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DESCRIPTION

FIELD

[0001] Provided herein are antigen-binding proteins (ABPs) with binding specificity for T cell immunoreceptor with Ig and ITIM domains (TIGIT) and compositions comprising such ABPs, including pharmaceutical compositions, diagnostic compositions, and kits. Also provided are methods of making TIGIT ABPs, and methods of using TIGIT ABPs, for example, for therapeutic purposes, diagnostic purposes, and research purposes.

BACKGROUND

[0002] TIGIT has been identified as a co-inhibitory receptor that limits the response of T cells to cancer and chronic infection. See Grogan et al., J. Immunol., 2014, 192: (1 Supplement) 203.15. Blockade of TIGIT has been shown to contribute to the enhancement CD8+ T cell effector function, and improvement of viral clearance and tumor rejection. See *id.*

[0003] Thus, there is a need for therapeutics that can antagonize TIGIT. Provided herein are ABPs that fulfill this need.

SUMMARY

[0004] The invention is as defined in the claims. Any references in the description to methods of treatment refer to the compounds, pharmaceutical compositions and medicaments of the present invention for use in a method for treatment of the human (or animal) body by therapy (or for diagnosis).

[0005] In a first aspect of the invention, there is provided an isolated antibody, or antigen-binding fragment thereof that specifically binds human TIGIT (hTIGIT; SEQ ID No: 1), comprising:

1. (a) a CDR-H3 of SEQ ID NO: 32, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 54, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71;
2. (b) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 54, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71;
3. (c) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 39, a CDR-H1 of SEQ ID NO: 51, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71;

4. (d) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 52, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71; or
5. (e) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 41, a CDR-H1 of SEQ ID NO: 53, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71.

[0006] In a second aspect of the invention, there is provided a pharmaceutical composition comprising an antibody, or antigen-binding fragment thereof of the first aspect and a pharmaceutically acceptable excipient.

[0007] In a third aspect of the invention, there is provided the antibody, or antigen-binding fragment thereof of the first aspect, or the pharmaceutical composition of the second aspect, for use as a medicament.

[0008] In a fourth aspect of the invention, there is provided the antibody, or antigen-binding fragment thereof of the first aspect or the pharmaceutical composition of the second aspect, for use in the treatment of a cancer or viral infection.

[0009] In a fifth aspect of the invention, there is provided the antibody, or antigen-binding fragment thereof of the first aspect or the pharmaceutical composition of the second aspect, for use as a medicament in the treatment of a disease or condition that was not responsive to a prior therapy.

[0010] In a sixth aspect of the invention, there is provided an isolated polynucleotide encoding an antibody, or antigen-binding fragment thereof of the first aspect.

[0011] In a seventh aspect of the invention, there is provided a vector comprising the polynucleotide of the sixth aspect.

[0012] In an eighth aspect of the invention, there is provided a host cell comprising the polynucleotide of the sixth aspect or the vector of the seventh aspect.

[0013] In a ninth aspect of the invention, there is provided a method of producing an antibody, or antigen-binding fragment thereof of the first aspect, comprising expressing the antibody, or antigen-binding fragment thereof in the host cell of the eighth aspect and isolating the expressed antibody, or antigen-binding fragment thereof.

[0014] In a tenth aspect of the invention, there is provided a kit comprising the pharmaceutical composition of the second aspect, and instructions for the use of such pharmaceutical composition.

[0015] Provided herein are ABPs that specifically bind TIGIT and methods of using such ABPs.

[0016] In some embodiments, the TIGIT is selected from human TIGIT ("hTIGIT", SEQ ID NO:1), cynomolgus monkey TIGIT ("cTIGIT", SEQ ID NO:2), and murine TIGIT ("mTIGIT", SEQ ID NO:3 or 138).

[0017] In some embodiments, the ABP comprises an antibody. In some aspects, the antibody is a monoclonal antibody. In some aspects, the antibody is a chimeric antibody. In some aspects, the antibody is a humanized antibody. In some aspects, the antibody is a human antibody. In some aspects, the ABP comprises an antibody fragment. In some embodiments, the ABP comprises an alternative scaffold.

[0018] In some embodiments, the TIGIT is expressed on the surface of a target cell. In some aspects, the ABP antagonizes TIGIT expressed on the surface of the target cell.

[0019] In some embodiments, the target cell is selected from an effector T cell, a regulatory T cell, a natural killer (NK) cell, and a natural killer T (NKT) cell. In some aspects, the target cell is an effector T cell selected from a helper (CD4-positive, "CD4+") T cell, a cytotoxic (CD8-positive, "CD8+") T cell, and combinations thereof. In some aspects, the target cell is a regulatory T cell selected from a CD4+CD25+Foxp3+ regulatory T cell, a CD8+CD25+ regulatory T cell, and combinations thereof.

[0020] In some embodiments, the ABPs provided herein induce various biological effects associated with inhibition of TIGIT. In some aspects, an ABP provided herein prevents inhibition of an effector T cell. In some aspects, the ABP co-stimulates an effector T cell. In some aspects, the ABP inhibits the suppression of an effector T cell by a regulatory T cell. In some aspects, the ABP increases the number of effector T cells in a tissue or in systemic circulation. In some aspects, the tissue is a tumor. In some aspects, the tissue is a tissue that is infected with a virus.

[0021] Also provided are kits comprising one or more of the ABPs provided herein, and instructions for use of the ABPs. Also provided are kits comprising one or more of the pharmaceutical compositions provided herein, and instructions for use of the pharmaceutical composition.

[0022] Also provided are isolated polynucleotides encoding the ABPs provided herein, and portions thereof.

[0023] Also provided are vectors comprising such polynucleotides.

[0024] Also provided are recombinant host cells comprising such polynucleotides and recombinant host cells comprising such vectors.

[0025] Also provided are methods of producing an ABP provided herein using the

polynucleotides, vectors, or host cells provided herein.

[0026] Also provided are pharmaceutical compositions comprising the ABPs provided herein and a pharmaceutically acceptable excipient.

[0027] In some examples, provided herein is a first family of ABPs, wherein an ABP of such family comprises: (a) a CDR-H3 of SEQ ID NO: 32, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 54, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71; (b) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 54, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71; (c) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 39, a CDR-H1 of SEQ ID NO: 51, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71; (d) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 52, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71; or (e) a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 41, a CDR-H1 of SEQ ID NO: 53, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71.

[0028] In some embodiments, an ABP of such first family comprises: (a) a V_H sequence of SEQ ID NO: 13 and a V_L sequence of SEQ ID NO: 26; (b) a V_H sequence of SEQ ID NO: 12 and a V_L sequence of SEQ ID NO: 26; (c) a V_H sequence of SEQ ID NO: 14 and a V_L sequence of SEQ ID NO: 26; (d) a V_H sequence of SEQ ID NO: 15 and a V_L sequence of SEQ ID NO: 26; (e) a V_H sequence of SEQ ID NO: 9 and a V_L sequence of SEQ ID NO: 26; (f) a V_H sequence of SEQ ID NO: 10 and a V_L sequence of SEQ ID NO: 26; or (g) a V_H sequence of SEQ ID NO: 11 and a V_L sequence of SEQ ID NO: 26.

[0029] In some embodiments, an ABP of such first family comprises: (a) (i) a heavy chain of SEQ ID NO: 99 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 100 and a light chain of SEQ ID NO: 92; (b) (i) a heavy chain of SEQ ID NO: 97 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 98 and a light chain of SEQ ID NO: 92; (c) (i) a heavy chain of SEQ ID NO: 101 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 102 and a light chain of SEQ ID NO: 92; (d) (i) a heavy chain of SEQ ID NO: 103 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 104 and a light chain of SEQ ID NO: 92; (e) (i) a heavy chain of SEQ ID NO: 90 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 91 and a light chain of SEQ ID NO: 92; (f) (i) a heavy chain of SEQ ID NO: 93 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 94 and a light chain of SEQ ID NO: 92; or (g) (i) a heavy chain of SEQ ID NO: 95 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 96 and a light chain of SEQ ID NO: 92.

