pro Thr
                85                  90                  95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
        115                 120                 125

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
    130                 135                 140

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala Asn
                165                 170                 175

Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys Gly
            180                 185                 190

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln
        195                 200                 205

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
225                 230                 235                 240
```

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
245 250

<210> 207
<211> 254
<212> PRT
<213> Artificial Sequence

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

<400> 207

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser

145 150 155 160

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
165 170 175

Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
180 185 190

Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser
195 200 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
210 215 220

Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Glu
225 230 235 240

Ser Phe Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 208
<211> 245
<212> PRT
<213> Artificial Sequence

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

<400> 208

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 Glu 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 Leu Glu Ser Tyr Pro Leu
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160


Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
                165                 170                 175


Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190


Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
        195                 200                 205


Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220


Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr Met
225                 230                 235                 240


Val Thr Val Ser Ser
                245


<210>  209
<211>  245
<212>  PRT
```

<213> Artificial Sequence

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

<400> 209

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


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


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


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140


Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Glu Ala Ser Ser Leu
```

180 185 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
195 200 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr
210 215 220

Tyr Cys Gln Gln Leu Glu Ser Tyr Pro Leu Thr Phe Gly Cys Gly Thr
225 230 235 240

Lys Val Glu Ile Lys
245

<210> 210
<211> 254
<212> PRT
<213> Artificial Sequence

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

<400> 210

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr
20 25 30

Thr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
35 40 45

Ser Ala Ile Val Gly Ser Gly Glu Ser Thr Tyr Phe 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 Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
            100                 105                 110


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


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140


Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser
145                 150                 155                 160


Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
                165                 170                 175


Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
            180                 185                 190


Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser
        195                 200                 205


Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
    210                 215                 220


Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp
225                 230                 235                 240


Asp Leu Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  211
<211>  255
<212>  PRT
<213>  Artificial Sequence

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

<400>  211

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 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 Leu Leu Ile Tyr 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 Asp
                85                  90                  95

Val Ala Leu Pro Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
    130                 135                 140

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
145                 150                 155                 160

Phe Ser Asp Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys
                165                 170                 175

Leu Glu Trp Met Gly Met Ile Asn Pro Ser Trp Gly Ser Thr Ser Tyr
            180                 185                 190

Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr
        195                 200                 205

Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
```

210 215 220

Val Tyr Tyr Cys Ala Arg Glu Ala Ala Asp Gly Phe Val Gly Glu Arg
225 230 235 240

Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
245 250 255

<210> 212
<211> 255
<212> PRT
<213> Artificial Sequence

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

<400> 212

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 Ser Asp Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Met Ile Asn Pro Ser Trp 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 Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
100 105 110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

```
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140


Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
145                 150                 155                 160


Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn
                165                 170                 175


Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
            180                 185                 190


Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
        195                 200                 205


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
    210                 215                 220


Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Asp Val
225                 230                 235                 240


Ala Leu Pro Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250                 255


<210>  213
<211>  246
<212>  PRT
<213>  Artificial Sequence

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

<400>  213

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 Gly Ser Tyr
            20                  25                  30


Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
```

```
        35                  40                  45

Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Glu Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Gln Ser Tyr Pro Pro Ile Thr Phe Gly Cys Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
```

245

<210> 214
<211> 246
<212> PRT
<213> Artificial Sequence

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

<400> 214

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 Glu 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 Gln Ser Tyr Pro Pro
85 90 95

Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
130 135 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Ser Tyr
145 150 155 160

```
Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
                165                 170                 175


Ala Thr Ile Lys Arg Asp Gly Ser Glu Lys Gly Tyr Val Asp Ser Val
            180                 185                 190


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
        195                 200                 205


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220


Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240


Met Val Thr Val Ser Ser
                245


<210>  215
<211>  246
<212>  PRT
<213>  Artificial Sequence

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

<400>  215

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 Pro Ser Tyr
            20                  25                  30


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


Ala Thr Ile Lys Arg Asp Gly Ser Glu Lys Gly 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145 150 155 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Glu Ala Ser Ser Leu
180 185 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
195 200 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr
210 215 220

Tyr Cys Gln Gln Ser Gln Ser Tyr Pro Pro Ile Thr Phe Gly Cys Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 216
<211> 247
<212> PRT
<213> Artificial Sequence

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

<400> 216

```
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 Ala His Ser Tyr Pro Leu
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125


Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
    130                 135                 140


Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Gly Thr Tyr Tyr
145                 150                 155                 160


Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met Gly
                165                 170                 175


Ile Ile Asn Pro Ser Arg Gly Ser Thr Val Tyr Ala Gln Lys Phe Gln
            180                 185                 190
```

```
Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met
        195                 200                 205


Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220


Arg Gly Ala Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys Gly
225                 230                 235                 240


Thr Thr Val Thr Val Ser Ser
                245


<210>  217
<211>  247
<212>  PRT
<213>  Artificial Sequence

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

<400>  217

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 Gly Thr Tyr
            20                  25                  30


Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Asn Pro Ser Arg Gly Ser Thr Val 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 Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys
```

100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Gly Ile Asp Ser Trp Leu Ala Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
180 185 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Ala His Ser Tyr Pro Leu Thr Phe Gly Cys
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 218
<211> 254
<212> PRT
<213> Artificial Sequence

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

<400> 218

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 Asn 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 Glu Ala Ser Ser Thr Lys 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 Asp Leu Pro Thr
                85                  90                  95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
        115                 120                 125

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly Ser Leu
    130                 135                 140

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Ala Met
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ser Ser
                165                 170                 175

Ile Ser Ser Ser Ser Glu Gly Ile Tyr Tyr Ala Asp Ser Val Lys Gly
            180                 185                 190

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln
        195                 200                 205

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220
```

```
Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
225                 230                 235                 240


Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                245                 250


<210>  219
<211>  254
<212>  PRT
<213>  Artificial Sequence

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

<400>  219

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


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


Ser Ser Ile Ser Ser Ser Ser Glu Gly Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
            100                 105                 110


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


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
```

130 135 140

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser
145 150 155 160

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Asn Ser
165 170 175

Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
180 185 190

Lys Leu Leu Ile Tyr Glu Ala Ser Ser Thr Lys Ser Gly Val Pro Ser
195 200 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
210 215 220

Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp
225 230 235 240

Asp Leu Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 220
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 220

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 Val Ile Tyr Ser Tyr
20 25 30

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

```
Tyr Ala Ala Ser Ser Leu Lys 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 Val Tyr Asp Thr Pro Leu
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
                165                 170                 175

Asn Ile Asn Thr Asp Gly Ser Glu Val Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
        195                 200                 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr Trp
225                 230                 235                 240

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
                245                 250
```

<210> 221
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 221

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

Ala Asn Ile Asn Thr Asp Gly Ser Glu Val 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 Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
130 135 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145 150 155 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Val Ile Tyr Ser Tyr Leu

165 170 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
180 185 190

Ala Ala Ser Ser Leu Lys Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
210 215 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Tyr Asp Thr Pro Leu Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 222
<211> 246
<212> PRT
<213> Artificial Sequence

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

<400> 222

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 His Ser Val Tyr 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 Tyr Asp Asn Leu Pro Thr
                85                  90                  95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
        115                 120                 125

Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu
    130                 135                 140

Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Thr Asp Tyr
145                 150                 155                 160

Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
                165                 170                 175

Gly Ser Ile Gly Tyr Ser Gly Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
        195                 200                 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220

Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240

Thr Val Thr Val Ser Ser
                245


<210>  223
<211>  246
<212>  PRT
<213>  Artificial Sequence

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

<400> 223

```
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 Thr
            20                  25                  30


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


Trp Ile Gly Ser Ile Gly Tyr Ser Gly Thr Tyr Tyr Asn Pro Ser Leu
    50                  55                  60


Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80


Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
    130                 135                 140


Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145                 150                 155                 160


Leu Ser Cys Arg Ala Ser His Ser Val Tyr Ser Tyr Leu Ala Trp Tyr
                165                 170                 175


Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
            180                 185                 190


Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
```

195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
210 215 220

Val Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Thr Phe Gly Cys Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 224
<211> 482
<212> PRT
<213> Artificial Sequence

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

<400> 224

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 Asp 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 Phe Pro Thr
85 90 95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
        115                 120                 125

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
    130                 135                 140

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala Asn
                165                 170                 175

Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys Gly
            180                 185                 190

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln
        195                 200                 205

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
225                 230                 235                 240

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
                245                 250                 255

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            260                 265                 270

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        275                 280                 285

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    290                 295                 300

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
305                 310                 315                 320
```

```
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
                325                 330                 335

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
            340                 345                 350

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
        355                 360                 365

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val
    370                 375                 380

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
385                 390                 395                 400

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
                405                 410                 415

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
            420                 425                 430

Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val
        435                 440                 445

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
    450                 455                 460

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
465                 470                 475                 480

Pro Gly
```

<210> 225
<211> 482
<212> PRT
<213> Artificial Sequence

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

<400> 225

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


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


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


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
            100                 105                 110


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


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140


Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser
145                 150                 155                 160


Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
                165                 170                 175


Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
            180                 185                 190


Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser
```

```
        195                 200                 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
    210                 215                 220

Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Glu
225                 230                 235                 240

Ser Phe Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ala Ser
                245                 250                 255

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            260                 265                 270

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        275                 280                 285

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    290                 295                 300

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
305                 310                 315                 320

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
                325                 330                 335

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
            340                 345                 350

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
        355                 360                 365

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val
    370                 375                 380

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
385                 390                 395                 400

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
```

405 410 415

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
420 425 430

Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val
435 440 445

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
450 455 460

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
465 470 475 480

Pro Gly

<210> 226
<211> 473
<212> PRT
<213> Artificial Sequence

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

<400> 226

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 Glu 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 Leu Glu Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
                165                 170                 175

Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
        195                 200                 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr Met
225                 230                 235                 240

Val Thr Val Ser Ser Ala Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285
```

```
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu
    370                 375                 380

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe Thr
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly
465                 470
```

<210> 227
<211> 473
<212> PRT

<213> Artificial Sequence

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

<400> 227

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


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


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


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140


Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Glu Ala Ser Ser Leu
```

```
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Leu Glu Ser Tyr Pro Leu Thr Phe Gly Cys Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys Ala Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu
    370                 375                 380

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
```

385 390 395 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
405 410 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe Thr
420 425 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
435 440 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
450 455 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470

<210> 228
<211> 482
<212> PRT
<213> Artificial Sequence

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

<400> 228

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 Lys Tyr
20 25 30

Thr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
35 40 45

Ser Ala Ile Val Gly Ser Gly Glu Ser Thr Tyr Phe 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 Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
            100                 105                 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser
145                 150                 155                 160

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
                165                 170                 175

Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
            180                 185                 190

Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser
        195                 200                 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
    210                 215                 220

Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp
225                 230                 235                 240

Asp Leu Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ala Ser
                245                 250                 255

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            260                 265                 270

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        275                 280                 285
```

```
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    290                 295                 300

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
305                 310                 315                 320

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
                325                 330                 335

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
            340                 345                 350

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
        355                 360                 365

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val
    370                 375                 380

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
385                 390                 395                 400

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
                405                 410                 415

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
            420                 425                 430

Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val
        435                 440                 445

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
    450                 455                 460

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
465                 470                 475                 480

Pro Gly
```

<210> 229
<211> 483
<212> PRT
<213> Artificial Sequence

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

<400> 229

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 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 Leu Leu Ile Tyr 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 Asp
85 90 95

Val Ala Leu Pro Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
130 135 140

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
145 150 155 160

Phe Ser Asp Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys

```
                165                 170                 175

Leu Glu Trp Met Gly Met Ile Asn Pro Ser Trp Gly Ser Thr Ser Tyr
            180                 185                 190

Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr
        195                 200                 205

Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
    210                 215                 220

Val Tyr Tyr Cys Ala Arg Glu Ala Ala Asp Gly Phe Val Gly Glu Arg
225                 230                 235                 240

Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Ala
                245                 250                 255

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
            260                 265                 270

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
        275                 280                 285

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
    290                 295                 300

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
305                 310                 315                 320

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
                325                 330                 335

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
            340                 345                 350

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
        355                 360                 365

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg
```

370 375 380

Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val
385 390 395 400

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
405 410 415

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
420 425 430

Pro Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr
435 440 445

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
450 455 460

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
465 470 475 480

Ser Pro Gly

<210> 230
<211> 483
<212> PRT
<213> Artificial Sequence

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

<400> 230

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asp Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

```
Gly Met Ile Asn Pro Ser Trp 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 Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
            100                 105                 110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140

Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
145                 150                 155                 160

Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn
                165                 170                 175

Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
            180                 185                 190

Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
        195                 200                 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
    210                 215                 220

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Asp Val
225                 230                 235                 240

Ala Leu Pro Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ala
                245                 250                 255
```

```
Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
            260                 265                 270

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
        275                 280                 285

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
    290                 295                 300

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
305                 310                 315                 320

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
                325                 330                 335

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
            340                 345                 350

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
        355                 360                 365

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg
    370                 375                 380

Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val
385                 390                 395                 400

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
                405                 410                 415

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
            420                 425                 430

Pro Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr
        435                 440                 445

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
    450                 455                 460
```

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
465                 470                 475                 480


Ser Pro Gly
```

<210> 231
<211> 474
<212> PRT
<213> Artificial Sequence

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

<400> 231

```
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 Gly Ser Tyr
            20                  25                  30


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


Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
```

```
    130                 135                 140

Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Glu Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Gln Ser Tyr Pro Pro Ile Thr Phe Gly Cys Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Ala Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                325                 330                 335

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
```

340 345 350

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
355 360 365

Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp
370 375 380

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
385 390 395 400

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
405 410 415

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
420 425 430

Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
435 440 445

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
450 455 460

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470

<210> 232
<211> 474
<212> PRT
<213> Artificial Sequence

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

<400> 232

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 Glu 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 Gln Ser Tyr Pro Pro
                85                  90                  95

Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
    130                 135                 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Ser Tyr
145                 150                 155                 160

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
                165                 170                 175

Ala Thr Ile Lys Arg Asp Gly Ser Glu Lys Gly Tyr Val Asp Ser Val
            180                 185                 190

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
        195                 200                 205

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240
```

```
Met Val Thr Val Ser Ser Ala Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                325                 330                 335

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
            340                 345                 350

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
        355                 360                 365

Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp
    370                 375                 380

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
385                 390                 395                 400

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
                405                 410                 415

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
            420                 425                 430

Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
        435                 440                 445
```

```
Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
    450                 455                 460


Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465                 470


<210>  233
<211>  474
<212>  PRT
<213>  Artificial Sequence

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

<400>  233

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 Pro Ser Tyr
            20                  25                  30


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


Ala Thr Ile Lys Arg Asp Gly Ser Glu Lys Gly 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 Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
```

```
    130                 135                 140

Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Glu Ala Ser Ser Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Gln Ser Tyr Pro Pro Ile Thr Phe Gly Cys Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Ala Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                325                 330                 335

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
```

340 345 350

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
355 360 365

Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp
370 375 380

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
385 390 395 400

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
405 410 415

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
420 425 430

Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
435 440 445

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
450 455 460

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470

<210> 234
<211> 475
<212> PRT
<213> Artificial Sequence

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

<400> 234

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 Ala His Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
    130                 135                 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Gly Thr Tyr Tyr
145                 150                 155                 160

Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met Gly
                165                 170                 175

Ile Ile Asn Pro Ser Arg Gly Ser Thr Val Tyr Ala Gln Lys Phe Gln
            180                 185                 190

Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met
        195                 200                 205

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Ala Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys Gly
225                 230                 235                 240
```

```
Thr Thr Val Thr Val Ser Ser Ala Ser Asp Lys Thr His Thr Cys Pro
                245                 250                 255

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
            260                 265                 270

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
        275                 280                 285

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
    290                 295                 300

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
305                 310                 315                 320

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
                325                 330                 335

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
            340                 345                 350

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
        355                 360                 365

Lys Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg
    370                 375                 380

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
385                 390                 395                 400

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
                405                 410                 415

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser
            420                 425                 430

Phe Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
        435                 440                 445
```

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
    450   455   460

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465   470   475

<210> 235
<211> 475
<212> PRT
<213> Artificial Sequence

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

<400> 235

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 Gly Thr Tyr
            20   25   30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
        35   40   45

Gly Ile Ile Asn Pro Ser Arg Gly Ser Thr Val 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 Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys
            100   105   110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met

130 135 140

Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Gly Ile Asp Ser Trp Leu Ala Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
180 185 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Ala His Ser Tyr Pro Leu Thr Phe Gly Cys
225 230 235 240

Gly Thr Lys Val Glu Ile Lys Ala Ser Asp Lys Thr His Thr Cys Pro
245 250 255

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
260 265 270

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
275 280 285

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
290 295 300

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
305 310 315 320

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
325 330 335

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val

340 345 350

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
355 360 365

Lys Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg
370 375 380

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
385 390 395 400

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
405 410 415

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser
420 425 430

Phe Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
435 440 445

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
450 455 460

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470 475

<210> 236
<211> 482
<212> PRT
<213> Artificial Sequence

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

<400> 236

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 Asn 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 Glu Ala Ser Ser Thr Lys 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 Asp Leu Pro Thr
                85                  90                  95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
        115                 120                 125

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly Ser Leu
    130                 135                 140

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Ala Met
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ser Ser
                165                 170                 175

Ile Ser Ser Ser Ser Glu Gly Ile Tyr Tyr Ala Asp Ser Val Lys Gly
            180                 185                 190

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln
        195                 200                 205

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
225                 230                 235                 240
```

```
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
                245                 250                 255

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            260                 265                 270

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        275                 280                 285

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    290                 295                 300

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
305                 310                 315                 320

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
                325                 330                 335

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
            340                 345                 350

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
        355                 360                 365

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val
    370                 375                 380

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
385                 390                 395                 400

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
                405                 410                 415

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
            420                 425                 430

Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val
        435                 440                 445
```

```
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
    450                 455                 460


His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
465                 470                 475                 480


Pro Gly
```

<210> 237
<211> 482
<212> PRT
<213> Artificial Sequence

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

<400> 237

```
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


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


Ser Ser Ile Ser Ser Ser Ser Glu Gly Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr
            100                 105                 110


Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
```

```
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser
145                 150                 155                 160

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Asn Ser
                165                 170                 175

Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
            180                 185                 190

Lys Leu Leu Ile Tyr Glu Ala Ser Ser Thr Lys Ser Gly Val Pro Ser
        195                 200                 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
    210                 215                 220

Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp
225                 230                 235                 240

Asp Leu Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ala Ser
                245                 250                 255

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            260                 265                 270

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        275                 280                 285

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    290                 295                 300

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
305                 310                 315                 320

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
```

325 330 335

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
340 345 350

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
355 360 365

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val
370 375 380

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
385 390 395 400

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
405 410 415

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
420 425 430

Val Leu Val Ser Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val
435 440 445

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
450 455 460

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
465 470 475 480

Pro Gly

<210> 238
<211> 478
<212> PRT
<213> Artificial Sequence

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

<400> 238

```
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 Val Ile Tyr Ser Tyr
            20                  25                  30

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

Tyr Ala Ala Ser Ser Leu Lys 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 Val Tyr Asp Thr Pro Leu
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
                165                 170                 175

Asn Ile Asn Thr Asp Gly Ser Glu Val Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
        195                 200                 205
```

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr Trp
225                 230                 235                 240

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Asp Lys Thr His
                245                 250                 255

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
            260                 265                 270

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
        275                 280                 285

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
    290                 295                 300

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
305                 310                 315                 320

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
                325                 330                 335

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
            340                 345                 350

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
        355                 360                 365

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro
    370                 375                 380

Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
385                 390                 395                 400

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
                405                 410                 415
```

```
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser
            420                 425                 430


Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
        435                 440                 445


Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
    450                 455                 460


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465                 470                 475


<210>  239
<211>  478
<212>  PRT
<213>  Artificial Sequence

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

<400>  239

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


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


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


Ala Asn Ile Asn Thr Asp Gly Ser Glu Val 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 Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
```

```
            100                 105                 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Val Ile Tyr Ser Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Leu Lys Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Tyr Asp Thr Pro Leu Thr
225                 230                 235                 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ala Ser Asp Lys Thr His
                245                 250                 255

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
            260                 265                 270

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
        275                 280                 285

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
    290                 295                 300

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
```

305 310 315 320

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
325 330 335

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
340 345 350

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
355 360 365

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro
370 375 380

Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
385 390 395 400

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
405 410 415

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser
420 425 430

Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
435 440 445

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
450 455 460

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470 475

<210> 240
<211> 474
<212> PRT
<213> Artificial Sequence

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

<400> 240

```
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 His Ser Val Tyr 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 Tyr Asp Asn Leu Pro Thr
                85                  90                  95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
        115                 120                 125

Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu
    130                 135                 140

Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Thr Asp Tyr
145                 150                 155                 160

Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
                165                 170                 175

Gly Ser Ile Gly Tyr Ser Gly Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
        195                 200                 205
```

```
Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220


Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240


Thr Val Thr Val Ser Ser Ala Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255


Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270


Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285


Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300


Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320


Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                325                 330                 335


Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
            340                 345                 350


Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
        355                 360                 365


Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp
    370                 375                 380


Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
385                 390                 395                 400


Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
                405                 410                 415
```

```
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
            420                 425                 430


Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
        435                 440                 445


Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
    450                 455                 460


Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465                 470


<210>  241
<211>  474
<212>  PRT
<213>  Artificial Sequence

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

<400>  241

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 Thr
            20                  25                  30


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


Trp Ile Gly Ser Ile Gly Tyr Ser Gly Thr Tyr Tyr Asn Pro Ser Leu
    50                  55                  60


Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80


Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly Gln
```

```
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
    130                 135                 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145                 150                 155                 160

Leu Ser Cys Arg Ala Ser His Ser Val Tyr Ser Tyr Leu Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
            180                 185                 190

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
    210                 215                 220

Val Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Thr Phe Gly Cys Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys Ala Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
```

305 310 315 320

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
325 330 335

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
340 345 350

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
355 360 365

Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Arg Asp
370 375 380

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
385 390 395 400

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
405 410 415

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
420 425 430

Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
435 440 445

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
450 455 460

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470

<210> 242
<211> 575
<212> PRT
<213> Artificial Sequence

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

<400> 242

```
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 Glu 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 Gln Ser Tyr Pro Pro
                85                  90                  95

Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
    130                 135                 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Ser Tyr
145                 150                 155                 160

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
                165                 170                 175

Ala Thr Ile Lys Gln Asp Gly Ser Glu Lys Ser Tyr Val Asp Ser Val
            180                 185                 190

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
        195                 200                 205
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Pro Leu Asn Ala Gly Glu Leu Asp Val Trp Gly Gln Gly Thr
225                 230                 235                 240

Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
                245                 250                 255

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
            260                 265                 270

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
        275                 280                 285

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
    290                 295                 300

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
305                 310                 315                 320

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
                325                 330                 335

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
            340                 345                 350

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
        355                 360                 365

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
    370                 375                 380

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
385                 390                 395                 400

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
                405                 410                 415
```

```
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
            420                 425                 430

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
        435                 440                 445

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
    450                 455                 460

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu
465                 470                 475                 480

Pro Pro Ser Arg Asp Glu Leu Thr Glu Asn Gln Val Ser Leu Thr Cys
                485                 490                 495

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
            500                 505                 510

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
        515                 520                 525

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Trp Leu Thr Val Asp Lys Ser
    530                 535                 540

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
545                 550                 555                 560

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
                565                 570                 575
```

<210> 243
<211> 583
<212> PRT
<213> Artificial Sequence

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

<400> 243

```
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 Asp Leu Pro Thr
                85                  90                  95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
        115                 120                 125

Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
    130                 135                 140

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr Thr Met
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ser Ala
                165                 170                 175

Ile Val Gly Ser Gly Glu Ser Thr Tyr Phe Ala Asp Ser Val Lys Gly
            180                 185                 190

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
        195                 200                 205

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
```

```
    210                 215                 220

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
225                 230                 235                 240

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
                245                 250                 255

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
            260                 265                 270

Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
        275                 280                 285

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
    290                 295                 300

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
305                 310                 315                 320

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
                325                 330                 335

Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val
            340                 345                 350

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
        355                 360                 365

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
    370                 375                 380

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
385                 390                 395                 400

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
                405                 410                 415

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
```

```
            420                 425                 430

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
        435                 440                 445

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
    450                 455                 460

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
465                 470                 475                 480

Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
                485                 490                 495

Glu Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
            500                 505                 510

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
        515                 520                 525

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
    530                 535                 540

Ser Trp Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
545                 550                 555                 560

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
                565                 570                 575

Ser Leu Ser Leu Ser Pro Gly
            580
```

<210> 244
<211> 347
<212> PRT
<213> Artificial Sequence

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

<400> 244

```
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 Ala Ser Asp Lys Thr His
        115                 120                 125

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
    130                 135                 140

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
145                 150                 155                 160

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
                165                 170                 175

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
            180                 185                 190

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
        195                 200                 205
```

```
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
    210                 215                 220


Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
225                 230                 235                 240


Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro
                245                 250                 255


Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
            260                 265                 270


Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
        275                 280                 285


Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser
    290                 295                 300


Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
305                 310                 315                 320


Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
                325                 330                 335


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
            340                 345


<210>  245
<211>  347
<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 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 Ile Gly Ala Ala Ala Gly Trp Phe Asp Pro Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Asp Lys Thr His
        115                 120                 125

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
    130                 135                 140

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
145                 150                 155                 160

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
                165                 170                 175

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
            180                 185                 190

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
        195                 200                 205

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
    210                 215                 220

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
```

225 230 235 240

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro
245 250 255

Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
260 265 270

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
275 280 285

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser
290 295 300

Asp Gly Ser Phe Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
305 310 315 320

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
325 330 335

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
340 345

<210> 246
<211> 762
<212> DNA
<213> Artificial Sequence

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

<400> 246
gacatccaga tgacccagag ccccagcacc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgac gccagcagcc tggagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgag ttcaccctga ccatcagcag cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag tacgagagct tccccacctt cggctgcggc 300

accaaggtgg agatcaaggg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 360

agcggcggcg gcggcagcga ggtgcagctg gtggagagcg gcggcggcct ggtgcagccc 420

ggcggcagcc tgaggctgag ctgcgccgcc agcggcttca ccttcagcag ctacggcatg 480

agctgggtga ggcaggcccc cggcaagtgc ctggagtggg tggccaacat caagcaggac 540

ggcagcgaga agtactacgt ggacagcgtg aagggcaggt tcaccatcag cagggacaac 600

gccaagaaca gcctgtacct gcagatgaac agcctgaggg ccgaggacac cgccgtgtac 660

tactgcgcca gggagggcgg cccctactac gacagcagcg gctacttcgt gtactacggc 720

atggacgtgt ggggccaggg caccaccgtg accgtgagca gc 762

<210> 247
<211> 762
<212> DNA
<213> Artificial Sequence

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

<400> 247
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctacggca tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaagcagg acggcagcga gaagtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggagggc 300

ggcccctact acgacagcag cggctacttc gtgtactacg gcatggacgt gtggggccag 360

ggcaccaccg tgaccgtgag cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg gcggcggcgg cagcgacatc cagatgaccc agagccccag caccctgagc 480

gccagcgtgg gcgacagggt gaccatcacc tgcagggcca gccagagcat cagcagctgg 540

ctggcctggt accagcagaa gcccggcaag gcccccaagc tgctgatcta cgacgccagc 600

agcctggaga gcggcgtgcc cagcaggttc agcggcagcg gcagcggcac cgagttcacc 660

ctgaccatca gcagcctgca gcccgacgac ttcgccacct actactgcca gcagtacgag 720

agcttcccca ccttcggctg cggcaccaag gtggagatca ag 762

<210> 248

<211> 735
<212> DNA
<213> Artificial Sequence

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

<400> 248
gacatccaga tgacccagag ccccagcacc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgag gccagcagcc tggagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgag ttcaccctga ccatcagcag cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag ctggagagct acccccctgac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttcag cagctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaagcag 540

gacggcagcg agaagtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccaggcccct gaacgccggc gagctggacg tgtggggcca gggcaccatg 720

gtgaccgtga gcagc 735

<210> 249
<211> 735
<212> DNA
<213> Artificial Sequence

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

<400> 249
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaagcagg acggcagcga gaagtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc caggcccctg 300

aacgccggcg agctggacgt gtggggccag ggcaccatgg tgaccgtgag cagcggcggc 360

ggcggcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcgacatc 420

cagatgaccc agagccccag caccctgagc gccagcgtgg gcgacagggt gaccatcacc 480

tgcagggcca gccagagcat cagcagctgg ctggcctggt accagcagaa gcccggcaag 540

gcccccaagc tgctgatcta cgaggccagc agcctggaga gcggcgtgcc cagcaggttc 600

agcggcagcg gcagcggcac cgagttcacc ctgaccatca gcagcctgca gcccgacgac 660

ttcgccacct actactgcca gcagctggag agctaccccc tgaccttcgg ctgcggcacc 720

aaggtggaga tcaag 735

<210> 250
<211> 762
<212> DNA
<213> Artificial Sequence

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

<400> 250
gacatccaga tgacccagag ccccagcacc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacaag gccagcagcc tggagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgag ttcaccctga ccatcagcag cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag tacgacgacc tgcccacctt cggctgcggc 300

accaaggtgg agatcaaggg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 360

agcggcggcg gcggcagcga ggtgcagctg ctggagagcg gcggcggcct ggtgcagccc 420

ggcggcagcc tgaggctgag ctgcgccgcc agcggcttca ccttcagcaa gtacaccatg 480

agctgggtga ggcaggcccc cggcaagtgc ctggagtggg tgagcgccat cgtgggcagc 540

ggcgagagca cctacttcgc cgacagcgtg aagggcaggt tcaccatcag cagggacaac 600

agcaagaaca ccctgtacct gcagatgaac agcctgaggg ccgaggacac cgccgtgtac 660

tactgcgcca gggagggcgg cccctactac gacagcagcg gctacttcgt gtactacggc 720

atggacgtgt ggggccaggg caccaccgtg accgtgagca gc 762

<210> 251
<211> 762
<212> DNA
<213> Artificial Sequence

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

<400> 251
gaggtgcagc tgctggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc aagtacacca tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtgagcgcc atcgtgggca gcggcgagag cacctacttc 180

gccgacagcg tgaagggcag gttcaccatc agcagggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggagggc 300

ggcccctact acgacagcag cggctacttc gtgtactacg gcatggacgt gtggggccag 360

ggcaccaccg tgaccgtgag cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg gcggcggcgg cagcgacatc cagatgaccc agagccccag caccctgagc 480

gccagcgtgg gcgacagggt gaccatcacc tgcagggcca gccagagcat cagcagctgg 540

ctggcctggt accagcagaa gcccggcaag gcccccaagc tgctgatcta caaggccagc 600

agcctggaga gcggcgtgcc cagcaggttc agcggcagcg gcagcggcac cgagttcacc 660

ctgaccatca gcagcctgca gcccgacgac ttcgccacct actactgcca gcagtacgac 720

gacctgccca ccttcggctg cggcaccaag gtggagatca ag 762

<210> 252
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 252
gacatcgtga tgacccagag ccccctgagc ctgcccgtga cccccggcga gcccgccagc 60

atcagctgca ggagcagcca gagcctgctg tacagcaacg gctacaacta cctggactgg 120

tacctgcaga agcccggcca gagcccccag ctgctgatct acctgggcag caacagggcc 180

agcggcgtgc ccgacaggtt cagcggcagc ggcagcggca ccgacttcac cctgaagatc 240

agcagggtgg aggccgagga cgtgggcgtg tactactgca tgcaggacgt ggccctgccc 300

atcaccttcg gctgcggcac caaggtggag atcaagggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cggcggcggc ggcagccagg tgcagctggt gcagagcggc 420

gccgaggtga agaagcccgg cgccagcgtg aaggtgagct gcaaggccag cggctacacc 480

ttcagcgact actacatgca ctgggtgagg caggcccccg gccagtgcct ggagtggatg 540

ggcatgatca accccagctg gggcagcacc agctacgccc agaagttcca gggcagggtg 600

accatgacca gggacaccag caccagcacc gtgtacatgg agctgagcag cctgaggagc 660

gaggacaccg ccgtgtacta ctgcgccagg gaggccgccg acggcttcgt gggcgagagg 720

tacttcgacc tgtggggcag gggcaccctg gtgaccgtga gcagc 765

<210> 253
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 253
caggtgcagc tggtgcagag cggcgccgag gtgaagaagc ccggcgccag cgtgaaggtg 60

agctgcaagg ccagcggcta caccttcagc gactactaca tgcactgggt gaggcaggcc 120

cccggccagt gcctggagtg gatgggcatg atcaacccca gctggggcag caccagctac 180

gcccagaagt tccagggcag ggtgaccatg accagggaca ccagcaccag caccgtgtac 240

atggagctga gcagcctgag gagcgaggac accgccgtgt actactgcgc cagggaggcc 300

gccgacggct tcgtgggcga gaggtacttc gacctgtggg gcaggggcac cctggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg acatcgtgat gacccagagc cccctgagcc tgcccgtgac ccccggcgag 480

cccgccagca tcagctgcag gagcagccag agcctgctgt acagcaacgg ctacaactac 540

ctggactggt acctgcagaa gcccggccag agcccccagc tgctgatcta cctgggcagc 600

aacagggcca gcggcgtgcc cgacaggttc agcggcagcg gcagcggcac cgacttcacc 660

ctgaagatca gcagggtgga ggccgaggac gtgggcgtgt actactgcat gcaggacgtg 720

gccctgccca tcaccttcgg ctgcggcacc aaggtggaga tcaag 765

<210> 254
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 254
gacatccaga tgacccagag ccccagcacc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgag gccagcagcc tggagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgag ttcaccctga ccatcagcag cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag agccagagct acccccccat caccttcggc 300