[0030] In some examples, provided herein is a second family of ABPs, wherein an ABP of such family comprises: (a) a CDR-H3 of SEQ ID NO: 29, a CDR-H2 of SEQ ID NO: 37, a CDR-H1 of SEQ ID NO: 49, a CDR-L3 of SEQ ID NO: 63, a CDR-L2 of SEQ ID NO: 67, and a CDR-L1 of

SEQ ID NO: 70; (b) a CDR-H3 of SEQ ID NO: 30, a CDR-H2 of SEQ ID NO: 37, a CDR-H1 of SEQ ID NO: 50, a CDR-L3 of SEQ ID NO: 63, a CDR-L2 of SEQ ID NO: 67, and a CDR-L1 of SEQ ID NO: 70; (c) a CDR-H3 of SEQ ID NO: 29, a CDR-H2 of SEQ ID NO: 38, a CDR-H1 of SEQ ID NO: 50, a CDR-L3 of SEQ ID NO: 63, a CDR-L2 of SEQ ID NO: 67, and a CDR-L1 of SEQ ID NO: 70; (d) a CDR-H3 of SEQ ID NO: 29, a CDR-H2 of SEQ ID NO: 36, a CDR-H1 of SEQ ID NO: 48, a CDR-L3 of SEQ ID NO: 63, a CDR-L2 of SEQ ID NO: 67, and a CDR-L1 of SEQ ID NO: 70; or (e) a CDR-H3 of SEQ ID NO: 29, a CDR-H2 of SEQ ID NO: 37, a CDR-H1 of SEQ ID NO: 50, a CDR-L3 of SEQ ID NO: 63, a CDR-L2 of SEQ ID NO: 67, and a CDR-L1 of SEQ ID NO: 70.

[0031] In some examples, an ABP of such second family comprises: (a) a V_H sequence of SEQ ID NO: 5 and a V_L sequence of SEQ ID NO: 25; (b) a V_H sequence of SEQ ID NO: 7 and a V_L sequence of SEQ ID NO: 25; (c) a V_H sequence of SEQ ID NO: 8 and a V_L sequence of SEQ ID NO: 25; (d) a V_H sequence of SEQ ID NO: 4 and a V_L sequence of SEQ ID NO: 25; or (e) a V_H sequence of SEQ ID NO: 6 and a V_L sequence of SEQ ID NO: 25.

[0032] In some examples, an ABP of such second family comprises: (a) (i) a heavy chain of SEQ ID NO: 82 and a light chain of SEQ ID NO: 81; or (ii) a heavy chain of SEQ ID NO: 83 and a light chain of SEQ ID NO: 81; (b) (i) a heavy chain of SEQ ID NO: 86 and a light chain of SEQ ID NO: 81; or (ii) a heavy chain of SEQ ID NO: 87 and a light chain of SEQ ID NO: 81; (c) (i) a heavy chain of SEQ ID NO: 88 and a light chain of SEQ ID NO: 81; or (ii) a heavy chain of SEQ ID NO: 89 and a light chain of SEQ ID NO: 81; (d) (i) a heavy chain of SEQ ID NO: 79 and a light chain of SEQ ID NO: 81; or (ii) a heavy chain of SEQ ID NO: 80 and a light chain of SEQ ID NO: 81; or (e) (i) a heavy chain of SEQ ID NO: 84 and a light chain of SEQ ID NO: 81; or (ii) a heavy chain of SEQ ID NO: 85 and a light chain of SEQ ID NO: 81.

[0033] In some examples, provided herein is a third family of ABPs, wherein an ABP of such family comprises (a) a CDR-H3 of SEQ ID NO: 33, a CDR-H2 of SEQ ID NO: 43, a CDR-H1 of SEQ ID NO: 60, a CDR-L3 of SEQ ID NO: 65, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72; (b) a CDR-H3 of SEQ ID NO: 34, a CDR-H2 of SEQ ID NO: 43, a CDR-H1 of SEQ ID NO: 60, a CDR-L3 of SEQ ID NO: 65, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72; (c) a CDR-H3 of SEQ ID NO: 33, a CDR-H2 of SEQ ID NO: 44, a CDR-H1 of SEQ ID NO: 59, a CDR-L3 of SEQ ID NO: 65, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72; (d) a CDR-H3 of SEQ ID NO: 33, a CDR-H2 of SEQ ID NO: 42, a CDR-H1 of SEQ ID NO: 58, a CDR-L3 of SEQ ID NO: 65, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72; (e) a CDR-H3 of SEQ ID NO: 33, a CDR-H2 of SEQ ID NO: 42, a CDR-H1 of SEQ ID NO: 59, a CDR-L3 of SEQ ID NO: 65, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72; or (f) a CDR-H3 of SEQ ID NO: 34, a CDR-H2 of SEQ ID NO: 44, a CDR-H1 of SEQ ID NO: 61, a CDR-L3 of SEQ ID NO: 65, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72.

[0034] In some examples, an ABP of such third family comprises: (a) a V_H sequence of SEQ ID NO: 18 and a V_L sequence of SEQ ID NO: 27; (b) a V_H sequence of SEQ ID NO: 19 and a V_L

sequence of SEQ ID NO: 27; (c) a V_H sequence of SEQ ID NO: 21 and a V_L sequence of SEQ ID NO: 27; (d) a V_H sequence of SEQ ID NO: 16 and a V_L sequence of SEQ ID NO: 27; (e) a V_H sequence of SEQ ID NO: 17 and a V_L sequence of SEQ ID NO: 27; or (f) a V_H sequence of SEQ ID NO: 20 and a V_L sequence of SEQ ID NO: 27.

[0035] In some examples, an ABP of such third family comprises: (a) (i) a heavy chain of SEQ ID NO: 110 and a light chain of SEQ ID NO: 107; or (ii) a heavy chain of SEQ ID NO: 111 and a light chain of SEQ ID NO: 107; (b) (i) a heavy chain of SEQ ID NO: 112 and a light chain of SEQ ID NO: 107; or (ii) a heavy chain of SEQ ID NO: 113 and a light chain of SEQ ID NO: 107; (c) (i) a heavy chain of SEQ ID NO: 116 and a light chain of SEQ ID NO: 107; or (ii) a heavy chain of SEQ ID NO: 117 and a light chain of SEQ ID NO: 107; (d) (i) a heavy chain of SEQ ID NO: 105 and a light chain of SEQ ID NO: 107; or (ii) a heavy chain of SEQ ID NO: 106 and a light chain of SEQ ID NO: 107; (e) (i) a heavy chain of SEQ ID NO: 108 and a light chain of SEQ ID NO: 107; or (ii) a heavy chain of SEQ ID NO: 109 and a light chain of SEQ ID NO: 107; or (f) (i) a heavy chain of SEQ ID NO: 114 and a light chain of SEQ ID NO: 107; or (ii) a heavy chain of SEQ ID NO: 115 and a light chain of SEQ ID NO: 107.

[0036] In some examples, provided herein is a fourth family of ABPs, wherein an ABP of such family comprises the following six CDR sequences: (a) a CDR-H3 of SEQ ID NO: 35, a CDR-H2 of SEQ ID NO: 46, a CDR-H1 of SEQ ID NO: 62, a CDR-L3 of SEQ ID NO: 66, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72; (b) a CDR-H3 of SEQ ID NO: 35, a CDR-H2 of SEQ ID NO: 47, a CDR-H1 of SEQ ID NO: 62, a CDR-L3 of SEQ ID NO: 66, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72; or (c) a CDR-H3 of SEQ ID NO: 35, a CDR-H2 of SEQ ID NO: 45, a CDR-H1 of SEQ ID NO: 62, a CDR-L3 of SEQ ID NO: 66, a CDR-L2 of SEQ ID NO: 69, and a CDR-L1 of SEQ ID NO: 72.

[0037] In some examples, an ABP of such fourth family comprises: (a) a V_H sequence of SEQ ID NO: 23 and a V_L sequence of SEQ ID NO: 28; (b) a V_H sequence of SEQ ID NO: 24 and a V_L sequence of SEQ ID NO: 28; or (c) a V_H sequence of SEQ ID NO: 22 and a V_L sequence of SEQ ID NO: 28.