tgcggcacca aggtggagat caagggcggc ggcggcagcg gcggcggcgg cagcggcggc 360

ggcggcagcg gcggcggcgg cagcgaggtg cagctggtgg agagcggcgg cggcctggtg 420

cagcccggcg gcagcctgag gctgagctgc gccgccagcg gcttcacctt cggcagctac 480

tggatgagct gggtgaggca ggcccccggc aagtgcctgg agtgggtggc caccatcaag 540

caggacggca gcgagaagag ctacgtggac agcgtgaagg gcaggttcac catcagcagg 600

gacaacgcca agaacagcct gtacctgcag atgaacagcc tgagggccga ggacaccgcc 660

gtgtactact gcgccaggcc cctgaacgcc ggcgagctgg acgtgtgggg ccagggcacc 720

atggtgaccg tgagcagc 738

<210> 255
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 255

gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcggc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccacc atcaagcagg acggcagcga gaagagctac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc caggcccctg 300

aacgccggcg agctggacgt gtggggccag ggcaccatgg tgaccgtgag cagcggcggc 360

ggcggcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcgacatc 420

cagatgaccc agagccccag caccctgagc gccagcgtgg gcgacagggt gaccatcacc 480

tgcagggcca gccagagcat cagcagctgg ctggcctggt accagcagaa gcccggcaag 540

gcccccaagc tgctgatcta cgaggccagc agcctggaga gcggcgtgcc cagcaggttc 600

agcggcagcg gcagcggcac cgagttcacc ctgaccatca gcagcctgca gcccgacgac 660

ttcgccacct actactgcca gcagagccag agctaccccc ccatcacctt cggctgcggc 720

accaaggtgg agatcaag 738

<210> 256
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 256
gacatccaga tgacccagag ccccagcacc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgag gccagcagcc tggagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgag ttcaccctga ccatcagcag cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag agccagagct acccccccat caccttcggc 300

tgcggcacca aggtggagat caagggcggc ggcggcagcg gcggcggcgg cagcggcggc 360

ggcggcagcg gcggcggcgg cagcgaggtg cagctggtgg agagcggcgg cggcctggtg 420

cagcccggcg gcagcctgag gctgagctgc gccgccagcg gcttcacctt ccccagctac 480

tggatgagct gggtgaggca ggcccccggc aagtgcctgg agtgggtggc caccatcaag 540

agggacggca gcgagaaggg ctacgtggac agcgtgaagg gcaggttcac catcagcagg 600

gacaacgcca agaacagcct gtacctgcag atgaacagcc tgagggccga ggacaccgcc 660

gtgtactact gcgccaggcc cctgaacgcc ggcgagctgg acgtgtgggg ccagggcacc 720

atggtgaccg tgagcagc 738

<210> 257
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 257
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcccc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccacc atcaagaggg acggcagcga gaagggctac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc caggcccctg 300

aacgccggcg agctggacgt gtggggccag ggcaccatgg tgaccgtgag cagcggcggc 360

ggcggcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcgacatc 420

cagatgaccc agagccccag caccctgagc gccagcgtgg gcgacagggt gaccatcacc 480

tgcagggcca gccagagcat cagcagctgg ctggcctggt accagcagaa gcccggcaag 540

gcccccaagc tgctgatcta cgaggccagc agcctggaga gcggcgtgcc cagcaggttc 600

agcggcagcg gcagcggcac cgagttcacc ctgaccatca gcagcctgca gcccgacgac 660

ttcgccacct actactgcca gcagagccag agctaccccc ccatcacctt cggctgcggc 720

accaaggtgg agatcaag 738

<210> 258
<211> 741
<212> DNA
<213> Artificial Sequence

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

<400> 258
gacatccaga tgacccagag ccccagcagc gtgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gggcatcgac agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcagcc tgcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gcccacagct acccccctgac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctggtgcaga gcggcgccga ggtgaagaag 420

cccggcgcca gcgtgaaggt gagctgcaag gccagcggct acaccttcgg cacctactac 480

atgcactggg tgaggcaggc ccccggccag tgcctggagt ggatgggcat catcaacccc 540

agcaggggca gcaccgtgta cgcccagaag ttccagggca gggtgaccat gaccagggac 600

accagcacca gcaccgtgta catggagctg agcagcctga ggagcgagga caccgccgtg 660

tactactgcg ccaggggcgc cggctacgac gacgaggaca tggacgtgtg gggcaagggc 720

accaccgtga ccgtgagcag c 741

<210> 259
<211> 741
<212> DNA
<213> Artificial Sequence

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

<400> 259
caggtgcagc tggtgcagag cggcgccgag gtgaagaagc ccggcgccag cgtgaaggtg 60

agctgcaagg ccagcggcta caccttcggc acctactaca tgcactgggt gaggcaggcc 120

cccggccagt gcctggagtg gatgggcatc atcaacccca gcaggggcag caccgtgtac 180

gcccagaagt tccagggcag ggtgaccatg accagggaca ccagcaccag caccgtgtac 240

atggagctga gcagcctgag gagcgaggac accgccgtgt actactgcgc caggggcgcc 300

ggctacgacg acgaggacat ggacgtgtgg ggcaagggca ccaccgtgac cgtgagcagc 360

ggcggcggcg gcagcggcgg cggcggcagc ggcggcggcg gcagcggcgg cggcggcagc 420

gacatccaga tgacccagag ccccagcagc gtgagcgcca gcgtgggcga cagggtgacc 480

atcacctgca gggccagcca gggcatcgac agctggctgg cctggtacca gcagaagccc 540

ggcaaggccc ccaagctgct gatctacgcc gccagcagcc tgcagagcgg cgtgcccagc 600

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 660

gaggacttcg ccacctacta ctgccagcag gcccacagct acccccctgac cttcggctgc 720

ggcaccaagg tggagatcaa g 741

<210> 260
<211> 762
<212> DNA
<213> Artificial Sequence

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

<400> 260
gacatccaga tgacccagag ccccagcacc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcaa cagcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgag gccagcagca ccaagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgag ttcaccctga ccatcagcag cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag tacgacgacc tgcccacctt cggctgcggc 300

accaaggtgg agatcaaggg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 360

agcggcggcg gcggcagcga ggtgcagctg gtggagagcg gcggcggcct ggtgaagccc 420

ggcggcagcc tgaggctgag ctgcgccgcc agcggcttca ccttcagcag ctacgccatg 480

agctgggtga ggcaggcccc cggcaagtgc ctggagtggg tgagcagcat cagcagcagc 540

agcgagggca tctactacgc cgacagcgtg aagggcaggt tcaccatcag cagggacaac 600

gccaagaaca gcctgtacct gcagatgaac agcctgaggg ccgaggacac cgccgtgtac 660

tactgcgcca gggagggcgg cccctactac gacagcagcg gctacttcgt gtactacggc 720

atggacgtgt ggggccaggg caccaccgtg accgtgagca gc 762

<210> 261

<211> 762
<212> DNA
<213> Artificial Sequence

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

<400> 261
gaggtgcagc tggtggagag cggcggcggc ctggtgaagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtgagcagc atcagcagca gcagcgaggg catctactac 180

gccgacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggagggc 300

ggcccctact acgacagcag cggctacttc gtgtactacg gcatggacgt gtggggccag 360

ggcaccaccg tgaccgtgag cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg gcggcggcgg cagcgacatc cagatgaccc agagccccag caccctgagc 480

gccagcgtgg gcgacagggt gaccatcacc tgcagggcca gcaacagcat cagcagctgg 540

ctggcctggt accagcagaa gcccggcaag gcccccaagc tgctgatcta cgaggccagc 600

agcaccaaga gcggcgtgcc cagcaggttc agcggcagcg gcagcggcac cgagttcacc 660

ctgaccatca gcagcctgca gcccgacgac ttcgccacct actactgcca gcagtacgac 720

gacctgccca ccttcggctg cggcaccaag gtggagatca ag 762

<210> 262
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 262
gacatccaga tgacccagag ccccagcagc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca ggtgatctac agctacctga actggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcagcc tgaagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gtgtacgaca ccccccctgac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttcag cagctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaacacc 540

gacggcagcg aggtgtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccagggacgt gggccccggc atcgcctacc agggccactt cgactactgg 720

ggccagggca ccctggtgac cgtgagcagc 750

<210> 263
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 263
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaacaccg acggcagcga ggtgtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggacgtg 300

ggccccggca tcgcctacca gggccacttc gactactggg gccagggcac cctggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg acatccagat gacccagagc cccagcagcc tgagcgccag cgtgggcgac 480

agggtgacca tcacctgcag ggccagccag gtgatctaca gctacctgaa ctggtaccag 540

cagaagcccg gcaaggcccc caagctgctg atctacgccg ccagcagcct gaagagcggc 600

gtgcccagca ggttcagcgg cagcggcagc ggcaccgact tcaccctgac catcagcagc 660

ctgcagcccg aggacttcgc cacctactac tgccagcagg tgtacgacac ccccctgacc 720

ttcggctgcg gcaccaaggt ggagatcaag 750

<210> 264
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 264
gagatcgtgc tgacccagag ccccgccacc ctgagcctga gccccggcga gagggccacc 60

ctgagctgca gggccagcca cagcgtgtac agctacctgg cctggtacca gcagaagccc 120

ggccaggccc ccaggctgct gatctacgac gccagcaaca gggccaccgg catccccgcc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctggagccc 240

gaggacttcg ccgtgtacta ctgccagcag tacgacaacc tgcccacctt cggctgcggc 300

accaaggtgg agatcaaggg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 360

agcggcggcg gcggcagcca gctgcagctg caggagagcg gccccggcct ggtgaagccc 420

agcgagaccc tgagcctgac ctgcaccgtg agcggcggca gcatcagcag caccgactac 480

tactggggct ggatcaggca gccccccggc aagtgcctgg agtggatcgg cagcatcggc 540

tacagcggca cctactacaa ccccagcctg aagagcaggg tgaccatcag cgtggacacc 600

agcaagaacc agttcagcct gaagctgagc agcgtgaccg ccgccgacac cgccgtgtac 660

tactgcgcca gggagaccgc ccacgacgtg cacggcatgg acgtgtgggg ccagggcacc 720

accgtgaccg tgagcagc 738

<210> 265
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 265
cagctgcagc tgcaggagag cggccccggc ctggtgaagc ccagcgagac cctgagcctg 60

acctgcaccg tgagcggcgg cagcatcagc agcaccgact actactgggg ctggatcagg 120

cagccccccg gcaagtgcct ggagtggatc ggcagcatcg gctacagcgg cacctactac 180

aaccccagcc tgaagagcag ggtgaccatc agcgtggaca ccagcaagaa ccagttcagc 240

ctgaagctga gcagcgtgac cgccgccgac accgccgtgt actactgcgc cagggagacc 300

gcccacgacg tgcacggcat ggacgtgtgg ggccagggca ccaccgtgac cgtgagcagc 360

ggcggcggcg gcagcggcgg cggcggcagc ggcggcggcg gcagcggcgg cggcggcagc 420

gagatcgtgc tgacccagag ccccgccacc ctgagcctga gccccggcga gagggccacc 480

ctgagctgca gggccagcca cagcgtgtac agctacctgg cctggtacca gcagaagccc 540

ggccaggccc ccaggctgct gatctacgac gccagcaaca gggccaccgg catccccgcc 600

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctggagccc 660

gaggacttcg ccgtgtacta ctgccagcag tacgacaacc tgcccacctt cggctgcggc 720

accaaggtgg agatcaag 738

<210> 266
<211> 127
<212> PRT
<213> Artificial Sequence

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

<400> 266

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 Ala 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

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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Pro Arg Ala Tyr Tyr Asp Ser Ser Gly Phe Lys Val Asn Tyr
            100                 105                 110


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


<210>  267
<211>  108
<212>  PRT
<213>  Artificial Sequence

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

<400>  267

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


Phe 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 Ala Ser Ser Ser Pro
                85                  90                  95


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


<210>  268
```

<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 268

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

Ser Gly Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly His Ser Ser Ser Tyr Tyr Asp His Ala Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 269
<211> 108
<212> PRT
<213> Artificial Sequence

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

<400> 269

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 Asp
            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 His Ser Ser Ala Pro
                85                  90                  95

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


<210>  270
<211>  123
<212>  PRT
<213>  Artificial Sequence

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

<400>  270

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
            20                  25                  30

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

Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60
```

```
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80


Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Arg Val Gly Gly Val Tyr Ser Thr Ile Glu Thr Tyr Gly Met Asp Val
            100                 105                 110


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


<210>  271
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  271

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 Thr Val Tyr Pro Pro
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
```

100 105

<210> 272
<211> 119
<212> PRT
<213> Artificial Sequence

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

<400> 272

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 Gln Gly Ile His Gly Leu Arg Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 273
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 273

Glu Ile Val Met 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 Asp His Asn Phe Pro Tyr
85 90 95

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

<210> 274
<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 274

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

```
Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys 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 Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  275
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  275

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


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


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


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


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

85 90 95

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

<210> 276
<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 276

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys 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 Glu Gly Gly Asp Ser Trp Tyr His Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 277
<211> 107
<212> PRT

<213> Artificial Sequence

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

<400> 277

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 Asn 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 Lys Leu Ser Leu Pro Leu
                85   90   95

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

<210> 278
<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 278

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1   5   10   15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20   25   30

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


Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


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


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


<210>  279
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  279

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


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


Tyr Gly 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 Val Tyr Ser Ala Pro Phe
85 90 95

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

<210> 280
<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 280

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 Tyr Ser Ile Ser Ser Gly
20 25 30

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

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

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 281
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 281

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 Val Asp Asn Tyr Pro Pro
85 90 95

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

<210> 282
<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 282

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


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


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  283
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  283

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


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


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
```

```
    50                  55                  60

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

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

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

<210> 284
<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 284

```
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly
            100                 105                 110
```

Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 285
<211> 106
<212> PRT
<213> Artificial Sequence

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

<400> 285

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 Tyr Asp Asn Leu Pro Thr
                85   90   95

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

<210> 286
<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 286

```
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 Ser 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 Glu Val Gly Tyr Gly Trp Tyr Thr Lys Ile Ala Phe Asp Ile
            100                 105                 110


Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210>  287
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  287

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 Lys 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 Ser Asn His Pro Ser
                85                  90                  95

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

<210> 288
<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 288

```
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 Thr 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 Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
100 105 110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 289
<211> 112
<212> PRT
<213> Artificial Sequence

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

<400> 289

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 Leu Leu His 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 Leu Leu Ile Tyr 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

Leu Gly Val Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 290
<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 290

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 Ser 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 Met Ile Asn Pro Tyr Gly Gly Ser Thr Arg 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 Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
            100   105   110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 291
<211> 112
<212> PRT
<213> Artificial Sequence

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

<400> 291

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 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 Leu Leu Ile Tyr 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 Asp
85 90 95

Val Ala Leu Pro Ile Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 292
<211> 120
<212> PRT
<213> Artificial Sequence

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

<400> 292

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 Glu Ile 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 Ser Gly Ser Thr Val 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 Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210>  293
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  293

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 Ala His Ser Tyr Pro Leu
                85                  90                  95


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


<210>  294
```

<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 294

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 Gly Gly Tyr
20 25 30

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

Ala Asn Ile Asn Gln Asp Gly Ser Glu Glu 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 Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 295
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 295

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 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 Asn Leu His 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 Phe His Val Pro Ile
                85                  90                  95

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


<210>  296
<211>  121
<212>  PRT
<213>  Artificial Sequence

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

<400>  296

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 Pro Gly Tyr
            20                  25                  30

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

Ala Asn Ile Asn Gln Asp Gly Ser Glu Val 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 Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  297
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  297

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 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 Thr 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 Phe His Val Pro Ile
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
```

100 105

<210> 298
<211> 123
<212> PRT
<213> Artificial Sequence

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

<400> 298

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

Ala Asn Ile Asn Gln Asp Gly Ser Glu Val 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 Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 299
<211> 107
<212> PRT
<213> Artificial Sequence

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

<400> 299

```
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 Tyr 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 Ala Ala Ser Ser Arg 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 Val Tyr Asp Thr Pro Leu
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
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<210> 300
<211> 121
<212> PRT
<213> Artificial Sequence

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

<400> 300

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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 Ser Asn 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 Phe Ser Gly Gly Thr Arg 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 Asp Val Gly Ser Ser Ala Tyr Tyr Tyr Met Asp Val Trp Gly
            100                 105                 110


Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210>  301
<211>  107
<212>  PRT
<213>  Artificial Sequence

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

<400>  301

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 Glu Ala Ser Lys 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 Asp 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 Phe Leu Phe Pro Pro
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85 90 95

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

<210> 302
<211> 122
<212> PRT
<213> Artificial Sequence

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

<400> 302

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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

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

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Glu Leu Ala Tyr Gly Asp Tyr Lys Gly Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 303
<211> 108
<212> PRT

<213> Artificial Sequence

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

<400> 303

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

Phe 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 Leu Asp Ser Pro Pro
85 90 95

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

<210> 304
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 304

Ser Tyr Ala Met Ser
1 5

<210> 305
<211> 17
<212> PRT

<213> Artificial Sequence

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

<400> 305

Ala Ile Ser Ala Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 306
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 306

Pro Arg Ala Tyr Tyr Asp Ser Ser Gly Phe Lys Val Asn Tyr Gly Met
1 5 10 15

Asp Val

<210> 307
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 307

Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala
1 5 10

<210> 308
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 308

Gly Ala Ser Ser Arg Ala Thr
1   5

<210> 309
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 309

Gln Gln Ala Ser Ser Ser Pro Pro Thr
1   5

<210> 310
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 310

Ser Tyr Ala Met Ser
1   5

<210> 311
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 311

Gly Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 312
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 312

Glu Gly His Ser Ser Ser Tyr Tyr Asp His Ala Phe Asp Ile
1   5   10

<210> 313
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 313

Arg Ala Ser Gln Ser Val Ser Ser Asp Tyr Leu Ala
1   5   10

<210> 314
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 314

Gly Ala Ser Ser Arg Ala Thr
1   5

<210> 315
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 315

Gln Gln His Ser Ser Ala Pro Pro Thr
1 5

<210> 316
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 316

Ser Tyr Tyr Trp Ser
1 5

<210> 317
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 317

Ser Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 318
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 318

Val Gly Gly Val Tyr Ser Thr Ile Glu Thr Tyr Gly Met Asp Val
1 5 10 15

<210> 319
<211> 11
<212> PRT

<213> Artificial Sequence

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

<400> 319

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1   5   10

<210> 320
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 320

Gly Ala Ser Thr Arg Ala Thr
1   5

<210> 321
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 321

Gln Gln Tyr Thr Val Tyr Pro Pro Thr
1   5

<210> 322
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 322

Gly Tyr Tyr Trp Ser
1   5

<210> 323
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 323

Glu Ile Asp His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 324
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 324

Gln Gly Ile His Gly Leu Arg Tyr Phe Asp Leu
1 5 10

<210> 325
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 325

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 326
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 326

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 327
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 327

Gln Gln Asp His Asn Phe Pro Tyr Thr
1 5

<210> 328
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 328

Ser Tyr Trp Met Ser
1 5

<210> 329
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 329

Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 330

<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 330

Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr
1 5 10

<210> 331
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 331

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 332
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 332

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 333
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 333

Gln Gln Gln Tyr Val Thr Pro Ile Thr

1 5

<210> 334
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 334

Ser Tyr Trp Met Ser
1 5

<210> 335
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 335

Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 336
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 336

Glu Gly Gly Asp Ser Trp Tyr His Ala Phe Asp Ile
1 5 10

<210> 337
<211> 11
<212> PRT

<213> Artificial Sequence

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

<400> 337

Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
1 5 10

<210> 338
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 338

Ala Ala Ser Asn Leu Gln Ser
1 5

<210> 339
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 339

Gln Gln Lys Leu Ser Leu Pro Leu Thr
1 5

<210> 340
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 340

Ser Gly Gly Tyr Tyr Trp Ser
1 5

<210> 341
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 341

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 342
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 342

Asp Arg Leu Asp Tyr Ser Tyr Asn Tyr Gly Met Asp Val
1 5 10

<210> 343
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 343

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 344
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 344

Gly Ala Ser Ser Leu Gln Ser
1 5

<210> 345
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 345

Gln Gln Val Tyr Ser Ala Pro Phe Thr
1 5

<210> 346
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 346

Ser Gly Tyr Tyr Trp Gly
1 5

<210> 347
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 347

Ser Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 348
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 348

Leu Pro Pro Trp Phe Gly Phe Ser Tyr Phe Asp Leu
1   5   10

<210> 349
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 349

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1   5   10

<210> 350
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 350

Asp Ala Ser Asn Arg Ala Thr
1   5

<210> 351
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 351

Gln Gln Val Asp Asn Tyr Pro Pro Thr
1   5

<210> 352

<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 352

Ser Tyr Trp Met Ser
1 5

<210> 353
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 353

Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 354
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 354

Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
1 5 10

<210> 355
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 355

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 356
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 356

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 357
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 357

Gln Gln Val Tyr Asp Thr Pro Leu Thr
1 5

<210> 358
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 358

Ser Ser Ser Tyr Tyr Trp Gly
1 5

<210> 359
<211> 16
<212> PRT

<213> Artificial Sequence

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

<400> 359

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1   5   10   15

<210> 360
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 360

Glu Thr Ala His Asp Val His Gly Met Asp Val
1   5   10

<210> 361
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 361

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1   5   10

<210> 362
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 362

Asp Ala Ser Asn Arg Ala Thr
1   5

<210> 363
<211> 8
<212> PRT
<213> Artificial Sequence

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

<400> 363

Gln Gln Tyr Asp Asn Leu Pro Thr
1 5

<210> 364
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 364

Ser Tyr Ala Ile Ser
1 5

<210> 365
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 365

Ser Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 366
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 366

Glu Val Gly Tyr Gly Trp Tyr Thr Lys Ile Ala Phe Asp Ile
1   5   10

<210> 367
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 367

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1   5   10

<210> 368
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 368

Asp Ala Ser Lys Arg Ala Thr
1   5

<210> 369
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 369

Gln Gln Ser Ser Asn His Pro Ser Thr
1   5

<210> 370

<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 370

Ser Tyr Tyr Met His
1 5

<210> 371
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 371

Ile Ile Asn Pro Ser Gly Gly Ser Thr Thr Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 372
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 372

Glu Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
1 5 10

<210> 373
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 373

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 374
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 374

Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 375
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 375

Met Gln Ala Leu Gly Val Pro Leu Thr
1 5

<210> 376
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 376

Gly Tyr Tyr Met His
1 5

<210> 377
<211> 17
<212> PRT

<213> Artificial Sequence

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

<400> 377

Met Ile Asn Pro Tyr Gly Gly Ser Thr Arg Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 378
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 378

Glu Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
1 5 10

<210> 379
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 379

Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 380
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 380

Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 381
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 381

Met Gln Asp Val Ala Leu Pro Ile Thr
1 5

<210> 382
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 382

Ile Tyr Tyr Met His
1 5

<210> 383
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 383

Ile Ile Asn Pro Ser Ser Gly Ser Thr Val Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 384

<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 384

Gly Ala Gly Tyr Asp Asp Glu Asp Met Asp Val
1 5 10

<210> 385
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 385

Arg Ala Ser Gln Gly Ile Asp Ser Trp Leu Ala
1 5 10

<210> 386
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 386

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 387
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 387

Gln Gln Ala His Ser Tyr Pro Leu Thr

1 5

<210> 388
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 388

Gly Tyr Trp Met Ser
1 5

<210> 389
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 389

Asn Ile Asn Gln Asp Gly Ser Glu Glu Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 390
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 390

Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr
1 5 10

<210> 391
<211> 11
<212> PRT

<213> Artificial Sequence

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

<400> 391

Arg Ala Ser Gln Ser Ile Tyr Asn Tyr Leu Asn
1 5 10

<210> 392
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 392

Ala Ala Ser Asn Leu His Ser
1 5

<210> 393
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 393

Gln Gln Ala Phe His Val Pro Ile Thr
1 5

<210> 394
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 394

Gly Tyr Trp Met Ser
1 5

<210> 395
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 395

Asn Ile Asn Gln Asp Gly Ser Glu Val Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 396
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 396

Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr
1 5 10

<210> 397
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 397

Arg Ala Ser Gln Ser Ile Tyr Asn Tyr Leu Asn
1 5 10

<210> 398
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 398

Ala Ala Ser Ser Thr Gln Ser
1   5

<210> 399
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 399

Gln Gln Ala Phe His Val Pro Ile Thr
1   5

<210> 400
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 400

Ser Tyr Trp Met Ser
1   5

<210> 401
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 401

Asn Ile Asn Gln Asp Gly Ser Glu Val Tyr Tyr Val Asp Ser Val Lys
1   5   10   15

Gly

<210> 402
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 402

Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
1 5 10

<210> 403
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 403

Arg Ala Ser Gln Ser Ile Tyr Tyr Tyr Leu Asn
1 5 10

<210> 404
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 404

Ala Ala Ser Ser Arg Gln Ser
1 5

<210> 405
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 405

Gln Gln Val Tyr Asp Thr Pro Leu Thr
1 5

<210> 406
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 406

Asn Tyr Tyr Met His
1 5

<210> 407
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 407

Trp Ile Asn Pro Phe Ser Gly Gly Thr Arg Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 408
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 408

Asp Val Gly Ser Ser Ala Tyr Tyr Tyr Met Asp Val
1 5 10

<210> 409
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 409

Glu Ala Ser Lys Gly Ile Ser Ser Trp Leu Ala
1 5 10

<210> 410
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 410

Ala Ala Ser Asp Leu Gln Ser
1 5

<210> 411
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 411

Gln Gln Ala Phe Leu Phe Pro Pro Thr
1 5

<210> 412
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 412

Ser Tyr Trp Ile Gly
1 5

<210> 413
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 413

Ser Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> 414
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 414

Glu Leu Ala Tyr Gly Asp Tyr Lys Gly Gly Val Asp Tyr
1 5 10

<210> 415
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 415

Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala
1 5 10

<210> 416

<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 416

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 417
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 417

Gln Gln Leu Asp Ser Pro Pro Pro Thr
1 5

<210> 418
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 418

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 Asp Tyr
20 25 30

Ala Ile Ser 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 Ala Asp Tyr Ala Gln Lys Phe
50 55 60

```
Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg 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 Asn Trp Ala Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
            100                 105                 110


Val Thr Val Ser Ser
        115


<210>  419
<211>  106
<212>  PRT
<213>  Artificial Sequence

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

<400>  419

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 Arg Ala Ser Gln Gly Ile Ser Ser Val
            20                  25                  30


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


Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


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


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


Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
```

100 105

<210> 420
<211> 116
<212> PRT
<213> Artificial Sequence

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

<400> 420

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 Asp Tyr
20 25 30

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

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

Lys Ser 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 Arg Pro Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 421
<211> 111
<212> PRT
<213> Artificial Sequence

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

<400> 421

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 Ser Val Asp Asn Tyr
20 25 30

Gly Ile Ser Phe Met Asn Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Gln Gly 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 Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Lys
85 90 95

Glu Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 422
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 422

Asp Tyr Ala Ile Ser
1 5

<210> 423
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 423

Arg Ile Ile Pro Ile Leu Gly Val Ala Asp Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 424
<211> 8
<212> PRT
<213> Artificial Sequence

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

<400> 424

Asn Trp Ala Asp Ala Phe Asp Ile
1 5

<210> 425
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 425

Arg Ala Ser Gln Gly Ile Ser Ser Val Leu Ala
1 5 10

<210> 426
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 426

Asp Ala Ser Ser Leu Glu Ser
1 5

<210> 427
<211> 8
<212> PRT
<213> Artificial Sequence

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

<400> 427

Gln Gln Phe Asp Ser Ser Ile Thr
1   5

<210> 428
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 428

Asp Tyr Asn Met His
1   5

<210> 429
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 429

Tyr Ile Tyr Pro Tyr Asn Gly Gly Thr Gly Tyr Asn Gln Lys Phe Lys
1   5   10   15

Ser

<210> 430
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 430

Gly Arg Pro Ala Met Asp Tyr
1   5

<210> 431
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 431

Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly Ile Ser Phe Met Asn
1   5   10   15

<210> 432
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 432

Ala Ala Ser Asn Gln Gly Ser
1   5

<210> 433
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 433

Gln Gln Ser Lys Glu Val Pro Trp Thr
1   5

<210> 434

<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 434

Ser Tyr Gly Met Ser
1 5

<210> 435
<211> 19
<212> PRT
<213> Artificial Sequence

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

<400> 435

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
1 5 10 15

Met Asp Val

<210> 436
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 436

Pro Leu Asn Ala Gly Glu Leu Asp Val
1 5

<210> 437
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 437

Asp Tyr Tyr Met His
1 5

<210> 438
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 438

Glu Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
1 5 10

<210> 439
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 439

Pro Leu Asn Ala Gly Glu Leu Asp Val
1 5

<210> 440
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 440

Thr Tyr Tyr Met His
1 5

<210> 441
<211> 11
<212> PRT

<213> Artificial Sequence

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

<400> 441

Gly Ala Gly Tyr Asp Asp Glu Asp Met Asp Val
1   5   10

<210> 442
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 442

Ser Tyr Ala Met Ser
1   5

<210> 443
<211> 19
<212> PRT
<213> Artificial Sequence

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

<400> 443

Glu Gly Gly Pro Tyr Tyr Asp Ser Ser Gly Tyr Phe Val Tyr Tyr Gly
1   5   10   15

Met Asp Val

<210> 444
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 444

Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
1 5 10

<210> 445
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 445

Ser Thr Asp Tyr Tyr Trp Gly
1 5

<210> 446
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 446

Glu Thr Ala His Asp Val His Gly Met Asp Val
1 5 10

<210> 447
<211> 255
<212> PRT
<213> Artificial Sequence

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

<400> 447

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

Phe 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 Ala Ser Ser Ser Pro
                85                  90                  95

Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
    130                 135                 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
145                 150                 155                 160

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
                165                 170                 175

Ser Ala Ile Ser Ala Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
            180                 185                 190

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
        195                 200                 205

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Pro Arg Ala Tyr Tyr Asp Ser Ser Gly Phe Lys Val Asn Tyr
225                 230                 235                 240

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
```

245 250 255

<210> 448
<211> 255
<212> PRT
<213> Artificial Sequence

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

<400> 448

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 Cys Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Ala Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Pro Arg Ala Tyr Tyr Asp Ser Ser Gly Phe Lys Val Asn Tyr
100 105 110

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

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu
145 150 155 160

```
Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val
                165                 170                 175


Ser Ser Ser Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
            180                 185                 190


Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp
        195                 200                 205


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
    210                 215                 220


Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ala Ser
225                 230                 235                 240


Ser Ser Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250                 255


<210>  449
<211>  251
<212>  PRT
<213>  Artificial Sequence

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

<400>  449

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 Asp
            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 His Ser Ser Ala Pro
85 90 95

Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
130 135 140

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
145 150 155 160

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
165 170 175

Ser Gly Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
180 185 190

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
195 200 205

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Gly His Ser Ser Ser Tyr Tyr Asp His Ala Phe Asp Ile
225 230 235 240

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
245 250

<210> 450
<211> 251
<212> PRT
<213> Artificial Sequence

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

<400> 450

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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 Cys Leu Glu Trp Val
        35                  40                  45


Ser Gly Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Gly His Ser Ser Ser Tyr Tyr Asp His Ala Phe Asp Ile
            100                 105                 110


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


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140


Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu
145                 150                 155                 160


Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asp Tyr
                165                 170                 175


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
            180                 185                 190
```

```
Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
        195                 200                 205


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro
    210                 215                 220


Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Ser Ser Ala Pro Pro
225                 230                 235                 240


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  451
<211>  250
<212>  PRT
<213>  Artificial Sequence

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

<400>  451

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 Thr Val Tyr Pro Pro
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
```

100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
130 135 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr Tyr
145 150 155 160

Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile Gly
165 170 175

Ser Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
210 215 220

Val Gly Gly Val Tyr Ser Thr Ile Glu Thr Tyr Gly Met Asp Val Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
245 250

<210> 452
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 452

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
            20                  25                  30

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

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

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Val Gly Gly Val Tyr Ser Thr Ile Glu Thr Tyr Gly Met Asp Val
            100                 105                 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140

Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly Glu
145                 150                 155                 160

Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn Leu
                165                 170                 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
            180                 185                 190

Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser Glu
    210                 215                 220
```

```
Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Thr Val Tyr Pro Pro Thr
225                 230                 235                 240


Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  453
<211>  246
<212>  PRT
<213>  Artificial Sequence

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

<400>  453

Glu Ile Val Met 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 Asp His Asn Phe Pro Tyr
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125


Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu Thr
```

130 135 140

Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr Tyr
145 150 155 160

Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile Gly
165 170 175

Glu Ile Asp His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
210 215 220

Gln Gly Ile His Gly Leu Arg Tyr Phe Asp Leu Trp Gly Arg Gly Thr
225 230 235 240

Leu Val Thr Val Ser Ser
245

<210> 454
<211> 246
<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 Pro Pro Gly Lys Cys 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 Gln Gly Ile His Gly Leu Arg Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
    130                 135                 140

Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
145                 150                 155                 160

Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn
            180                 185                 190

Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val
    210                 215                 220

Tyr Tyr Cys Gln Gln Asp His Asn Phe Pro Tyr Thr Phe Gly Cys Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 455
<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 455

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


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


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


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


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gln Tyr Val Thr Pro Ile
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160


Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
```

```
                165                 170                 175

Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
        195                 200                 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly Gln
225                 230                 235                 240

Gly Thr Leu Val Thr Val Ser Ser
                245
```

<210> 456
<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 456

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

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

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

Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys 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 Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190


Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Gln Tyr Val Thr Pro Ile Thr Phe Gly
225                 230                 235                 240


Cys Gly Thr Lys Val Glu Ile Lys
                245


<210>  457
<211>  248
<212>  PRT
<213>  Artificial Sequence

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

<400> 457

```
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 Asn 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 Lys Leu Ser Leu Pro Leu
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160


Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
                165                 170                 175


Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190


Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
```

195 200 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Glu Gly Gly Asp Ser Trp Tyr His Ala Phe Asp Ile Trp Gly Gln
225 230 235 240

Gly Thr Met Val Thr Val Ser Ser
245

<210> 458
<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 458

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys 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 Glu Gly Gly Asp Ser Trp Tyr His Ala Phe Asp Ile Trp Gly
100 105 110