[0038] In some examples, an ABP of such fourth family comprises: (a) (i) a heavy chain of SEQ ID NO: 121 and a light chain of SEQ ID NO: 120; or (ii) a heavy chain of SEQ ID NO: 122 and a light chain of SEQ ID NO: 120; (b) (i) a heavy chain of SEQ ID NO: 123 and a light chain of SEQ ID NO: 120; or (ii) a heavy chain of SEQ ID NO: 124 and a light chain of SEQ ID NO: 120; or (c) (i) a heavy chain of SEQ ID NO: 118 and a light chain of SEQ ID NO: 120; or (ii) a heavy chain of SEQ ID NO: 119 and a light chain of SEQ ID NO: 120.

[0039] In some embodiments, any of the foregoing ABPs: (a) competes for binding to TIGIT with an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure; (b) inhibits binding of CD155 to TIGIT; (c) inhibits binding of CD112 to TIGIT; (d) inhibits association of CD226 with TIGIT; (e)

activates an effector T cell or a natural killer (NK) cell; (f) decreases the number of regulatory T cells in a tissue or in circulation; (g) inhibits the suppression of an effector T cell by a regulatory T cell; (h) does not bind specifically to any of PVRL1, PVRL2, PVRL3, or PVRL4; or (i) is capable of any combination of (a)- (h).

[0040] In some embodiments, any of the foregoing ABPs: (a) specifically binds cynomolgus monkey TIGIT (cTIGIT; SEQ ID NO: 2); (b) binds murine TIGIT (mTIGIT; SEQ ID NO: 3) with an affinity lower (as indicated by higher K_D) than the affinity of the ABP for hTIGIT, or does not bind mTIGIT; or (c) is capable of any combination of (a) - (b).

[0041] In some embodiments, any of the foregoing ABPs: (a) specifically binds cTIGIT (SEQ ID NO: 2); (b) binds mTIGIT (SEQ ID NO: 3) with an affinity lower (as indicated by higher K_D) than the affinity of the ABP for hTIGIT and cTIGIT; and (c) inhibits binding of CD155 to TIGIT.

[0042] In some embodiments, provided herein is an ABP that competes for binding to TIGIT with any of the foregoing ABPs, wherein the ABP: (a) specifically binds cTIGIT (SEQ ID NO: 2); (b) binds mTIGIT (SEQ ID NO: 3) with an affinity lower (as indicated by higher K_D) than the affinity of the ABP for hTIGIT and cTIGIT; and (c) inhibits binding of CD155 to TIGIT.

[0043] In some embodiments, any of the foregoing ABPs comprises an antibody. In some embodiments, the antibody is a monoclonal antibody. In some embodiments, the antibody is selected from a human antibody, a humanized antibody or a chimeric antibody.

[0044] In some embodiments, any of the foregoing ABPs is multispecific. In some embodiments, the multispecific ABP binds more than one antigen (i.e., TIGIT and a different (non-TIGIT) antigen). In some embodiments, the multispecific ABP binds more than one epitope on a single antigen (i.e., two or more epitopes on TIGIT).

[0045] In some embodiments, any of the foregoing ABPs comprises an antibody fragment.

[0046] In some embodiments, any of the foregoing ABPs comprises an alternative scaffold.

[0047] In some embodiments, any of the foregoing ABPs comprises an immunoglobulin constant region. In some embodiments, the ABP comprises heavy chain constant region of a class selected from IgA, IgD, IgE, IgG, or IgM. In some embodiments, the ABP comprises a heavy chain constant region of the class IgG and a subclass selected from IgG4, IgG1, IgG2, or IgG3.

[0048] In some embodiments, any of the foregoing ABPs binds hTIGIT (SEQ ID NO: 1) with a K_D of less than about 10 nM, as measured by biolayer interferometry. In some embodiments, any of the foregoing ABPs binds hTIGIT (SEQ ID NO: 1) with a K_D of less than about 5 nM, as measured by biolayer interferometry. In some embodiments, any of the foregoing ABPs binds hTIGIT (SEQ ID NO: 1) with a K_D of less than about 2 nM, as measured by biolayer

interferometry. In some embodiments, any of the foregoing ABPs binds cTIGIT (SEQ ID NO: 2) with a K_D of less than about 100 nM, as measured by biolayer interferometry. In some embodiments, any of the foregoing ABPs binds cTIGIT (SEQ ID NO: 2) with a K_D of less than about 10 nM, as measured by biolayer interferometry. In some embodiments, any of the foregoing ABPs shows no significant binding to mTIGIT in a biolayer interferometry assay. In some embodiments, any of the foregoing ABPs binds to cell surface mTIGIT with a K_D of less than about 50 nM. In some embodiments, mTIGIT comprises SEQ ID NO: 3. In some embodiments, mTIGIT comprises SEQ ID NO: 138.

[0049] In some examples, any of the foregoing ABPs comprises a polypeptide sequence having a pyroglutamate (pE) residue at its N-terminus. In some examples, any of the foregoing ABPs comprises a V_H sequence in which an N-terminal Q is substituted with pE. In some examples, any of the foregoing ABPs comprises a V_L sequence in which an N-terminal E is substituted with pE. In some examples, any of the foregoing ABPs comprises a heavy chain sequence in which an N-terminal Q is substituted with pE. In some examples, any of the foregoing ABPs comprises a light chain sequence in which an N-terminal E is substituted with pE.

[0050] In some embodiments, provided herein are any of the foregoing ABPs for use as a medicament. In some embodiments, provided herein are any of the foregoing ABPs for use in the treatment of a cancer or viral infection. In some embodiments, provided herein are any of the foregoing ABPs for use in the treatment of a cancer, wherein the cancer is selected from a solid tumor and a hematological tumor. In some embodiments, provided herein are any of the foregoing ABPs for use as a medicament in the treatment of a disease or condition that was not responsive to a prior therapy. In some embodiments, the prior therapy was a therapy comprising an agent that inhibits the interaction between PD-1 and PD-L1.

[0051] In some embodiments, provided herein is an isolated polynucleotide encoding any of the foregoing ABPs, a V_H thereof, a V_L thereof, a light chain thereof, a heavy chain thereof or an antigen-binding portion thereof. In some embodiments, provided herein is a vector comprising the polynucleotide. In some embodiments, provided herein is a host cell comprising the polynucleotide and/or the vector. In some embodiments, provided herein is a method of producing any of the foregoing ABPs, comprising expressing the ABP in the host cell and isolating the expressed ABP.

[0052] In some embodiments, provided herein is a pharmaceutical composition comprising any of the foregoing ABPs. In some embodiments, the amount of the ABP in the pharmaceutical composition is sufficient to (a) increase effector T cell activity; (b) increase cytolytic T cell activity; (c) increase NK cell activity; (d) inhibit TIGIT-mediated signaling; (e) inhibit or block the binding of CD155 and or CD112 to TIGIT; or (f) any combination of (a) - (e), in a subject. In some embodiments, the any of the foregoing pharmaceutical compositions further comprises an antibody that antagonizes PD-1 or blocks PD-L1 from interacting with PD-1. In some embodiments, any of the foregoing pharmaceutical compositions is for use as a medicament.

In some embodiments, any of the foregoing pharmaceutical compositions is for use in the treatment of a cancer or a viral infection. In some embodiments, any of the foregoing pharmaceutical compositions is for use in the treatment of a cancer, wherein the cancer is selected from a solid tumor and a hematological tumor. In some embodiments, any of the foregoing pharmaceutical compositions is for use as a medicament in the treatment of a disease or condition that was not responsive to a prior therapy. In some embodiments, the prior therapy was a therapy comprising an agent that inhibits the interaction between PD-1 and PD-L1.

[0053] In some embodiments, the additional therapeutic agent for use in any of the foregoing uses of an ABP or uses of a pharmaceutical composition is an agent that inhibits the interaction between PD-1 and PD-L1, and wherein the agent that inhibits the interaction between PD-1 and PD-L1 is selected from an antibody, a peptidomimetic, a small molecule or a nucleic acid encoding such agent. In some embodiments, the agent that inhibits the interaction between PD-1 and PD-L1 is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, BMS-936559, sulfamonomethoxine 1, and sulfamethizole 2.