```
Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190


Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Lys Leu Ser Leu Pro Leu Thr Phe Gly
225                 230                 235                 240


Cys Gly Thr Lys Val Glu Ile Lys
                245


<210>  459
<211>  250
<212>  PRT
<213>  Artificial Sequence

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

<400>  459

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
```

```
            20                  25                  30

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

Tyr Gly 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 Val Tyr Ser Ala Pro Phe
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln Thr
    130                 135                 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly Gly
145                 150                 155                 160

Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Cys Leu Glu Trp
                165                 170                 175

Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu
            180                 185                 190

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
        195                 200                 205

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Asp Arg Leu Asp Tyr Ser Tyr Asn Tyr Gly Met Asp Val Trp
```

225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
245 250

<210> 460
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 460

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

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

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
130 135 140

```
Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160


Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175


Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190


Gly Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Tyr Ser Ala Pro Phe Thr
225                 230                 235                 240


Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  461
<211>  248
<212>  PRT
<213>  Artificial Sequence

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

<400>  461

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 Val Asp Asn Tyr Pro Pro
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
    130                 135                 140

Leu Ser Leu Thr Cys Ala Val Ser Gly Tyr Ser Ile Ser Ser Gly Tyr
145                 150                 155                 160

Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
                165                 170                 175

Gly Ser Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
            180                 185                 190

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
        195                 200                 205

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Leu Pro Pro Trp Phe Gly Phe Ser Tyr Phe Asp Leu Trp Gly Arg
225                 230                 235                 240

Gly Thr Leu Val Thr Val Ser Ser
                245
```

<210> 462

<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 462

```
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 Tyr Ser Ile Ser Ser Gly
            20                  25                  30


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


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


Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80


Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


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


Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
    130                 135                 140


Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145                 150                 155                 160


Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp
                165                 170                 175
```

```
Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala
            180                 185                 190


Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe
    210                 215                 220


Ala Val Tyr Tyr Cys Gln Gln Val Asp Asn Tyr Pro Pro Thr Phe Gly
225                 230                 235                 240


Cys Gly Thr Lys Val Glu Ile Lys
                245


<210>  463
<211>  250
<212>  PRT
<213>  Artificial Sequence

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

<400>  463

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


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


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


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


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Tyr Asp Thr Pro Leu
```

```
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
                165                 170                 175

Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
        195                 200                 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr Trp
225                 230                 235                 240

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
                245                 250
```

<210> 464
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 464

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


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


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


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys 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 Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
            100                 105                 110


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


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140


Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160


Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175


Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190


Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205
```

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
210 215 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Tyr Asp Thr Pro Leu Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 465
<211> 247
<212> PRT
<213> Artificial Sequence

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

<400> 465

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 Tyr Asp Asn Leu Pro Thr
85 90 95

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu

```
        115                 120                 125


Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu
    130                 135                 140


Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser Ser Tyr
145                 150                 155                 160


Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
                165                 170                 175


Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys
            180                 185                 190


Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
        195                 200                 205


Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220


Arg Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly Gln Gly
225                 230                 235                 240


Thr Thr Val Thr Val Ser Ser
                245


<210>  466
<211>  247
<212>  PRT
<213>  Artificial Sequence

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

<400>  466

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 Cys Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Glu Thr Ala His Asp Val His Gly Met Asp Val Trp Gly
            100                 105                 110

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

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
    130                 135                 140

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145                 150                 155                 160

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala
            180                 185                 190

Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe
    210                 215                 220

Ala Val Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Thr Phe Gly Cys
225                 230                 235                 240
```

Gly Thr Lys Val Glu Ile Lys
245

<210> 467
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 467

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 Lys 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 Ser Asn His Pro Ser
85 90 95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser
130 135 140

Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr Ala

145 150 155 160

Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met Gly
165 170 175

Ser Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
180 185 190

Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr Met
195 200 205

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Glu Val Gly Tyr Gly Trp Tyr Thr Lys Ile Ala Phe Asp Ile Trp
225 230 235 240

Gly Gln Gly Thr Met Val Thr Val Ser Ser
245 250

<210> 468
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 468

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 Cys Leu Glu Trp Met
35 40 45

Gly Ser 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 Glu Val Gly Tyr Gly Trp Tyr Thr Lys Ile Ala Phe Asp Ile
            100                 105                 110


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


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140


Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
145                 150                 155                 160


Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu
                165                 170                 175


Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
            180                 185                 190


Asp Ala Ser Lys Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser
        195                 200                 205


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
    210                 215                 220


Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn His Pro Ser Thr
225                 230                 235                 240


Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  469
<211>  255
<212>  PRT
```

<213> Artificial Sequence

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

<400> 469

```
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 Leu Leu His 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 Leu Leu Ile Tyr 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


Leu Gly Val Pro Leu Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
            100                 105                 110


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
    130                 135                 140


Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
145                 150                 155                 160


Phe Thr Ser Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys
                165                 170                 175


Leu Glu Trp Met Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Thr Tyr
```

180 185 190

Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr
195 200 205

Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
210 215 220

Val Tyr Tyr Cys Ala Arg Glu Ala Ala Asp Gly Phe Val Gly Glu Arg
225 230 235 240

Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
245 250 255

<210> 470
<211> 255
<212> PRT
<213> Artificial Sequence

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

<400> 470

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 Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Thr 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 Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
            100                 105                 110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140

Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
145                 150                 155                 160

Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn
                165                 170                 175

Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
            180                 185                 190

Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
        195                 200                 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
    210                 215                 220

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu
225                 230                 235                 240

Gly Val Pro Leu Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250                 255
```

<210> 471
<211> 255
<212> PRT
<213> Artificial Sequence

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

<400> 471

```
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 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 Leu Leu Ile Tyr 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 Asp
                85                  90                  95

Val Ala Leu Pro Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
    130                 135                 140

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
145                 150                 155                 160

Phe Ser Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys
                165                 170                 175

Leu Glu Trp Met Gly Met Ile Asn Pro Tyr Gly Gly Ser Thr Arg Tyr
            180                 185                 190

Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr
        195                 200                 205

Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
```

210 215 220

Val Tyr Tyr Cys Ala Arg Glu Ala Ala Asp Gly Phe Val Gly Glu Arg
225 230 235 240

Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
245 250 255

<210> 472
<211> 255
<212> PRT
<213> Artificial Sequence

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

<400> 472

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 Ser Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Met Ile Asn Pro Tyr Gly Gly Ser Thr Arg 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 Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
100 105 110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

```
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140


Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
145                 150                 155                 160


Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn
                165                 170                 175


Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
            180                 185                 190


Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
        195                 200                 205


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
    210                 215                 220


Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Asp Val
225                 230                 235                 240


Ala Leu Pro Ile Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250                 255


<210>  473
<211>  247
<212>  PRT
<213>  Artificial Sequence

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

<400>  473

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 Ala His Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
    130                 135                 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Glu Ile Tyr Tyr
145                 150                 155                 160

Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met Gly
                165                 170                 175

Ile Ile Asn Pro Ser Ser Gly Ser Thr Val Tyr Ala Gln Lys Phe Gln
            180                 185                 190

Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met
        195                 200                 205

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Ala Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys Gly
225                 230                 235                 240

Thr Thr Val Thr Val Ser Ser
```

245

<210> 474
<211> 247
<212> PRT
<213> Artificial Sequence

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

<400> 474

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 Glu Ile Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Ser Gly Ser Thr Val 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 Gly Tyr Asp Asp Glu Asp Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

```
Ile Thr Cys Arg Ala Ser Gln Gly Ile Asp Ser Trp Leu Ala Trp Tyr
                165                 170                 175


Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190


Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220


Thr Tyr Tyr Cys Gln Gln Ala His Ser Tyr Pro Leu Thr Phe Gly Cys
225                 230                 235                 240


Gly Thr Lys Val Glu Ile Lys
                245


<210>  475
<211>  248
<212>  PRT
<213>  Artificial Sequence

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

<400>  475

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 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 Asn Leu His 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 Phe His Val Pro Ile
85 90 95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
115 120 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
130 135 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Gly Tyr Trp
145 150 155 160

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
165 170 175

Asn Ile Asn Gln Asp Gly Ser Glu Glu Tyr Tyr Val Asp Ser Val Lys
180 185 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
195 200 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Leu Val Thr Val Ser Ser
245

<210> 476
<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 476

```
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 Gly Gly Tyr
            20                  25                  30


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


Ala Asn Ile Asn Gln Asp Gly Ser Glu Glu 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 Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Asn Tyr Leu Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190
```

```
Ser Asn Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Ala Phe His Val Pro Ile Thr Phe Gly
225                 230                 235                 240


Cys Gly Thr Lys Val Glu Ile Lys
                245


<210>  477
<211>  248
<212>  PRT
<213>  Artificial Sequence

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

<400>  477

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 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 Thr 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 Phe His Val Pro Ile
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
```

100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
115 120 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
130 135 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Gly Tyr Trp
145 150 155 160

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
165 170 175

Asn Ile Asn Gln Asp Gly Ser Glu Val Tyr Tyr Val Asp Ser Val Lys
180 185 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
195 200 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Leu Val Thr Val Ser Ser
245

<210> 478
<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 478

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 Pro Gly Tyr
            20                  25                  30

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

Ala Asn Ile Asn Gln Asp Gly Ser Glu Val 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 Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Asn Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Thr Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220
```

```
Ala Thr Tyr Tyr Cys Gln Gln Ala Phe His Val Pro Ile Thr Phe Gly
225                 230                 235                 240


Cys Gly Thr Lys Val Glu Ile Lys
                245


<210>  479
<211>  250
<212>  PRT
<213>  Artificial Sequence

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

<400>  479

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 Tyr 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 Ala Ala Ser Ser Arg 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 Val Tyr Asp Thr Pro Leu
                85                  90                  95


Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
```

```
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Trp
145                 150                 155                 160

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala
                165                 170                 175

Asn Ile Asn Gln Asp Gly Ser Glu Val Tyr Tyr Val Asp Ser Val Lys
            180                 185                 190

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
        195                 200                 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr Trp
225                 230                 235                 240

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
                245                 250


<210>  480
<211>  250
<212>  PRT
<213>  Artificial Sequence

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

<400>  480

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

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

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
        35                  40                  45
```

```
Ala Asn Ile Asn Gln Asp Gly Ser Glu Val 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 Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
            100                 105                 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Tyr Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Arg Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Tyr Asp Thr Pro Leu Thr
225                 230                 235                 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250
```

<210> 481
<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 481

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 Glu Ala Ser Lys 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 Asp 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 Phe Leu Phe Pro Pro
85 90 95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
130 135 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Tyr Tyr
145 150 155 160

Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met Gly

165 170 175

Trp Ile Asn Pro Phe Ser Gly Gly Thr Arg Tyr Ala Gln Lys Phe Gln
180 185 190

Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met
195 200 205

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Asp Val Gly Ser Ser Ala Tyr Tyr Tyr Met Asp Val Trp Gly Lys
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser
245

<210> 482
<211> 248
<212> PRT
<213> Artificial Sequence

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

<400> 482

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 Ser Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Phe Ser Gly Gly Thr Arg 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 Asp Val Gly Ser Ser Ala Tyr Tyr Tyr Met Asp Val Trp Gly
            100                 105                 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Glu Ala Ser Lys Gly Ile Ser Ser Trp Leu Ala Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Asp Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ala Phe Leu Phe Pro Pro Thr Phe Gly
225                 230                 235                 240

Cys Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 483
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 483

```
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


Phe 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 Leu Asp Ser Pro Pro
                85                  90                  95


Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly
            100                 105                 110


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
    130                 135                 140


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
145                 150                 155                 160


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Cys Leu Glu Trp Met
                165                 170                 175


Gly Ser Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
            180                 185                 190


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
```

195 200 205

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
210 215 220

Ala Arg Glu Leu Ala Tyr Gly Asp Tyr Lys Gly Gly Val Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
245 250

<210> 484
<211> 250
<212> PRT
<213> Artificial Sequence

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

<400> 484

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Cys Leu Glu Trp Met
35 40 45

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

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Glu Leu Ala Tyr Gly Asp Tyr Lys Gly Gly Val Asp Tyr Trp
100 105 110

```
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140


Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160


Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu
                165                 170                 175


Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
            180                 185                 190


Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
        195                 200                 205


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu
    210                 215                 220


Asp Phe Ala Val Tyr Tyr Cys Gln Gln Leu Asp Ser Pro Pro Pro Thr
225                 230                 235                 240


Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
                245                 250


<210>  485
<211>  243
<212>  PRT
<213>  Artificial Sequence

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

<400>  485

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 Arg Ala Ser Gln Gly Ile Ser Ser Val
```

```
            20                  25                  30

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

Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

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

Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
        115                 120                 125

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val
    130                 135                 140

Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Asp Tyr Ala Ile
145                 150                 155                 160

Ser Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met Gly Arg
                165                 170                 175

Ile Ile Pro Ile Leu Gly Val Ala Asp Tyr Ala Gln Lys Phe Gln Gly
            180                 185                 190

Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr Met Glu
        195                 200                 205

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    210                 215                 220

Asn Trp Ala Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr
```

225 230 235 240

Val Ser Ser

<210> 486
<211> 243
<212> PRT
<213> Artificial Sequence

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

<400> 486

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 Asp Tyr
20 25 30

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

Gly Arg Ile Ile Pro Ile Leu Gly Val Ala Asp Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg 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 Asn Trp Ala Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
130 135 140

```
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160


Arg Ala Ser Gln Gly Ile Ser Ser Val Leu Ala Trp Tyr Gln Gln Lys
                165                 170                 175


Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu
            180                 185                 190


Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205


Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220


Cys Gln Gln Phe Asp Ser Ser Ile Thr Phe Gly Cys Gly Thr Lys Leu
225                 230                 235                 240


Glu Ile Lys



<210>  487
<211>  247
<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 Glu Ser Val Asp Asn Tyr
            20                  25                  30


Gly Ile Ser Phe Met Asn Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro
        35                  40                  45


Lys Leu Leu Ile Tyr Ala Ala Ser Asn Gln Gly 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 Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Lys
                85                  90                  95

Glu Val Pro Trp Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
    130                 135                 140

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
145                 150                 155                 160

Thr Asp Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu
                165                 170                 175

Glu Trp Ile Gly Tyr Ile Tyr Pro Tyr Asn Gly Gly Thr Gly Tyr Asn
            180                 185                 190

Gln Lys Phe Lys Ser Lys Ala Thr Ile Thr Ala Asp Glu Ser Thr Asn
        195                 200                 205

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
    210                 215                 220

Tyr Tyr Cys Ala Arg Gly Arg Pro Ala Met Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240

Thr Leu Val Thr Val Ser Ser
                245
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<210> 488

<211> 247
<212> PRT
<213> Artificial Sequence

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

<400> 488

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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 Asp Tyr
            20                  25                  30


Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Ile
        35                  40                  45


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


Lys Ser 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 Arg Pro Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140


Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160


Ala Ser Glu Ser Val Asp Asn Tyr Gly Ile Ser Phe Met Asn Trp Phe
                165                 170                 175
```

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
180 185 190

Asn Gln Gly Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Ser Lys Glu Val Pro Trp Thr Phe Gly Cys
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 489
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 489
gagatcgtgc tgacccagag ccccggcacc ctgagcctga gccccggcga gagggccacc 60

ctgagctgca gggccagcca gagcgtgagc agcagcttcc tggcctggta ccagcagaag 120

cccggccagg cccccaggct gctgatctac ggcgccagca gcagggccac cggcatcccc 180

gacaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag caggctggag 240

cccgaggact tcgccgtgta ctactgccag caggccagca gcagcccccc caccttcggc 300

tgcggcacca aggtggagat caagggcggc ggcggcagcg gcggcggcgg cagcggcggc 360

ggcggcagcg gcggcggcgg cagcgaggtg cagctgctgg agagcggcgg cggcctggtg 420

cagcccggcg gcagcctgag gctgagctgc gccgccagcg gcttcacctt cagcagctac 480

gccatgagct gggtgaggca ggcccccggc aagtgcctgg agtgggtgag cgccatcagc 540

gccagcggcg gcagcaccta ctacgccgac agcgtgaagg gcaggttcac catcagcagg 600

gacaacagca agaacaccct gtacctgcag atgaacagcc tgagggccga ggacaccgcc 660

gtgtactact gcgccaggcc cagggcctac tacgacagca gcggcttcaa ggtgaactac 720

ggcatggacg tgtggggcca gggcaccacc gtgaccgtga gcagc 765

<210> 490
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 490
gaggtgcagc tgctggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtgagcgcc atcagcgcca gcggcggcag cacctactac 180

gccgacagcg tgaagggcag gttcaccatc agcagggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc caggcccagg 300

gcctactacg acagcagcgg cttcaaggtg aactacggca tggacgtgtg gggccagggc 360

accaccgtga ccgtgagcag cggcggcggc ggcagcggcg gcggcggcag cggcggcggc 420

ggcagcggcg gcggcggcag cgagatcgtg ctgacccaga gccccggcac cctgagcctg 480

agccccggcg agagggccac cctgagctgc agggccagcc agagcgtgag cagcagcttc 540

ctggcctggt accagcagaa gcccggccag gcccccaggc tgctgatcta cggcgccagc 600

agcagggcca ccggcatccc cgacaggttc agcggcagcg gcagcggcac cgacttcacc 660

ctgaccatca gcaggctgga gcccgaggac ttcgccgtgt actactgcca gcaggccagc 720

agcagccccc ccaccttcgg ctgcggcacc aaggtggaga tcaag 765

<210> 491
<211> 753
<212> DNA
<213> Artificial Sequence

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

<400> 491
gagatcgtgc tgacccagag ccccggcacc ctgagcctga gccccggcga gagggccacc 60

ctgagctgca gggccagcca gagcgtgagc agcgactacc tggcctggta ccagcagaag 120

cccggccagg cccccaggct gctgatctac ggcgccagca gcagggccac cggcatcccc 180

gacaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag caggctggag 240

cccgaggact tcgccgtgta ctactgccag cagcacagca gcgccccccc caccttcggc 300

tgcggcacca aggtggagat caagggcggc ggcggcagcg gcggcggcgg cagcggcggc 360

ggcggcagcg gcggcggcgg cagcgaggtg cagctgctgg agagcggcgg cggcctggtg 420

cagcccggcg gcagcctgag gctgagctgc gccgccagcg gcttcacctt cagcagctac 480

gccatgagct gggtgaggca ggcccccggc aagtgcctgg agtgggtgag cggcatcagc 540

ggcagcggcg gcagcaccta ctacgccgac agcgtgaagg gcaggttcac catcagcagg 600

gacaacagca agaacaccct gtacctgcag atgaacagcc tgagggccga ggacaccgcc 660

gtgtactact gcgccaggga gggccacagc agcagctact acgaccacgc cttcgacatc 720

tggggccagg gcaccatggt gaccgtgagc agc 753

<210> 492
<211> 753
<212> DNA
<213> Artificial Sequence

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

<400> 492
gaggtgcagc tgctggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtgagcggc atcagcggca gcggcggcag cacctactac 180

gccgacagcg tgaagggcag gttcaccatc agcagggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggagggc 300

cacagcagca gctactacga ccacgccttc gacatctggg gccagggcac catggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg agatcgtgct gacccagagc cccggcaccc tgagcctgag ccccggcgag 480

agggccaccc tgagctgcag ggccagccag agcgtgagca gcgactacct ggcctggtac 540

cagcagaagc ccggccaggc ccccaggctg ctgatctacg gcgccagcag cagggccacc 600

ggcatccccg acaggttcag cggcagcggc agcggcaccg acttcaccct gaccatcagc 660

aggctggagc ccgaggactt cgccgtgtac tactgccagc agcacagcag cgcccccccc 720

accttcggct gcggcaccaa ggtggagatc aag 753

<210> 493
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 493
gagatcgtga tgacccagag ccccgccacc ctgagcgtga gccccggcga gagggccacc 60

ctgagctgca gggccagcca gagcgtgagc agcaacctgg cctggtacca gcagaagccc 120

ggccaggccc ccaggctgct gatctacggc gccagcacca gggccaccgg catccccgcc 180

aggttcagcg gcagcggcag cggcaccgag ttcaccctga ccatcagcag cctgcagagc 240

gaggacttcg ccgtgtacta ctgccagcag tacaccgtgt acccccccac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctgcaggaga gcggccccgg cctggtgaag 420

cccagcgaga ccctgagcct gacctgcacc gtgagcggcg gcagcatcag cagctactac 480

tggagctgga tcaggcagcc ccccggcaag tgcctggagt ggatcggcag catctactac 540

agcggcagca ccaactacaa ccccagcctg aagagcaggg tgaccatcag cgtggacacc 600

agcaagaacc agttcagcct gaagctgagc agcgtgaccg ccgccgacac cgccgtgtac 660

tactgcgcca gggtgggcgg cgtgtacagc accatcgaga cctacggcat ggacgtgtgg 720

ggccagggca ccaccgtgac cgtgagcagc 750

<210> 494
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 494
caggtgcagc tgcaggagag cggccccggc ctggtgaagc ccagcgagac cctgagcctg 60

acctgcaccg tgagcggcgg cagcatcagc agctactact ggagctggat caggcagccc 120

cccggcaagt gcctggagtg gatcggcagc atctactaca gcggcagcac caactacaac 180

cccagcctga agagcagggt gaccatcagc gtggacacca gcaagaacca gttcagcctg 240

aagctgagca gcgtgaccgc cgccgacacc gccgtgtact actgcgccag ggtgggcggc 300

gtgtacagca ccatcgagac ctacggcatg gacgtgtggg gccagggcac caccgtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg agatcgtgat gacccagagc cccgccaccc tgagcgtgag ccccggcgag 480

agggccaccc tgagctgcag ggccagccag agcgtgagca gcaacctggc ctggtaccag 540

cagaagcccg gccaggcccc caggctgctg atctacggcg ccagcaccag ggccaccggc 600

atccccgcca ggttcagcgg cagcggcagc ggcaccgagt tcaccctgac catcagcagc 660

ctgcagagcg aggacttcgc cgtgtactac tgccagcagt acaccgtgta ccccccccacc 720

ttcggctgcg gcaccaaggt ggagatcaag 750

<210> 495
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 495
gagatcgtga tgacccagag ccccgccacc ctgagcctga gccccggcga gagggccacc 60

ctgagctgca gggccagcca gagcgtgagc agctacctgg cctggtacca gcagaagccc 120

ggccaggccc ccaggctgct gatctacgac gccagcaaca gggccaccgg catccccgcc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctggagccc 240

gaggacttcg ccgtgtacta ctgccagcag gaccacaact tcccctacac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctgcagcagt ggggcgccgg cctgctgaag 420

cccagcgaga ccctgagcct gacctgcgcc gtgtacggcg gcagcttcag cggctactac 480

tggagctgga tcaggcagcc ccccggcaag tgcctggagt ggatcggcga gatcgaccac 540

agcggcagca ccaactacaa ccccagcctg aagagcaggg tgaccatcag cgtggacacc 600

agcaagaacc agttcagcct gaagctgagc agcgtgaccg ccgccgacac cgccgtgtac 660

tactgcgcca ggcagggcat ccacggcctg aggtacttcg acctgtgggg caggggcacc 720

ctggtgaccg tgagcagc 738

<210> 496
<211> 738
<212> DNA
<213> Artificial Sequence

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

<400> 496
caggtgcagc tgcagcagtg gggcgccggc ctgctgaagc ccagcgagac cctgagcctg 60

acctgcgccg tgtacggcgg cagcttcagc ggctactact ggagctggat caggcagccc 120

cccggcaagt gcctggagtg gatcggcgag atcgaccaca gcggcagcac caactacaac 180

cccagcctga agagcagggt gaccatcagc gtggacacca gcaagaacca gttcagcctg 240

aagctgagca gcgtgaccgc cgccgacacc gccgtgtact actgcgccag gcagggcatc 300

cacggcctga ggtacttcga cctgtggggc aggggcaccc tggtgaccgt gagcagcggc 360

ggcggcggca gcggcggcgg cggcagcggc ggcggcggca gcggcggcgg cggcagcgag 420

atcgtgatga cccagagccc cgccaccctg agcctgagcc ccggcgagag ggccaccctg 480

agctgcaggg ccagccagag cgtgagcagc tacctggcct ggtaccagca gaagcccggc 540

caggccccca ggctgctgat ctacgacgcc agcaacaggg ccaccggcat ccccgccagg 600

ttcagcggca gcggcagcgg caccgacttc accctgacca tcagcagcct ggagcccgag 660

gacttcgccg tgtactactg ccagcaggac cacaacttcc cctacacctt cggctgcggc 720

accaaggtgg agatcaag 738

<210> 497
<211> 744
<212> DNA

<213> Artificial Sequence

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

<400> 497
gacatccaga tgacccagag ccccagcagc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctacctga actggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcagcc tgcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag cagtacgtga ccccccatcac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttcag cagctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaaccag 540

gacggcagcg agaagtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccagggaggc caactactac ggcaacgtgg gcgacgacta ctggggccag 720

ggcaccctgg tgaccgtgag cagc 744

<210> 498
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 498
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaaccagg acggcagcga gaagtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggaggcc 300

aactactacg gcaacgtggg cgacgactac tggggccagg gcaccctggt gaccgtgagc 360

agcggcggcg gcggcagcgg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 420

agcgacatcc agatgaccca gagccccagc agcctgagcg ccagcgtggg cgacagggtg 480

accatcacct gcagggccag ccagagcatc agcagctacc tgaactggta ccagcagaag 540

cccggcaagg cccccaagct gctgatctac gccgccagca gcctgcagag cggcgtgccc 600

agcaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag cagcctgcag 660

cccgaggact tcgccaccta ctactgccag cagcagtacg tgacccccat caccttcggc 720

tgcggcacca aggtggagat caag 744

<210> 499
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 499
gacatccaga tgacccagag ccccagcagc gtgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gggcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcaacc tgcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag aagctgagcc tgcccctgac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttcag cagctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaaccag 540

gacggcagcg agaagtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccagggaggg cggcgacagc tggtaccacg ccttcgacat ctggggccag 720

ggcaccatgg tgaccgtgag cagc 744

<210> 500
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 500
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaaccagg acggcagcga gaagtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggagggc 300

ggcgacagct ggtaccacgc cttcgacatc tggggccagg gcaccatggt gaccgtgagc 360

agcggcggcg gcggcagcgg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 420

agcgacatcc agatgaccca gagccccagc agcgtgagcg ccagcgtggg cgacagggtg 480

accatcacct gcagggccag ccagggcatc agcagctggc tggcctggta ccagcagaag 540

cccggcaagg cccccaagct gctgatctac gccgccagca acctgcagag cggcgtgccc 600

agcaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag cagcctgcag 660

cccgaggact tcgccaccta ctactgccag cagaagctga gcctgcccct gaccttcggc 720

tgcggcacca aggtggagat caag 744

<210> 501
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 501
gacatccaga tgacccagag ccccagcagc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctacctga actggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacggc gccagcagcc tgcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gtgtacagcg ccccccttcac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctgcaggaga gcggccccgg cctggtgaag 420

cccagccaga ccctgagcct gacctgcacc gtgagcggcg gcagcatcag cagcggcggc 480

tactactgga gctggatcag gcagcacccc ggcaagtgcc tggagtggat cggcagcatc 540

tactacagcg gcagcaccta ctacaacccc agcctgaaga gcagggtgac catcagcgtg 600

gacaccagca agaaccagtt cagcctgaag ctgagcagcg tgaccgccgc cgacaccgcc 660

gtgtactact gcgccaggga caggctggac tacagctaca actacggcat ggacgtgtgg 720

ggccagggca ccaccgtgac cgtgagcagc 750

<210> 502
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 502
caggtgcagc tgcaggagag cggccccggc ctggtgaagc ccagccagac cctgagcctg 60

acctgcaccg tgagcggcgg cagcatcagc agcggcggct actactggag ctggatcagg 120

cagcaccccg gcaagtgcct ggagtggatc ggcagcatct actacagcgg cagcacctac 180

tacaacccca gcctgaagag cagggtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gaccgccgcc gacaccgccg tgtactactg cgccagggac 300

aggctggact acagctacaa ctacggcatg gacgtgtggg gccagggcac caccgtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg acatccagat gacccagagc cccagcagcc tgagcgccag cgtgggcgac 480

agggtgacca tcacctgcag ggccagccag agcatcagca gctacctgaa ctggtaccag 540

cagaagcccg gcaaggcccc caagctgctg atctacggcg ccagcagcct gcagagcggc 600

gtgcccagca ggttcagcgg cagcggcagc ggcaccgact tcaccctgac catcagcagc 660

ctgcagcccg aggacttcgc cacctactac tgccagcagg tgtacagcgc ccccttcacc 720

ttcggctgcg gcaccaaggt ggagatcaag 750

<210> 503
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 503
gagatcgtgc tgacccagag ccccgccacc ctgagcctga gccccggcga gagggccacc 60

ctgagctgca gggccagcca gagcgtgagc agctacctgg cctggtacca gcagaagccc 120

ggccaggccc ccaggctgct gatctacgac gccagcaaca gggccaccgg catccccgcc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctggagccc 240

gaggacttcg ccgtgtacta ctgccagcag gtggacaact acccccccac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctgcaggaga gcggccccgg cctggtgaag 420

cccagcgaga ccctgagcct gacctgcgcc gtgagcggct acagcatcag cagcggctac 480

tactggggct ggatcaggca gccccccggc aagtgcctgg agtggatcgg cagcatctac 540

cacagcggca gcaccaacta caaccccagc ctgaagagca gggtgaccat cagcgtggac 600

accagcaaga accagttcag cctgaagctg agcagcgtga ccgccgccga caccgccgtg 660

tactactgcg ccaggctgcc cccctggttc ggcttcagct acttcgacct gtggggcagg 720

ggcaccctgg tgaccgtgag cagc 744

<210> 504
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 504
caggtgcagc tgcaggagag cggccccggc ctggtgaagc ccagcgagac cctgagcctg 60

acctgcgccg tgagcggcta cagcatcagc agcggctact actggggctg gatcaggcag 120

ccccccggca agtgcctgga gtggatcggc agcatctacc acagcggcag caccaactac 180

aaccccagcc tgaagagcag ggtgaccatc agcgtggaca ccagcaagaa ccagttcagc 240

ctgaagctga gcagcgtgac cgccgccgac accgccgtgt actactgcgc caggctgccc 300

ccctggttcg gcttcagcta cttcgacctg tggggcaggg gcaccctggt gaccgtgagc 360

agcggcggcg gcggcagcgg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 420

agcgagatcg tgctgaccca gagccccgcc accctgagcc tgagccccgg cgagagggcc 480

accctgagct gcagggccag ccagagcgtg agcagctacc tggcctggta ccagcagaag 540

cccggccagg cccccaggct gctgatctac gacgccagca acagggccac cggcatcccc 600

gccaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag cagcctggag 660

cccgaggact tcgccgtgta ctactgccag caggtggaca actacccccc caccttcggc 720

tgcggcacca aggtggagat caag 744

<210> 505
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 505
gacatccaga tgacccagag ccccagcagc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatcagc agctacctga actggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcagcc tgcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gtgtacgaca ccccccctgac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttcag cagctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaagcag 540

gacggcagcg agaagtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccagggacgt gggccccggc atcgcctacc agggccactt cgactactgg 720

ggccagggca ccctggtgac cgtgagcagc 750

<210> 506
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 506
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcagc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaagcagg acggcagcga gaagtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggacgtg 300

ggccccggca tcgcctacca gggccacttc gactactggg gccagggcac cctggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg acatccagat gacccagagc cccagcagcc tgagcgccag cgtgggcgac 480

agggtgacca tcacctgcag ggccagccag agcatcagca gctacctgaa ctggtaccag 540

cagaagcccg gcaaggcccc caagctgctg atctacgccg ccagcagcct gcagagcggc 600

gtgcccagca ggttcagcgg cagcggcagc ggcaccgact tcaccctgac catcagcagc 660

ctgcagcccg aggacttcgc cacctactac tgccagcagg tgtacgacac ccccctgacc 720

ttcggctgcg gcaccaaggt ggagatcaag 750

<210> 507
<211> 741
<212> DNA
<213> Artificial Sequence

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

<400> 507
gagatcgtgc tgacccagag ccccgccacc ctgagcctga gccccggcga gagggccacc 60

ctgagctgca gggccagcca gagcgtgagc agctacctgg cctggtacca gcagaagccc 120

ggccaggccc ccaggctgct gatctacgac gccagcaaca gggccaccgg catccccgcc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctggagccc 240

gaggacttcg ccgtgtacta ctgccagcag tacgacaacc tgcccacctt cggctgcggc 300

accaaggtgg agatcaaggg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 360

agcggcggcg gcggcagcca gctgcagctg caggagagcg gccccggcct ggtgaagccc 420

agcgagaccc tgagcctgac ctgcaccgtg agcggcggca gcatcagcag cagcagctac 480

tactggggct ggatcaggca gccccccggc aagtgcctgg agtggatcgg cagcatctac 540

tacagcggca gcacctacta caaccccagc ctgaagagca gggtgaccat cagcgtggac 600

accagcaaga accagttcag cctgaagctg agcagcgtga ccgccgccga caccgccgtg 660

tactactgcg ccagggagac cgcccacgac gtgcacggca tggacgtgtg gggccagggc 720

accaccgtga ccgtgagcag c 741

<210> 508
<211> 741
<212> DNA
<213> Artificial Sequence

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

<400> 508
cagctgcagc tgcaggagag cggccccggc ctggtgaagc ccagcgagac cctgagcctg 60

acctgcaccg tgagcggcgg cagcatcagc agcagcagct actactgggg ctggatcagg 120

cagccccccg gcaagtgcct ggagtggatc ggcagcatct actacagcgg cagcacctac 180

tacaacccca gcctgaagag cagggtgacc atcagcgtgg acaccagcaa gaaccagttc 240

agcctgaagc tgagcagcgt gaccgccgcc gacaccgccg tgtactactg cgccagggag 300

accgcccacg acgtgcacgg catggacgtg tggggccagg gcaccaccgt gaccgtgagc 360

agcggcggcg gcggcagcgg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 420

agcgagatcg tgctgaccca gagccccgcc accctgagcc tgagccccgg cgagagggcc 480

accctgagct gcagggccag ccagagcgtg agcagctacc tggcctggta ccagcagaag 540

cccggccagg cccccaggct gctgatctac gacgccagca acagggccac cggcatcccc 600

gccaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag cagcctggag 660

cccgaggact tcgccgtgta ctactgccag cagtacgaca acctgcccac cttcggctgc 720

ggcaccaagg tggagatcaa g 741

<210> 509
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 509
gagatcgtgc tgacccagag ccccgccacc ctgagcctga gccccggcga gagggccacc 60