[0054] In some embodiments, the additional therapeutic agent for use in any of the foregoing uses of an ABP or uses of a pharmaceutical composition is an immunostimulatory agent selected from (a) an agent that blocks signaling of an inhibitory receptor of an immune cell or a ligand thereof or a nucleic acid encoding such agent; (b) an agonist to a stimulatory receptor of an immune cell or a nucleic acid encoding such agonist; (c) a cytokine or a nucleic acid encoding a cytokine; (d) an oncolytic virus or a nucleic acid encoding an oncolytic virus; (e) a T cell expressing a chimeric antigen receptor; (f) a bi- or multi-specific T cell directed antibody or a nucleic acid encoding such antibody; (g) an anti-TGF- β antibody or a nucleic acid encoding such antibody; (h) a TGF- β trap or a nucleic acid encoding such trap; (i) a vaccine to a cancer-associated antigen, including such antigen or a nucleic acid encoding such antigen and (j) combinations thereof. In some embodiments, the additional therapeutic agent is an agent that blocks signaling of an inhibitory receptor of an immune cell or a ligand thereof or a nucleic acid encoding such agent, and the inhibitory receptor or ligand thereof is selected from CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5, VISTA, LAIR1, CD160, 2B4, TGF-R, KIR, and combinations thereof. In some embodiments, the additional therapeutic agent is an agonist to a stimulatory receptor of an immune cell or a nucleic acid encoding such agonist, and the stimulatory receptor of an immune cell is selected from OX40, CD2, CD27, CD28, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, CD83 ligand, and combinations thereof. In some embodiments, the additional therapeutic agent is a cytokine or a nucleic acid encoding a cytokine selected from IL-2, IL-5, IL-7, IL-12, IL-15, IL-21, and combinations thereof. In some embodiments, the additional therapeutic agent is an oncolytic virus or a nucleic acid encoding an oncolytic virus selected from herpes simplex virus, vesicular stomatitis virus, adenovirus, Newcastle disease virus, vaccinia virus, a maraba virus, and combinations thereof.

[0055] In some embodiments, the additional therapeutic agent is formulated in the same

pharmaceutical composition as the ABP. In some embodiments, the additional therapeutic agent is formulated in a different pharmaceutical composition from the ABP. In some embodiments, the additional therapeutic agent is administered prior to administering the ABP. In some embodiments, the additional therapeutic agent is administered after administering the ABP. In some embodiments, the additional therapeutic agent is administered contemporaneously with the ABP.

[0056] In some embodiments, the subject is a subject that has been treated with an agent that inhibits the interaction between PD-1 and PD-L1 prior to performing such method.

[0057] In some embodiments, the disease or condition afflicting the subject was not responsive to a prior therapy. In some embodiments, the prior therapy was a therapy comprising an agent that inhibits the interaction between PD-1 and PD-L1.

[0058] In some embodiments, provided herein is a kit comprising any of the foregoing pharmaceutical compositions, and instructions for the use of such pharmaceutical composition. In some embodiments, the kit further comprises an additional pharmaceutical composition comprising an additional therapeutic agent and instructions for the use of such additional therapeutic agent. In some embodiments, the additional therapeutic agent is selected from an agent that inhibits the interaction between PD-1 and PD-L1, a chemotherapy, an immunostimulatory agent, radiation, and combinations thereof. In some embodiments, the additional therapeutic agent is an agent that inhibits the interaction between PD-1 and PD-L1, and wherein the agent inhibits the interaction between PD-1 and PD-L1 is selected from an antibody, a peptidomimetic, a small molecule or a nucleic acid encoding such agent. In some embodiments, the agent that inhibits the interaction between PD-1 and PD-L1 is selected from is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, BMS-936559, sulfamonomethoxine 1, and sulfamethizole 2. In some embodiments, the additional therapeutic agent is an immunostimulatory agent selected from (a) an agent that blocks signaling of an inhibitory receptor of an immune cell or a ligand thereof or a nucleic acid encoding such agent; (b) an agonist to a stimulatory receptor of an immune cell or a nucleic acid encoding such agonist; (c) a cytokine or a nucleic acid encoding a cytokine; (d) an oncolytic virus or a nucleic acid encoding an oncolytic virus; (e) a T cell expressing a chimeric antigen receptor; (f) a bi- or multi-specific T cell directed antibody or a nucleic acid encoding such antibody; (g) an anti-TGF- β antibody or a nucleic acid encoding such antibody; (h) a TGF- β trap or a nucleic acid encoding such trap; (i) a vaccine to a cancer-associated antigen, including such antigen or a nucleic acid encoding such antigen and (j) combinations thereof. In some embodiments, the additional therapeutic agent is an agent that blocks signaling of an inhibitory receptor of an immune cell or a ligand thereof or a nucleic acid encoding such agent, and the inhibitory receptor or ligand thereof is selected from CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5, VISTA, LAIR1, CD160, 2B4, TGF-R, KIR, and combinations thereof. In some embodiments, the additional therapeutic agent is an agonist to a stimulatory receptor of an immune cell or a nucleic acid encoding such agonist, and the stimulatory receptor of an immune cell is selected from OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD28, CD30, CD40,

BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, Nkp80, CD160, B7-H3, CD83 ligand, and combinations thereof. In some embodiments, the additional therapeutic agent is a cytokine or a nucleic acid encoding a cytokine selected from IL-2, IL-5, IL-7, IL-12, IL-15, IL-21, and combinations thereof. In some embodiments, the additional therapeutic agent is an oncolytic virus or a nucleic acid encoding an oncolytic virus selected from herpes simplex virus, vesicular stomatitis virus, adenovirus, Newcastle disease virus, vaccinia virus, a maraba virus, and combinations thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0059]

Figures 1A-1B show sequence alignments of various molecules described further in the Examples. **Figure 1A** shows sequence alignments of the TIGIT extracellular domains from human, cynomolgus monkey, mouse (SEQ ID NO: 3), and rat TIGIT reference sequences. **Figure 1B** shows an alignment of the human TIGIT and PVRL4 extracellular domains.

Figure 2 is an illustration of the similarity between the CD28-CTLA4 and CD226-TIGIT pathways and thus the utility of TIGIT as an immune checkpoint target. The CD226/TIGIT costimulation/coinhibition biology is analogous to that of CD28/CTLA4; TIGIT provides an inhibitory signal to T cells while CD226 provides a costimulation signal to T cells. TIGIT ligands CD155 and CD112 are widely expressed in tumors providing an immune suppressive environment.

Figure 3 shows a schematic diagram of the TIGIT Jurkat/anti-CD3 HT-1080 co-culture assay described in Example 7.

Figure 4A shows the EC₅₀ curves from exemplary experiments comparing the ability of MAB10 and an IgG4 isotype control to induce IL-2 production in engineered Jurkat cells expressing human TIGIT. **Figure 4B** shows the EC₅₀ curves from exemplary experiments comparing the ability of MAB10 and an IgG4 isotype control to induce IL-2 production in engineered Jurkat cells expressing cynomolgus monkey TIGIT.

Figure 5A-5C show TIGIT expression analysis on human CD4⁺ T cells by FACS. **Figure 5A** and **Figure 5B** show a series of graphs showing expression analysis of TIGIT, PVR and CD226 on unstimulated (**Figure 5A**) and stimulated (**Figure 5B**) CD4⁺ T cells. **Figure 5C** shows analysis of TIGIT expression on naive (positive for CD45RA, a marker of naive T cells, top right panel) and memory (positive for CD45RO, a marker of activated T cells, bottom right panel) CD4⁺ T cells.

Figures 6A-6O show the effect of treatment with MABs on sub-optimally stimulated PBMCs from human donors. MABs were tested for their ability to induce IFN- γ in PBMCs from human donors, including a control IgG4 antibody (**Figure 6A**), MAB2 (**Figure 6B**), MAB3 (**Figure 6C**), MAB4 (**Figure 6D**), MAB5 (**Figure 6E**), MAB10 (**Figure 6F**), MAB11 (**Figure 6G**), MAB12

(**Figure 6H**), MAB15 (**Figure 6I**), MAB16 (**Figure 6J**), and SEC1 (hamster anti-mouse TIGIT, **Figure 6K**). Treatment of the PBMCs from Donor 1 with MAB10 induces the upregulation of several pro-inflammatory cytokines, including tumor necrosis factor alpha (TNF, **Figure 6L**), lymphotoxin alpha (LT- α , **Figure 6M**), and interferon gamma (IFN- γ , **Figure 6N**). **Figure 6O** shows a graph illustrating the EC₅₀ of MAB10 in PBMCs from Donor 1, as measured by IFN- γ production.

Figures 7A-7E provide a series of graphs showing the effect of MAB10 on cytokine secretion in sub-optimally stimulated PBMCs from Donor 2, including IFN- γ (**Figure 7A**), TNF (**Figure 7B**), interleukin 6 (IL-6, **Figure 7C**), granulocyte macrophage colony-stimulating factor (GM-CSF, **Figure 7D**), and LT- α (**Figure 7E**). Data from cells treated with MAB10 are shown as black bars and data from cells treated with the IgG4 isotype control are shown as light gray bars. Antibody concentration for each bar is in $\mu\text{g/mL}$.

Figures 8A-8C provide a series of graphs showing that the antagonist anti-TIGIT antibody MAB10 increases IFN- γ in a CD4⁺ cell assay using cells obtained from three different donors. **Figure 8A** shows results obtained from CD4⁺ cells obtained from Donor 1. **Figure 8B** shows results obtained from CD4⁺ cells obtained from Donor 2. **Figure 8C** shows results obtained from CD4⁺ cells obtained from Donor 3. IFN- γ production in cells treated with either MAB10 (black bars) or the IgG4 isotype control (light gray bars) is shown in the left panel of each of Figures 8A-8C. The average EC₅₀ value for MAB10 in this assay was calculated by determining the concentration of MAB10 required to induce 50% of the increase in IFN- γ signal (plotted in the right panel of each of Figures 8A-8C).

Figure 9A shows the results of the assay in which a 1:1 ratio of MAB10 and pembrolizumab (anti-PD-1 antibody) were used in a mechanism-of-action based PD-1/TIGIT Combination Bioassay. Concentrations for each antibody were 25, 10, 4, 1.6, 0.64, 0.256, 0.1024, 0.04096, and 0.016384 $\mu\text{g/mL}$. An untargeted IgG4 was used as a control. As shown in Figure 9A, only the combination of MAB10 and pembrolizumab (EC₅₀ of 5.06 nM) blocked binding sufficiently to induce luciferase activity in the Jurkat cells. **Figure 9B** shows the results of the assay with a fixed dose (1 $\mu\text{g/mL}$) of pembrolizumab (or IgG4 control) and a varying dose of MAB10 (50, 20, 8, 3.2, 1.28, 0.512, 0.2048, 0.08192, and 0.032768 $\mu\text{g/mL}$). In Figures 9A and 9B, neither the IgG4 control alone or the IgG4 + MAB10 combination induced luciferase activity.

Figures 10A-10D are a series of graphs showing the effect of MAB10 on CMV-stimulated CD4⁺ T-cells from a human donor using intracellular cytokine staining. Incubation of CD4⁺ cells with MAB10 (black bars) increases the production of the effector cytokines in a dose-dependent manner, including TNF (**Figure 10A**), IL-2 (**Figure 10B**), and IFN- γ (**Figure 10C**) compared to cells incubated with the IgG4 control (white bars). **Figure 10D** shows that incubation with MAB10 increases the proportion of antigen-specific activated CD4⁺ T-cells. In Figure 10D, cells that were treated with 20 $\mu\text{g/mL}$ of the IgG4 control or MAB10 were analyzed by FACS for expression of CD3 (a marker of mature T-cells) and expression of TNF and IL-2. Statistical differences were calculated between MAB10 and IgG4 control groups (same concentration treatments) using Student's T test (*= $p < 0.05$, **= $p < 0.01$, ***= $p < 0.005$, ****= $p < 0.001$).

Figures 11A-11D are a series of graphs similar to Figure 10, but using CD8+ cells, and show the production of TNF (**Figure 11A**), perforin (**Figure 11B**), and granzyme B (**Figure 11C**) by such cells treated with MAB10 or the IgG4 control. **Figure 11D** shows that incubation with MAB10 also increases the proportion of antigen-specific activated CD8+ T-cells. Cells that were treated with 20 µg/ml of the IgG4 control or MAB10 were analyzed by FACS for expression of CD3 and expression of perforin and granzyme B. Statistical differences were calculated between MAB10 and IgG4 control groups (same concentration treatments) using Student's T test (*=p<0.05, **=p<0.01, ***=p<0.005, ****=p<0.001).

Figures 12A-12D show the results of treatment of cells from the same donor, wherein blockade by MAB10 amplifies CMV-specific CD8+ T-cell responses. Cells were incubated with a range of concentrations of MAB10 (black bars) or the IgG4 control (white bars), and the percentage of double positive population perforin + granzyme B+ (**Figure 12A**) or IFN-γ + TNF+ (**Figure 12C**) was analyzed. Statistical differences were calculated between MAB10 and IgG4 control groups (same concentration treatments) using Student's T test (*=p<0.05, **=p<0.01, ***=p<0.005, ****=p<0.001). **Figure 12B** (perforin + granzyme B+ analysis) and **Figure 12D** (IFN-γ + TNF+ analysis) show the proportion of double positive cells comparing cells treated with 20 µg/ml of the control antibody (left panels) or 20 µg/ml of MAB10 (right panels).

Figure 13 is a graph showing the combinatorial effect of MAB10 and the PD-1 antibody pembrolizumab on cells from the same donor as used for Figures 10-12. Cells were stimulated with CMV lysates and treated with 2 µg/ml pembrolizumab or control IgG4, and 10, 20, or 40 µg/ml control antibody or MAB10, and production of TNF was measured. Four groups of cells were tested, and treated with IgG4 control (white bars, left most group), a constant amount of IgG4 control and a titration of MAB10 (dark gray bars, second group from left), a constant amount of pembrolizumab and a titration of IgG4 control (light gray bars, second group from right), or a constant amount of pembrolizumab and a titration of MAB10 (black bars, right hand group).

Figures 14A-14C are a series of graphs showing the effect of MAB10 + pembrolizumab treatment on cells from three different donors. Cells were stimulated with 0.1 µg/ml of CMV lysate and treated with 20 µg/ml of MAB10 or 20 µg/ml of control IgG4 antibody and a titration of pembrolizumab, then the production of TNF was measured. **Figure 14A** shows the results of the assay using cells from Donor 1; **Figure 14B** shows the results of the assay using cells from Donor 2; **Figure 14C** shows the results of the assay using cells from Donor 3. The addition of MAB10 (black bars) alone or in combination with increasing concentrations of pembrolizumab results in a greater production of TNF compared to control antibody + pembrolizumab group (white bars). Additionally, MAB10 (black bars) in combination with pembrolizumab also resulted in increased activation compared to MAB10 alone. Statistic differences were calculated between MAB10 alone and MAB10+pembro groups using Student T test analysis (*=p<0.05, **=p<0.01, ***=p<0.005, ****=p<0.001)

DETAILED DESCRIPTION

1. Definitions

[0060] Unless otherwise defined, all terms of art, notations and other scientific terminology used herein are intended to have the meanings commonly understood by those of skill in the art to which this invention pertains. In some cases, terms with commonly understood meanings are defined herein for clarity and/or for ready reference, and the inclusion of such definitions herein should not necessarily be construed to represent a difference over what is generally understood in the art. The techniques and procedures described or referenced herein are generally well understood and commonly employed using conventional methodologies by those skilled in the art, such as, for example, the widely utilized molecular cloning methodologies described in Sambrook et al., *Molecular Cloning: A Laboratory Manual* 4th ed. (2012) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. As appropriate, procedures involving the use of commercially available kits and reagents are generally carried out in accordance with manufacturer-defined protocols and conditions unless otherwise noted.

[0061] As used herein, the singular forms "a," "an," and "the" include the plural referents unless the context clearly indicates otherwise. The terms "include," "such as," and the like are intended to convey inclusion without limitation, unless otherwise specifically indicated.

[0062] As used herein, the term "comprising" also specifically includes embodiments "consisting of" and "consisting essentially of" the recited elements, unless specifically indicated otherwise. For example, a multispecific ABP "comprising a diabody" includes a multispecific ABP "consisting of a diabody" and a multispecific ABP "consisting essentially of a diabody."