ctgagctgca gggccagcca gagcgtgagc agctacctgg cctggtacca gcagaagccc 120

ggccaggccc ccaggctgct gatctacgac gccagcaaga gggccaccgg catccccgcc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctggagccc 240

gaggacttcg ccgtgtacta ctgccagcag agcagcaacc accccagcac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctggtgcaga gcggcgccga ggtgaagaag 420

cccggcagca gcgtgaaggt gagctgcaag gccagcggcg gcaccttcag cagctacgcc 480

atcagctggg tgaggcaggc ccccggccag tgcctggagt ggatgggcag catcatcccc 540

atcttcggca ccgccaacta cgcccagaag ttccagggca gggtgaccat caccgccgac 600

gagagcacca gcaccgccta catggagctg agcagcctga ggagcgagga caccgccgtg 660

tactactgcg ccagggaggt gggctacggc tggtacacca agatcgcctt cgacatctgg 720

ggccagggca ccatggtgac cgtgagcagc 750

<210> 510
<211> 750
<212> DNA

<213> Artificial Sequence

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

<400> 510
caggtgcagc tggtgcagag cggcgccgag gtgaagaagc ccggcagcag cgtgaaggtg 60

agctgcaagg ccagcggcgg caccttcagc agctacgcca tcagctgggt gaggcaggcc 120

cccggccagt gcctggagtg gatgggcagc atcatcccca tcttcggcac cgccaactac 180

gcccagaagt tccagggcag ggtgaccatc accgccgacg agagcaccag caccgcctac 240

atggagctga gcagcctgag gagcgaggac accgccgtgt actactgcgc cagggaggtg 300

ggctacggct ggtacaccaa gatcgccttc gacatctggg gccagggcac catggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg agatcgtgct gacccagagc cccgccaccc tgagcctgag ccccggcgag 480

agggccaccc tgagctgcag ggccagccag agcgtgagca gctacctggc ctggtaccag 540

cagaagcccg gccaggcccc caggctgctg atctacgacg ccagcaagag ggccaccggc 600

atccccgcca ggttcagcgg cagcggcagc ggcaccgact tcaccctgac catcagcagc 660

ctggagcccg aggacttcgc cgtgtactac tgccagcaga gcagcaacca ccccagcacc 720

ttcggctgcg gcaccaaggt ggagatcaag 750

<210> 511
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 511
gacatcgtga tgacccagag ccccctgagc ctgcccgtga cccccggcga gcccgccagc 60

atcagctgca ggagcagcca gagcctgctg cacagcaacg gctacaacta cctggactgg 120

tacctgcaga agcccggcca gagcccccag ctgctgatct acctgggcag caacagggcc 180

agcggcgtgc ccgacaggtt cagcggcagc ggcagcggca ccgacttcac cctgaagatc 240

agcagggtgg aggccgagga cgtgggcgtg tactactgca tgcaggccct gggcgtgccc 300

ctgaccttcg gctgcggcac caaggtggag atcaagggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cggcggcggc ggcagccagg tgcagctggt gcagagcggc 420

gccgaggtga agaagcccgg cgccagcgtg aaggtgagct gcaaggccag cggctacacc 480

ttcaccagct actacatgca ctgggtgagg caggcccccg gccagtgcct ggagtggatg 540

ggcatcatca accccagcgg cggcagcacc acctacgccc agaagttcca gggcagggtg 600

accatgacca gggacaccag caccagcacc gtgtacatgg agctgagcag cctgaggagc 660

gaggacaccg ccgtgtacta ctgcgccagg gaggccgccg acggcttcgt gggcgagagg 720

tacttcgacc tgtggggcag gggcaccctg gtgaccgtga gcagc 765

<210> 512
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 512
caggtgcagc tggtgcagag cggcgccgag gtgaagaagc ccggcgccag cgtgaaggtg 60

agctgcaagg ccagcggcta caccttcacc agctactaca tgcactgggt gaggcaggcc 120

cccggccagt gcctggagtg gatgggcatc atcaacccca gcggcggcag caccacctac 180

gcccagaagt tccagggcag ggtgaccatg accagggaca ccagcaccag caccgtgtac 240

atggagctga gcagcctgag gagcgaggac accgccgtgt actactgcgc cagggaggcc 300

gccgacggct tcgtgggcga gaggtacttc gacctgtggg gcaggggcac cctggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg acatcgtgat gacccagagc cccctgagcc tgcccgtgac ccccggcgag 480

cccgccagca tcagctgcag gagcagccag agcctgctgc acagcaacgg ctacaactac 540

ctggactggt acctgcagaa gcccggccag agcccccagc tgctgatcta cctgggcagc 600

aacagggcca gcggcgtgcc cgacaggttc agcggcagcg gcagcggcac cgacttcacc 660

ctgaagatca gcagggtgga ggccgaggac gtgggcgtgt actactgcat gcaggccctg 720

ggcgtgcccc tgaccttcgg ctgcggcacc aaggtggaga tcaag 765

<210> 513
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 513
gacatcgtga tgacccagag ccccctgagc ctgcccgtga cccccggcga gcccgccagc 60

atcagctgca ggagcagcca gagcctgctg tacagcaacg gctacaacta cctggactgg 120

tacctgcaga agcccggcca gagcccccag ctgctgatct acctgggcag caacagggcc 180

agcggcgtgc ccgacaggtt cagcggcagc ggcagcggca ccgacttcac cctgaagatc 240

agcagggtgg aggccgagga cgtgggcgtg tactactgca tgcaggacgt ggccctgccc 300

atcaccttcg gctgcggcac caaggtggag atcaagggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cggcggcggc ggcagccagg tgcagctggt gcagagcggc 420

gccgaggtga agaagcccgg cgccagcgtg aaggtgagct gcaaggccag cggctacacc 480

ttcagcggct actacatgca ctgggtgagg caggcccccg gccagtgcct ggagtggatg 540

ggcatgatca acccctacgg cggcagcacc aggtacgccc agaagttcca gggcagggtg 600

accatgacca gggacaccag caccagcacc gtgtacatgg agctgagcag cctgaggagc 660

gaggacaccg ccgtgtacta ctgcgccagg gaggccgccg acggcttcgt gggcgagagg 720

tacttcgacc tgtggggcag gggcaccctg gtgaccgtga gcagc 765

<210> 514
<211> 765
<212> DNA
<213> Artificial Sequence

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

<400> 514
caggtgcagc tggtgcagag cggcgccgag gtgaagaagc ccggcgccag cgtgaaggtg 60

agctgcaagg ccagcggcta caccttcagc ggctactaca tgcactgggt gaggcaggcc 120

cccggccagt gcctggagtg gatgggcatg atcaacccct acggcggcag caccaggtac 180

gcccagaagt tccagggcag ggtgaccatg accagggaca ccagcaccag caccgtgtac 240

atggagctga gcagcctgag gagcgaggac accgccgtgt actactgcgc cagggaggcc 300

gccgacggct tcgtgggcga gaggtacttc gacctgtggg gcaggggcac cctggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg acatcgtgat gacccagagc cccctgagcc tgcccgtgac ccccggcgag 480

cccgccagca tcagctgcag gagcagccag agcctgctgt acagcaacgg ctacaactac 540

ctggactggt acctgcagaa gcccggccag agcccccagc tgctgatcta cctgggcagc 600

aacagggcca gcggcgtgcc cgacaggttc agcggcagcg gcagcggcac cgacttcacc 660

ctgaagatca gcagggtgga ggccgaggac gtgggcgtgt actactgcat gcaggacgtg 720

gccctgccca tcaccttcgg ctgcggcacc aaggtggaga tcaag 765

<210> 515
<211> 741
<212> DNA
<213> Artificial Sequence

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

<400> 515
gacatccaga tgacccagag ccccagcagc gtgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gggcatcgac agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcagcc tgcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gcccacagct acccccctgac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctggtgcaga gcggcgccga ggtgaagaag 420

cccggcgcca gcgtgaaggt gagctgcaag gccagcggct acaccttcga gatctactac 480

atgcactggg tgaggcaggc ccccggccag tgcctggagt ggatgggcat catcaacccc 540

agcagcggca gcaccgtgta cgcccagaag ttccagggca gggtgaccat gaccagggac 600

accagcacca gcaccgtgta catggagctg agcagcctga ggagcgagga caccgccgtg 660

tactactgcg ccaggggcgc cggctacgac gacgaggaca tggacgtgtg gggcaagggc 720

accaccgtga ccgtgagcag c 741

<210> 516
<211> 741
<212> DNA
<213> Artificial Sequence

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

<400> 516
caggtgcagc tggtgcagag cggcgccgag gtgaagaagc ccggcgccag cgtgaaggtg 60

agctgcaagg ccagcggcta caccttcgag atctactaca tgcactgggt gaggcaggcc 120

cccggccagt gcctggagtg gatgggcatc atcaacccca gcagcggcag caccgtgtac 180

gcccagaagt tccagggcag ggtgaccatg accagggaca ccagcaccag caccgtgtac 240

atggagctga gcagcctgag gagcgaggac accgccgtgt actactgcgc caggggcgcc 300

ggctacgacg acgaggacat ggacgtgtgg ggcaagggca ccaccgtgac cgtgagcagc 360

ggcggcggcg gcagcggcgg cggcggcagc ggcggcggcg gcagcggcgg cggcggcagc 420

gacatccaga tgacccagag ccccagcagc gtgagcgcca gcgtgggcga cagggtgacc 480

atcacctgca gggccagcca gggcatcgac agctggctgg cctggtacca gcagaagccc 540

ggcaaggccc ccaagctgct gatctacgcc gccagcagcc tgcagagcgg cgtgcccagc 600

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 660

gaggacttcg ccacctacta ctgccagcag gcccacagct acccccctgac cttcggctgc 720

ggcaccaagg tggagatcaa g 741

<210> 517
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 517
gacatccaga tgacccagag ccccagcagc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatctac aactacctga actggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcaacc tgcacagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gccttccacg tgcccatcac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttcgg cggctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaaccag 540

gacggcagcg aggagtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccagggaggc caactactac ggcaacgtgg gcgacgacta ctggggccag 720

ggcaccctgg tgaccgtgag cagc 744

<210> 518
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 518
gaggtgcagc tggtggagag cggcggcggc ctggtgcagc ccggcggcag cctgaggctg 60

agctgcgccg ccagcggctt caccttcggc ggctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaaccagg acggcagcga ggagtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggaggcc 300

aactactacg gcaacgtggg cgacgactac tggggccagg gcaccctggt gaccgtgagc 360

agcggcggcg gcggcagcgg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 420

agcgacatcc agatgaccca gagccccagc agcctgagcg ccagcgtggg cgacagggtg 480

accatcacct gcagggccag ccagagcatc tacaactacc tgaactggta ccagcagaag 540

cccggcaagg cccccaagct gctgatctac gccgccagca acctgcacag cggcgtgccc 600

agcaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag cagcctgcag 660

cccgaggact tcgccaccta ctactgccag caggccttcc acgtgcccat caccttcggc 720

tgcggcacca aggtggagat caag 744

<210> 519
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 519
gacatccaga tgacccagag ccccagcagc ctgagcgcca gcgtgggcga cagggtgacc 60

atcacctgca gggccagcca gagcatctac aactacctga actggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcagca cccagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gccttccacg tgcccatcac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttccc cggctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaaccag 540

gacggcagcg aggtgtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccagggaggc caactactac ggcaacgtgg gcgacgacta ctggggccag 720

ggcaccctgg tgaccgtgag cagc 744

<210> 520
<211> 744
<212> DNA
<213> Artificial Sequence

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

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agctgcgccg ccagcggctt caccttcccc ggctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaaccagg acggcagcga ggtgtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggaggcc 300

aactactacg gcaacgtggg cgacgactac tggggccagg gcaccctggt gaccgtgagc 360

agcggcggcg gcggcagcgg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 420

agcgacatcc agatgaccca gagccccagc agcctgagcg ccagcgtggg cgacagggtg 480

accatcacct gcagggccag ccagagcatc tacaactacc tgaactggta ccagcagaag 540

cccggcaagg cccccaagct gctgatctac gccgccagca gcacccagag cggcgtgccc 600

agcaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag cagcctgcag 660

cccgaggact tcgccaccta ctactgccag caggccttcc acgtgcccat caccttcggc 720

tgcggcacca aggtggagat caag 744

<210> 521
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 521
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ggcaaggccc ccaagctgct gatctacgcc gccagcagca ggcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gtgtacgaca ccccctgac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag cgaggtgcag ctggtggaga gcggcggcgg cctggtgcag 420

cccggcggca gcctgaggct gagctgcgcc gccagcggct tcaccttcag cagctactgg 480

atgagctggg tgaggcaggc ccccggcaag tgcctggagt gggtggccaa catcaaccag 540

gacggcagcg aggtgtacta cgtggacagc gtgaagggca ggttcaccat cagcagggac 600

aacgccaaga acagcctgta cctgcagatg aacagcctga gggccgagga caccgccgtg 660

tactactgcg ccagggacgt gggccccggc atcgcctacc agggccactt cgactactgg 720

ggccagggca ccctggtgac cgtgagcagc 750

<210> 522
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 522
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agctgcgccg ccagcggctt caccttcagc agctactgga tgagctgggt gaggcaggcc 120

cccggcaagt gcctggagtg ggtggccaac atcaaccagg acggcagcga ggtgtactac 180

gtggacagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa cagcctgtac 240

ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagggacgtg 300

ggccccggca tcgcctacca gggccacttc gactactggg gccagggcac cctggtgacc 360

gtgagcagcg gcggcggcgg cagcggcggc ggcggcagcg gcggcggcgg cagcggcggc 420

ggcggcagcg acatccagat gacccagagc cccagcagcc tgagcgccag cgtgggcgac 480

agggtgacca tcacctgcag ggccagccag agcatctact actacctgaa ctggtaccag 540

cagaagcccg gcaaggcccc caagctgctg atctacgccg ccagcagcag gcagagcggc 600

gtgcccagca ggttcagcgg cagcggcagc ggcaccgact tcaccctgac catcagcagc 660

ctgcagcccg aggacttcgc cacctactac tgccagcagg tgtacgacac ccccctgacc 720

ttcggctgcg gcaccaaggt ggagatcaag 750

<210> 523
<211> 744
<212> DNA

<213> Artificial Sequence

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

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gacatccaga tgacccagag ccccagcagc gtgagcgcca gcgtgggcga cagggtgacc 60

atcacctgcg aggccagcaa gggcatcagc agctggctgg cctggtacca gcagaagccc 120

ggcaaggccc ccaagctgct gatctacgcc gccagcgacc tgcagagcgg cgtgcccagc 180

aggttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagccc 240

gaggacttcg ccacctacta ctgccagcag gccttcctgt tccccccccac cttcggctgc 300

ggcaccaagg tggagatcaa gggcggcggc ggcagcggcg gcggcggcag cggcggcggc 360

ggcagcggcg gcggcggcag ccaggtgcag ctggtgcaga gcggcgccga ggtgaagaag 420

cccggcgcca gcgtgaaggt gagctgcaag gccagcggct acaccttcag caactactac 480

atgcactggg tgaggcaggc ccccggccag tgcctggagt ggatgggctg gatcaacccc 540

ttcagcggcg gcaccaggta cgcccagaag ttccagggca gggtgaccat gaccagggac 600

accagcacca gcaccgtgta catggagctg agcagcctga ggagcgagga caccgccgtg 660

tactactgcg ccagggacgt gggcagcagc gcctactact acatggacgt gtggggcaag 720

ggcaccaccg tgaccgtgag cagc 744

<210> 524
<211> 744
<212> DNA
<213> Artificial Sequence

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

<400> 524
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agctgcaagg ccagcggcta caccttcagc aactactaca tgcactgggt gaggcaggcc 120

cccggccagt gcctggagtg gatgggctgg atcaacccct tcagcggcgg caccaggtac 180

gcccagaagt tccagggcag ggtgaccatg accagggaca ccagcaccag caccgtgtac 240

atggagctga gcagcctgag gagcgaggac accgccgtgt actactgcgc cagggacgtg 300

ggcagcagcg cctactacta catggacgtg tggggcaagg gcaccaccgt gaccgtgagc 360

agcggcggcg gcggcagcgg cggcggcggc agcggcggcg gcggcagcgg cggcggcggc 420

agcgacatcc agatgaccca gagccccagc agcgtgagcg ccagcgtggg cgacagggtg 480

accatcacct gcgaggccag caagggcatc agcagctggc tggcctggta ccagcagaag 540

cccggcaagg cccccaagct gctgatctac gccgccagcg acctgcagag cggcgtgccc 600

agcaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag cagcctgcag 660

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tgcggcacca aggtggagat caag 744