[0063] The term "about" indicates and encompasses an indicated value and a range above and below that value. In certain embodiments, the term "about" indicates the designated value $\pm 10\%$, $\pm 5\%$, or $\pm 1\%$. In certain embodiments, where applicable, the term "about" indicates the designated value(s) $\pm$ one standard deviation of that value(s).

[0064] The terms "TIGIT," "TIGIT protein," and "TIGIT antigen" are used interchangeably herein to refer to human TIGIT, or any variants (e.g., splice variants and allelic variants), isoforms, and species homologs of human TIGIT that are naturally expressed by cells, or that are expressed by cells transfected with a *tigit* gene. In some aspects, the TIGIT protein is a TIGIT protein naturally expressed by a primate (e.g., a monkey or a human), a rodent (e.g., a mouse or a rat), a dog, a camel, a cat, a cow, a goat, a horse, or a sheep. In some aspects, the TIGIT protein is human TIGIT (hTIGIT; SEQ ID NO:1). Without being bound by theory, it is believed that positions 1-21 of SEQ ID NO:1 encode a signal peptide; positions 22-141 of SEQ ID NO:1 encode the extracellular domain of the mature TIGIT protein; positions 142-162 of SEQ ID NO:1 encode a transmembrane domain; and positions 163-244 of SEQ ID NO:1

encode a cytoplasmic domain. See UniProt KB - Q495A1 (TIGIT_HUMAN), at www.uniprot.org/uniprot/Q495A1, accessed September 28, 2015. In some aspects, the TIGIT protein is a cynomolgus monkey TIGIT (cTIGIT; SEQ ID NO:2). In some aspects, the TIGIT protein is a murine TIGIT (mTIGIT) having the sequence provided in SEQ ID NO:3. In some aspects, the TIGIT protein is a murine TIGIT (mTIGIT) having the sequence provided in SEQ ID NO: 138. As used herein, if a SEQ ID NO is not specified, the terms "mTIGIT," "murine TIGIT" and "mouse TIGIT" mean SEQ ID NO: 3 and/or SEQ ID NO: 138. In some aspects, the TIGIT protein is a full-length or unprocessed TIGIT protein. In some aspects, the TIGIT protein is a truncated or processed TIGIT protein produced by post-translational modification. TIGIT is also known by a variety of synonyms, including WUCAM, VSIG9, and Vstm3.

[0065] The term "immunoglobulin" refers to a class of structurally related proteins generally comprising two pairs of polypeptide chains: one pair of light (L) chains and one pair of heavy (H) chains. In an "intact immunoglobulin," all four of these chains are interconnected by disulfide bonds. The structure of immunoglobulins has been well characterized. See, e.g., Paul, *Fundamental Immunology* 7th ed., Ch. 5 (2013) Lippincott Williams & Wilkins, Philadelphia, PA. Briefly, each heavy chain typically comprises a heavy chain variable region (V_H) and a heavy chain constant region (C_H). The heavy chain constant region typically comprises three domains, abbreviated C_{H1} , C_{H2} , and C_{H3} . Each light chain typically comprises a light chain variable region (V_L) and a light chain constant region. The light chain constant region typically comprises one domain, abbreviated C_L .

[0066] The term "antigen-binding protein" (ABP) refers to a protein comprising one or more antigen-binding domains that specifically bind to an antigen or epitope. In some embodiments, the antigen-binding domain binds the antigen or epitope with specificity and affinity similar to that of naturally occurring antibodies. In some embodiments, the ABP comprises an antibody. In some embodiments, the ABP consists of an antibody. In some embodiments, the ABP consists essentially of an antibody. In some embodiments, the ABP comprises an alternative scaffold. In some embodiments, the ABP consists of an alternative scaffold. In some embodiments, the ABP consists essentially of an alternative scaffold. In some embodiments, the ABP comprises an antibody fragment. In some embodiments, the ABP consists of an antibody fragment. In some embodiments, the ABP consists essentially of an antibody fragment. A "TIGIT ABP," "anti-TIGIT ABP," or "TIGIT-specific ABP" is an ABP, as provided herein, which specifically binds to the antigen TIGIT. In some embodiments, the ABP binds the extracellular domain of TIGIT. In certain embodiments, a TIGIT ABP provided herein binds to an epitope of TIGIT that is conserved between or among TIGIT proteins from different species.

[0067] The term "antibody" is used herein in its broadest sense and includes certain types of immunoglobulin molecules comprising one or more antigen-binding domains that specifically bind to an antigen or epitope. An antibody specifically includes intact antibodies (e.g., intact immunoglobulins), antibody fragments, and multi-specific antibodies. An antibody is one type of ABP.

[0068] The term "alternative scaffold" refers to a molecule in which one or more regions may be diversified to produce one or more antigen-binding domains that specifically bind to an antigen or epitope. In some embodiments, the antigen-binding domain binds the antigen or epitope with specificity and affinity similar to that of an antibody. Exemplary alternative scaffolds include those derived from fibronectin (e.g., Adnectins™), the β -sandwich (e.g., iMab), lipocalin (e.g., Anticalins®), EETI-II/AGRP, BPTI/LACI-D1/ITI-D2 (e.g., Kunitz domains), thioredoxin peptide aptamers, protein A (e.g., Affibody®), ankyrin repeats (e.g., DARPin), gamma-B-crystallin/ubiquitin (e.g., Affilins), CTLD₃ (e.g., Tetranectins), Fynomers, and (LDLR-A module) (e.g., Avimers). Additional information on alternative scaffolds is provided in Binz et al., Nat. Biotechnol., 2005 23:1257-1268; Skerra, Current Opin. in Biotech., 2007 18:295-304; and Silacci et al., J. Biol. Chem., 2014, 289:14392-14398. An alternative scaffold is one type of ABP.

[0069] The term "antigen-binding domain" means the portion of an ABP that is capable of specifically binding to an antigen or epitope. One example of an antigen-binding domain is an antigen-binding domain formed by a V_H-V_L dimer of an antibody. Another example of an antigen-binding domain is an antigen-binding domain formed by diversification of certain loops from the tenth fibronectin type III domain of an Adnectin.

[0070] The terms "full length antibody," "intact antibody," and "whole antibody" are used herein interchangeably to refer to an antibody having a structure substantially similar to a naturally occurring antibody structure and having heavy chains that comprise an Fc region. For example, when used to refer to an IgG molecule, a "full length antibody" is an antibody that comprises two heavy chains and two light chains.

[0071] The term "Fc region" means the C-terminal region of an immunoglobulin heavy chain that, in naturally occurring antibodies, interacts with Fc receptors and certain proteins of the complement system. The structures of the Fc regions of various immunoglobulins, and the glycosylation sites contained therein, are known in the art. See Schroeder and Cavacini, J. Allergy Clin. Immunol., 2010, 125:S41-52. The Fc region may be a naturally occurring Fc region, or an Fc region modified as described in the art or elsewhere in this disclosure.

[0072] The V_H and V_L regions may be further subdivided into regions of hypervariability ("hypervariable regions (HVRs);" also called "complementarity determining regions" (CDRs)) interspersed with regions that are more conserved. The more conserved regions are called framework regions (FRs). Each V_H and V_L generally comprises three CDRs and four FRs, arranged in the following order (from N-terminus to C-terminus): FR1 - CDR1 - FR2 - CDR2 - FR3 - CDR3 - FR4. The CDRs are involved in antigen binding, and influence antigen specificity and binding affinity of the antibody. See Kabat et al., Sequences of Proteins of Immunological Interest 5th ed. (1991) Public Health Service, National Institutes of Health, Bethesda, MD.

[0073] The light chain from any vertebrate species can be assigned to one of two types, called kappa (κ) and lambda (λ), based on the sequence of its constant domain.

[0074] The heavy chain from any vertebrate species can be assigned to one of five different classes (or isotypes): IgA, IgD, IgE, IgG, and IgM. These classes are also designated α , δ , ϵ , γ , and μ , respectively. The IgG and IgA classes are further divided into subclasses on the basis of differences in sequence and function. Humans express the following subclasses: IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

[0075] The amino acid sequence boundaries of a CDR can be determined by one of skill in the art using any of a number of known numbering schemes, including those described by Kabat et al., *supra* ("Kabat" numbering scheme); Al-Lazikani et al., 1997, J. Mol. Biol., 273:927-948 ("Chothia" numbering scheme); MacCallum et al., 1996, J. Mol. Biol. 262:732-745 ("Contact" numbering scheme); Lefranc et al., Dev. Comp. Immunol., 2003, 27:55-77 ("IMGT" numbering scheme); and Honegge and Plückthun, J. Mol. Biol., 2001, 309:657-70 ("Aho" numbering scheme).

[0076] Table 1 provides the positions of CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, and CDR-H3 as identified by the Kabat and Chothia schemes. For CDR-H1, residue numbering is provided using both the Kabat and Chothia numbering schemes.

[0077] CDRs may be assigned, for example, using antibody numbering software, such as Abnum, available at www.bioinf.org.uk/abs/abnum/, and described in Abhinandan and Martin, Immunology, 2008, 45:3832-3839.

Table 1. Residues in CDRs according to Kabat and Chothia numbering schemes.

CDR	Kabat	Chothia
L1	L24-L34	L24-L34
L2	L50-L56	L50-L56
L3	L89-L97	L89-L97
H1 (Kabat Numbering)	H31-H35B	H26-H32 or H34*
H1 (Chothia Numbering)	H31-H35	H26-H32
H2	H50-H65	H52-H56
H3	H95-H102	H95-H102
* The C-terminus of CDR-H1, when numbered using the Kabat numbering convention, varies between H32 and H34, depending on the length of the CDR.		

[0078] The "EU numbering scheme" is generally used when referring to a residue in an antibody heavy chain constant region (e.g., as reported in Kabat et al., *supra*). Unless stated otherwise, the EU numbering scheme is used to refer to residues in antibody heavy chain constant regions described herein.

[0079] An "antibody fragment" comprises a portion of an intact antibody, such as the antigen-binding or variable region of an intact antibody. Antibody fragments include, for example, Fv

fragments, Fab fragments, $F(ab')_2$ fragments, Fab' fragments, scFv (sFv) fragments, and scFv-Fc fragments.

[0080] "Fv" fragments comprise a non-covalently-linked dimer of one heavy chain variable domain and one light chain variable domain.

[0081] "Fab" fragments comprise, in addition to the heavy and light chain variable domains, the constant domain of the light chain and the first constant domain (C_{H1}) of the heavy chain. Fab fragments may be generated, for example, by recombinant methods or by papain digestion of a full-length antibody.

[0082] " $F(ab')_2$ " fragments contain two Fab' fragments joined, near the hinge region, by disulfide bonds. $F(ab')_2$ fragments may be generated, for example, by recombinant methods or by pepsin digestion of an intact antibody. The $F(ab')$ fragments can be dissociated, for example, by treatment with β -mercaptoethanol.

[0083] "Single-chain Fv" or "sFv" or "scFv" antibody fragments comprise a V_H domain and a V_L domain in a single polypeptide chain. The V_H and V_L are generally linked by a peptide linker. See Plückthun A. (1994). Any suitable linker may be used. In some embodiments, the linker is a $(GGGGS)_n$ (SEQ ID NO: 127). In some embodiments, $n = 1, 2, 3, 4, 5$, or 6 . See Antibodies from *Escherichia coli*. In Rosenberg M. & Moore G.P. (Eds.), The Pharmacology of Monoclonal Antibodies vol. 113 (pp. 269-315). Springer-Verlag, New York,.

[0084] "scFv-Fc" fragments comprise an scFv attached to an Fc domain. For example, an Fc domain may be attached to the C-terminal of the scFv. The Fc domain may follow the V_H or V_L , depending on the orientation of the variable domains in the scFv (i.e., V_H - V_L or V_L - V_H). Any suitable Fc domain known in the art or described herein may be used. In some cases, the Fc domain comprises an IgG4 Fc domain.

[0085] The term "single domain antibody" refers to a molecule in which one variable domain of an antibody specifically binds to an antigen without the presence of the other variable domain. Single domain antibodies, and fragments thereof, are described in Arabi Ghahroudi et al., FEBS Letters, 1998, 414:521-526 and Muyldermans et al., Trends in Biochem. Sci., 2001, 26:230-245. Single domain antibodies are also known as sdAbs or nanobodies.

[0086] A "multispecific ABP" is an ABP that comprises two or more different antigen-binding domains that collectively specifically bind two or more different epitopes. The two or more different epitopes may be epitopes on the same antigen (e.g., a single TIGIT molecule expressed by a cell) or on different antigens (e.g., different TIGIT molecules expressed by the same cell, or a TIGIT molecule and a non-TIGIT molecule). In some aspects, a multi-specific ABP binds two different epitopes (i.e., a "bispecific ABP"). In some aspects, a multi-specific ABP binds three different epitopes (i.e., a "trispecific ABP"). In some aspects, a multi-specific ABP binds four different epitopes (i.e., a "quadspecific ABP"). In some aspects, a multi-specific

ABP binds five different epitopes (i.e., a "quintspecific ABP"). In some aspects, a multi-specific ABP binds 6, 7, 8, or more different epitopes. Each binding specificity may be present in any suitable valency. Examples of multispecific ABPs are provided elsewhere in this disclosure.

[0087] A "monospecific ABP" is an ABP that comprises one or more binding sites that specifically bind to a single epitope. An example of a monospecific ABP is a naturally occurring IgG molecule which, while divalent (i.e., having two antigen-binding domains), recognizes the same epitope at each of the two antigen-binding domains. The binding specificity may be present in any suitable valency.

[0088] The term "monoclonal antibody" refers to an antibody from a population of substantially homogeneous antibodies. A population of substantially homogeneous antibodies comprises antibodies that are substantially similar and that bind the same epitope(s), except for variants that may normally arise during production of the monoclonal antibody. Such variants are generally present in only minor amounts. A monoclonal antibody is typically obtained by a process that includes the selection of a single antibody from a plurality of antibodies. For example, the selection process can be the selection of a unique clone from a plurality of clones, such as a pool of hybridoma clones, phage clones, yeast clones, bacterial clones, or other recombinant DNA clones. The selected antibody can be further altered, for example, to improve affinity for the target ("affinity maturation"), to humanize the antibody, to improve its production in cell culture, and/or to reduce its immunogenicity in a subject.

[0089] The term "chimeric antibody" refers to an antibody in which a portion of the heavy and/or light chain is derived from a particular source or species, while the remainder of the heavy and/or light chain is derived from a different source or species.

[0090] "Humanized" forms of non-human antibodies are chimeric antibodies that contain minimal sequence derived from the non-human antibody. A humanized antibody is generally a human antibody (recipient antibody) in which residues from one or more CDRs are replaced by residues from one or more CDRs of a non-human antibody (donor antibody). The donor antibody can be any suitable non-human antibody, such as a mouse, rat, rabbit, chicken, or non-human primate antibody having a desired specificity, affinity, or biological effect. In some instances, selected framework region residues of the recipient antibody are replaced by the corresponding framework region residues from the donor antibody. Humanized antibodies may also comprise residues that are not found in either the recipient antibody or the donor antibody. Such modifications may be made to further refine antibody function. For further details, see Jones et al., *Nature*, 1986, 321:522-525; Riechmann et al., *Nature*, 1988, 332:323-329; and Presta, *Curr. Op. Struct. Biol.*, 1992, 2:593-596.

[0091] A "human antibody" is one which possesses an amino acid sequence corresponding to that of an antibody produced by a human or a human cell, or derived from a non-human source that utilizes a human antibody repertoire or human antibody-encoding sequences (e.g., obtained from human sources or designed *de novo*). Human antibodies specifically exclude humanized antibodies.