<210> 525
<211> 750
<212> DNA
<213> Artificial Sequence

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

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ctgagctgca gggccagcca gagcgtgagc agcagcttcc tggcctggta ccagcagaag 120

cccggccagg cccccaggct gctgatctac ggcgccagca gcagggccac cggcatcccc 180

gacaggttca gcggcagcgg cagcggcacc gacttcaccc tgaccatcag caggctggag 240

cccgaggact tcgccgtgta ctactgccag cagctggaca gccccccccc caccttcggc 300

tgcggcacca aggtggagat caagggcggc ggcggcagcg gcggcggcgg cagcggcggc 360

ggcggcagcg gcggcggcgg cagcgaggtg cagctggtgc agagcggcgc cgaggtgaag 420

aagcccggcg agagcctgaa gatcagctgc aagggcagcg gctacagctt caccagctac 480

tggatcggct gggtgaggca gatgcccggc aagtgcctgg agtggatggg cagcatctac 540

cccggcgaca gcgacaccag gtacagcccc agcttccagg gccaggtgac catcagcgcc 600

gacaagagca tcagcaccgc ctacctgcag tggagcagcc tgaaggccag cgacaccgcc 660

atgtactact gcgccaggga gctggcctac ggcgactaca agggcggcgt ggactactgg 720

ggccagggca ccctggtgac cgtgagcagc 750

<210> 526
<211> 750
<212> DNA
<213> Artificial Sequence

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

<400> 526
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agctgcaagg gcagcggcta cagcttcacc agctactgga tcggctgggt gaggcagatg 120

cccggcaagt gcctggagtg gatgggcagc atctaccccg gcgacagcga caccaggtac 180

agccccagct tccagggcca ggtgaccatc agcgccgaca agagcatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggccagcgac accgccatgt actactgcgc cagggagctg 300

gcctacggcg actacaaggg cggcgtggac tactggggcc agggcaccct ggtgaccgtg 360

agcagcggcg gcggcggcag cggcggcggc ggcagcggcg gcggcggcag cggcggcggc 420

ggcagcgaga tcgtgctgac ccagagcccc ggcaccctga gcctgagccc cggcgagagg 480

gccaccctga gctgcagggc cagccagagc gtgagcagca gcttcctggc ctggtaccag 540

cagaagcccg gccaggcccc caggctgctg atctacggcg ccagcagcag ggccaccggc 600

atccccgaca ggttcagcgg cagcggcagc ggcaccgact tcaccctgac catcagcagg 660

ctggagcccg aggacttcgc cgtgtactac tgccagcagc tggacagccc ccccccccacc 720

ttcggctgcg gcaccaaggt ggagatcaag 750

<210> 527
<211> 13
<212> PRT
<213> Artificial Sequence

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

<220>
<221> VARIANT
<222> (4)..(4)
<223> Ala, Val, Leu, Ile, Pro, Phe, Trp, Gly, Ser, Thr, Cys, Asn, Gln, or Tyr

<400> 527

Gly Ala Pro Xaa Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 528
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 528

Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5

<210> 529
<211> 20
<212> PRT
<213> Artificial Sequence

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

<400> 529

Ala Arg Pro Arg Ala Tyr Tyr Asp Ser Ser Gly Phe Lys Val Asn Tyr
1 5 10 15

Gly Met Asp Val
20

<210> 530
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 530

Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5

<210> 531
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 531

Ala Arg Glu Gly His Ser Ser Ser Tyr Tyr Asp His Ala Phe Asp Ile
1 5 10 15

<210> 532
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 532

Gly Ser Ile Ser Ser Tyr Tyr Trp Ser
1 5

<210> 533
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 533

Ala Arg Val Gly Gly Val Tyr Ser Thr Ile Glu Thr Tyr Gly Met Asp
1 5 10 15

Val

<210> 534
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 534

Gly Ser Phe Ser Gly Tyr Tyr Trp Ser
1 5

<210> 535
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 535

Ala Arg Gln Gly Ile His Gly Leu Arg Tyr Phe Asp Leu
1 5 10

<210> 536
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 536

Phe Thr Phe Ser Ser Tyr Trp Met Ser
1 5

<210> 537
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 537

Ala Arg Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr
1 5 10

<210> 538
<211> 9

<212> PRT
<213> Artificial Sequence

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

<400> 538

Phe Thr Phe Ser Ser Tyr Trp Met Ser
1 5

<210> 539
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 539

Ala Arg Glu Gly Gly Asp Ser Trp Tyr His Ala Phe Asp Ile
1 5 10

<210> 540
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 540

Gly Ser Ile Ser Ser Gly Gly Tyr Tyr Trp Ser
1 5 10

<210> 541
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 541

Ala Arg Asp Arg Leu Asp Tyr Ser Tyr Asn Tyr Gly Met Asp Val
1 5 10 15

<210> 542
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 542

Tyr Ser Ile Ser Ser Gly Tyr Tyr Trp Gly
1   5   10

<210> 543
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 543

Ala Arg Leu Pro Pro Trp Phe Gly Phe Ser Tyr Phe Asp Leu
1   5   10

<210> 544
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 544

Phe Thr Phe Ser Ser Tyr Trp Met Ser
1   5

<210> 545
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 545

Ala Arg Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
1 5 10 15

<210> 546
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 546

Gly Ser Ile Ser Ser Ser Ser Tyr Tyr Trp Gly
1 5 10

<210> 547
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 547

Ala Arg Glu Thr Ala His Asp Val His Gly Met Asp Val
1 5 10

<210> 548
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 548

Gly Thr Phe Ser Ser Tyr Ala Ile Ser
1 5

<210> 549
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 549

Ala Arg Glu Val Gly Tyr Gly Trp Tyr Thr Lys Ile Ala Phe Asp Ile
1   5   10   15

<210> 550
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 550

Tyr Thr Phe Thr Ser Tyr Tyr Met His
1   5

<210> 551
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 551

Ala Arg Glu Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
1   5   10   15

<210> 552
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 552

Tyr Thr Phe Ser Gly Tyr Tyr Met His
1   5

<210> 553
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 553

Ala Arg Glu Ala Ala Asp Gly Phe Val Gly Glu Arg Tyr Phe Asp Leu
1 5 10 15

<210> 554
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 554

Tyr Thr Phe Glu Ile Tyr Tyr Met His
1 5

<210> 555
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 555

Ala Arg Gly Ala Gly Tyr Asp Asp Glu Asp Met Asp Val
1 5 10

<210> 556
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 556

Phe Thr Phe Gly Gly Tyr Trp Met Ser
1   5

<210> 557
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 557

Ala Arg Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr
1   5   10

<210> 558
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 558

Phe Thr Phe Pro Gly Tyr Trp Met Ser
1   5

<210> 559
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 559

Ala Arg Glu Ala Asn Tyr Tyr Gly Asn Val Gly Asp Asp Tyr
1   5   10

<210> 560
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 560

Phe Thr Phe Ser Ser Tyr Trp Met Ser
1 5

<210> 561
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 561

Ala Arg Asp Val Gly Pro Gly Ile Ala Tyr Gln Gly His Phe Asp Tyr
1 5 10 15

<210> 562
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 562

Tyr Thr Phe Ser Asn Tyr Tyr Met His
1 5

<210> 563
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 563

Ala Arg Asp Val Gly Ser Ser Ala Tyr Tyr Tyr Met Asp Val
1 5 10

<210> 564
<211> 9

<212> PRT
<213> Artificial Sequence

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

<400> 564

Tyr Ser Phe Thr Ser Tyr Trp Ile Gly
1 5

<210> 565
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 565

Ala Arg Glu Leu Ala Tyr Gly Asp Tyr Lys Gly Gly Val Asp Tyr
1 5 10 15

<210> 566
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 566

Ser Tyr Tyr Met His
1 5

<210> 567
<211> 17
<212> PRT
<213> Artificial Sequence

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

<400> 567

Gly Ala Pro Asn Tyr Gly Asp Thr Thr His Asp Tyr Tyr Tyr Met Asp
1 5 10 15

Val

<210> 568
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 568

Gly Tyr Tyr Met His
1 5

<210> 569
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 569

Asp Thr Gly Glu Tyr Tyr Asp Thr Asp Asp His Gly Met Asp Val
1 5 10 15

<210> 570
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 570

Ser Tyr Ala Met Ser
1 5

<210> 571
<211> 12
<212> PRT
<213> Artificial Sequence

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

<400> 571

Asp Gly Gly Tyr Tyr Asp Ser Gly Ala Gly Asp Tyr
1   5   10

<210> 572
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 572

Ser Tyr Tyr Met His
1   5

<210> 573
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 573

Glu Gly Ala Gly Phe Ala Tyr Gly Met Asp Tyr Tyr Tyr Met Asp Val
1   5   10   15

<210> 574
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 574

Gly Tyr Tyr Trp Ser
1   5

<210> 575
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 575

Ala Arg Gly Pro Trp Ser Phe Asp Pro
1 5

<210> 576
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 576

Ser Tyr Ala Ile Ser
1 5

<210> 577
<211> 16
<212> PRT
<213> Artificial Sequence

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

<400> 577

Gly Asp Ser Ser Ile Arg His Ala Tyr Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 578
<211> 7
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 578

Ser Ser Ser Tyr Tyr Trp Gly
1 5

<210> 579
<211> 11
<212> PRT
<213> Artificial Sequence

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

<400> 579

Gly Ser Asp Arg Phe His Pro Tyr Phe Asp Tyr
1 5 10

<210> 580
<211> 113
<212> PRT
<213> Artificial Sequence

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

<400> 580

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> 581
<211> 7
<212> PRT
<213> Artificial Sequence

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

<400> 581

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 582
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 582

Gln Gln Phe Asp Thr Trp Pro Pro Thr
1 5

<210> 583
<211> 117
<212> PRT
<213> Artificial Sequence

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

<400> 583

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>  584
<211>  106
<212>  PRT
<213>  Artificial Sequence

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

<400>  584

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> 585
<211> 126
<212> PRT
<213> Artificial Sequence

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

<400> 585

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> 586
<211> 122
<212> PRT
<213> Artificial Sequence

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

<400> 586

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 Gln 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> 587
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 587

Ala Arg Gly Ala Pro Gln Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10 15

<210> 588
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 588

Gly Ala Pro Gln Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 589
<211> 122
<212> PRT
<213> Artificial Sequence

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

<400> 589

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 Leu 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> 590
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 590

Ala Arg Gly Ala Pro Leu Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10 15

<210> 591
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 591

Gly Ala Pro Leu Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 592
<211> 122
<212> PRT
<213> Artificial Sequence

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

<400> 592

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 Phe 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> 593
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 593

Ala Arg Gly Ala Pro Phe Gly Ala Ala Ala Gly Trp Phe Asp Pro
1   5   10   15

<210> 594
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 594

Gly Ala Pro Phe Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 595
<211> 122
<212> PRT
<213> Artificial Sequence

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

<400> 595

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 Val 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> 596
<211> 15
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 596

Ala Arg Gly Ala Pro Val Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10 15

<210> 597
<211> 13
<212> PRT
<213> Artificial Sequence

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

<400> 597

Gly Ala Pro Val Gly Ala Ala Ala Gly Trp Phe Asp Pro
1 5 10

<210> 598
<211> 347
<212> PRT
<213> Homo sapiens

<400> 598

Asp Pro Asn Phe Trp Leu Gln Val Gln Glu Ser Val Thr Val Gln Glu
1 5 10 15

Gly Leu Cys Val Leu Val Pro Cys Thr Phe Phe His Pro Ile Pro Tyr
20 25 30

Tyr Asp Lys Asn Ser Pro Val His Gly Tyr Trp Phe Arg Glu Gly Ala
35 40 45

Ile Ile Ser Arg Asp Ser Pro Val Ala Thr Asn Lys Leu Asp Gln Glu
50 55 60

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

Arg Asn Asn Cys Ser Leu Ser Ile Val Asp Ala Arg Arg Arg Asp Asn
85 90 95

```
Gly Ser Tyr Phe Phe Arg Met Glu Arg Gly Ser Thr Lys Tyr Ser Tyr
            100                 105                 110

Lys Ser Pro Gln Leu Ser Val His Val Thr Asp Leu Thr His Arg Pro
        115                 120                 125

Lys Ile Leu Ile Pro Gly Thr Leu Glu Pro Gly His Ser Lys Asn Leu
    130                 135                 140

Thr Cys Ser Val Ser Trp Ala Cys Glu Gln Gly Thr Pro Pro Ile Phe
145                 150                 155                 160

Ser Trp Leu Ser Ala Ala Pro Thr Ser Leu Gly Pro Arg Thr Thr His
                165                 170                 175

Ser Ser Val Leu Ile Ile Thr Pro Arg Pro Gln Asp His Gly Thr Asn
            180                 185                 190

Leu Thr Cys Gln Val Lys Phe Ala Gly Ala Gly Val Thr Thr Glu Arg
        195                 200                 205

Thr Ile Gln Leu Asn Val Thr Tyr Val Pro Gln Asn Pro Thr Thr Gly
    210                 215                 220

Ile Phe Pro Gly Asp Gly Ser Gly Lys Gln Glu Thr Arg Ala Gly Val
225                 230                 235                 240

Val His Gly Ala Ile Gly Gly Ala Gly Val Thr Ala Leu Leu Ala Leu
                245                 250                 255

Cys Leu Cys Leu Ile Phe Phe Ile Val Lys Thr His Arg Arg Lys Ala
            260                 265                 270

Ala Arg Thr Ala Val Gly Arg Asn Asp Thr His Pro Thr Thr Gly Ser
        275                 280                 285

Ala Ser Pro Lys His Gln Lys Lys Ser Lys Leu His Gly Pro Thr Glu
    290                 295                 300
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Thr Ser Ser Cys Ser Gly Ala Ala Pro Thr Val Glu Met Asp Glu Glu
305                 310                 315                 320


Leu His Tyr Ala Ser Leu Asn Phe His Gly Met Asn Pro Ser Lys Asp
                325                 330                 335


Thr Ser Thr Glu Tyr Ser Glu Val Arg Thr Gln
            340                 345


<210>  599
<211>  343
<212>  PRT
<213>  Macaca fascicularis

<400>  599

Asp Pro Arg Val Arg Leu Glu Val Gln Glu Ser Val Thr Val Gln Glu
1               5                   10                  15


Gly Leu Cys Val Leu Val Pro Cys Thr Phe Phe His Pro Val Pro Tyr
            20                  25                  30


His Thr Arg Asn Ser Pro Val His Gly Tyr Trp Phe Arg Glu Gly Ala
        35                  40                  45


Ile Val Ser Leu Asp Ser Pro Val Ala Thr Asn Lys Leu Asp Gln Glu
    50                  55                  60


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


Arg Asn Asn Cys Ser Leu Ser Ile Val Asp Ala Arg Arg Arg Asp Asn
                85                  90                  95


Gly Ser Tyr Phe Phe Arg Met Glu Lys Gly Ser Thr Lys Tyr Ser Tyr
            100                 105                 110


Lys Ser Thr Gln Leu Ser Val His Val Thr Asp Leu Thr His Arg Pro
        115                 120                 125
```

```
Gln Ile Leu Ile Pro Gly Ala Leu Asp Pro Asp His Ser Lys Asn Leu
    130                 135                 140

Thr Cys Ser Val Pro Trp Ala Cys Glu Gln Gly Thr Pro Pro Ile Phe
145                 150                 155                 160

Ser Trp Met Ser Ala Ala Pro Thr Ser Leu Gly Leu Arg Thr Thr His
                165                 170                 175

Ser Ser Val Leu Ile Ile Thr Pro Arg Pro Gln Asp His Gly Thr Asn
            180                 185                 190

Leu Thr Cys Gln Val Lys Phe Pro Gly Ala Gly Val Thr Thr Glu Arg
        195                 200                 205

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

Ile Phe Leu Gly Asp Gly Ser Gly Lys Gln Gly Val Val Gln Gly Ala
225                 230                 235                 240

Ile Gly Gly Ala Gly Val Thr Val Leu Leu Ala Leu Cys Leu Cys Leu
                245                 250                 255

Ile Phe Phe Thr Val Lys Thr His Arg Arg Lys Ala Ala Arg Thr Ala
            260                 265                 270

Val Gly Arg Ile Asp Thr His Pro Ala Thr Gly Pro Thr Ser Ser Lys
        275                 280                 285

His Gln Lys Lys Ser Lys Leu His Gly Ala Thr Glu Thr Ser Gly Cys
    290                 295                 300

Ser Gly Thr Thr Leu Thr Val Glu Met Asp Glu Glu Leu His Tyr Ala
305                 310                 315                 320

Ser Leu Asn Phe His Gly Met Asn Pro Ser Glu Asp Thr Ser Thr Glu
                325                 330                 335
```

Tyr Ser Glu Val Arg Thr Gln
340