[0092] An "isolated ABP" or "isolated nucleic acid" is an ABP or nucleic acid that has been separated and/or recovered from a component of its natural environment. Components of the natural environment may include enzymes, hormones, and other proteinaceous or nonproteinaceous materials. In some embodiments, an isolated ABP is purified to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence, for example by use of a spinning cup sequenator. In some embodiments, an isolated ABP is purified to homogeneity by gel electrophoresis (e.g., SDS-PAGE) under reducing or nonreducing conditions, with detection by Coomassie blue or silver stain. In some embodiments, an isolated ABP may include an ABP *in situ* within recombinant cells, since at least one component of the ABP's natural environment is not present. In some aspects, an isolated ABP or isolated nucleic acid is prepared by at least one purification step. In some embodiments, an isolated ABP or isolated nucleic acid is purified to at least 80%, 85%, 90%, 95%, or 99% by weight. In some embodiments, an isolated ABP or isolated nucleic acid is purified to at least 80%, 85%, 90%, 95%, or 99% by volume. In some embodiments, an isolated ABP or isolated nucleic acid is provided as a solution comprising at least 85%, 90%, 95%, 98%, 99% to 100% ABP or nucleic acid by weight. In some embodiments, an isolated ABP or isolated nucleic acid is provided as a solution comprising at least 85%, 90%, 95%, 98%, 99% to 100% ABP or nucleic acid by volume.

[0093] "Affinity" refers to the strength of the sum total of non-covalent interactions between a single binding site of a molecule (e.g., an ABP) and its binding partner (e.g., an antigen or epitope). Unless indicated otherwise, as used herein, "affinity" refers to intrinsic binding affinity, which reflects a 1:1 interaction between members of a binding pair (e.g., ABP and antigen or epitope). The affinity of a molecule X for its partner Y can be represented by the dissociation equilibrium constant (K_D). The kinetic components that contribute to the dissociation equilibrium constant are described in more detail below. Affinity can be measured by common methods known in the art, including those described herein, such as surface plasmon resonance (SPR) technology (e.g., BIACORE®) or biolayer interferometry (e.g., FORTEBIO®).

[0094] With regard to the binding of an ABP to a target molecule, the terms "bind," "specific binding," "specifically binds to," "specific for," "selectively binds," and "selective for" a particular antigen (e.g., a polypeptide target) or an epitope on a particular antigen mean binding that is measurably different from a non-specific or non-selective interaction (e.g., with a non-target molecule). Specific binding can be measured, for example, by measuring binding to a target molecule and comparing it to binding to a non-target molecule. Specific binding can also be determined by competition with a control molecule that mimics the epitope recognized on the target molecule. In that case, specific binding is indicated if the binding of the ABP to the target molecule is competitively inhibited by the control molecule. In some aspects, the affinity of a TIGIT ABP for a non-target molecule is less than about 50% of the affinity for TIGIT. In some aspects, the affinity of a TIGIT ABP for a non-target molecule is less than about 40% of the affinity for TIGIT. In some aspects, the affinity of a TIGIT ABP for a non-target molecule is less than about 30% of the affinity for TIGIT. In some aspects, the affinity of a TIGIT ABP for a non-target molecule is less than about 20% of the affinity for TIGIT. In some aspects, the affinity of

a TIGIT ABP for a non-target molecule is less than about 10% of the affinity for TIGIT. In some aspects, the affinity of a TIGIT ABP for a non-target molecule is less than about 1% of the affinity for TIGIT. In some aspects, the affinity of a TIGIT ABP for a non-target molecule is less than about 0.1% of the affinity for TIGIT.

[0095] The term " k_d " (sec^{-1}), as used herein, refers to the dissociation rate constant of a particular ABP- antigen interaction. This value is also referred to as the k_{off} value.

[0096] The term " k_a " ($\text{M}^{-1} \times \text{sec}^{-1}$), as used herein, refers to the association rate constant of a particular ABP-antigen interaction. This value is also referred to as the k_{on} value.

[0097] The term " K_D " (M), as used herein, refers to the dissociation equilibrium constant of a particular ABP-antigen interaction. $K_D = k_d/k_a$. In some embodiments, the affinity of an ABP is described in terms of the K_D for an interaction between such ABP and its antigen. For clarity, as known in the art, a smaller K_D value indicates a higher affinity interaction, while a larger K_D value indicates a lower affinity interaction.

[0098] The term " K_A " (M^{-1}), as used herein, refers to the association equilibrium constant of a particular ABP-antigen interaction. $K_A = k_a/k_d$.

[0099] An "affinity matured" ABP is an ABP with one or more alterations (e.g., in one or more CDRs or FRs) relative to a parent ABP (i.e., an ABP from which the altered ABP is derived or designed) that result in an improvement in the affinity of the ABP for its antigen, compared to the parent ABP which does not possess the alteration(s). In some embodiments, an affinity matured ABP has nanomolar or picomolar affinity for the target antigen. Affinity matured ABPs may be produced using a variety of methods known in the art. For example, Marks et al. (Bio/Technology, 1992, 10:779-783) describes affinity maturation by V_H and V_L domain shuffling. Random mutagenesis of CDR and/or framework residues is described by, for example, Barbas et al. (Proc. Nat. Acad. Sci. U.S.A., 1994, 91:3809-3813); Schier et al., Gene, 1995, 169:147-155; Yelton et al., J. Immunol., 1995, 155:1994-2004; Jackson et al., J. Immunol., 1995, 154:3310-3319; and Hawkins et al, J. Mol. Biol., 1992, 226:889-896.

[0100] An "immunoconjugate" is an ABP conjugated to one or more heterologous molecule(s), such as a therapeutic or diagnostic agent.

[0101] "Effector functions" refer to those biological activities mediated by the Fc region of an antibody, which activities may vary depending on the antibody isotype. Examples of antibody effector functions include C1q binding to activate complement dependent cytotoxicity (CDC), Fc receptor binding to activate antibody-dependent cellular cytotoxicity (ADCC), and antibody dependent cellular phagocytosis (ADCP).

[0102] When used herein in the context of two or more ABPs, the term "competes with" or

"cross-competes with" indicates that the two or more ABPs compete for binding to an antigen (e.g., TIGIT). In one exemplary assay, TIGIT is coated on a surface and contacted with a first TIGIT ABP, after which a second TIGIT ABP is added. In another exemplary assay, a first TIGIT ABP is coated on a surface and contacted with TIGIT, and then a second TIGIT ABP is added. If the presence of the first TIGIT ABP reduces binding of the second TIGIT ABP, in either assay, then the ABPs compete with each other. The term "competes with" also includes combinations of ABPs where one ABP reduces binding of another ABP, but where no competition is observed when the ABPs are added in the reverse order. However, in some embodiments, the first and second ABPs inhibit binding of each other, regardless of the order in which they are added. In some embodiments, one ABP reduces binding of another ABP to its antigen by at least 25%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95%. A skilled artisan can select the concentrations of the antibodies used in the competition assays based on the affinities of the ABPs for TIGIT and the valency of the ABPs. The assays described in this definition are illustrative, and a skilled artisan can utilize any suitable assay to determine if antibodies compete with each other. Suitable assays are described, for example, in Cox et al., "Immunoassay Methods," in Assay Guidance Manual [Internet], Updated December 24, 2014 (www.ncbi.nlm.nih.gov/books/NBK92434/; accessed September 29, 2015); Silman et al., Cytometry, 2001, 44:30-37; and Finco et al., J. Pharm. Biomed. Anal., 2011, 54:351-358.

[0103] The term "epitope" means a portion of an antigen that specifically binds to an ABP. Epitopes frequently consist of surface-accessible amino acid residues and/or sugar side chains and may have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and non-conformational epitopes are distinguished in that the binding to the former but not the latter may be lost in the presence of denaturing solvents. An epitope may comprise amino acid residues that are directly involved in the binding, and other amino acid residues, which are not directly involved in the binding. The epitope to which an ABP binds can be determined using known techniques for epitope determination such as, for example, testing for ABP binding to TIGIT variants with different point-mutations, or to chimeric TIGIT variants.

[0104] Percent "identity" between a polypeptide sequence and a reference sequence, is defined as the percentage of amino acid residues in the polypeptide sequence that are identical to the amino acid residues in the reference sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN, MEGALIGN (DNASTAR), CLUSTALW, CLUSTAL OMEGA, or MUSCLE software. Those skilled in the art can determine appropriate parameters for aligning sequences, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared.

[0105] A "conservative substitution" or a "conservative amino acid substitution," refers to the substitution an amino acid with a chemically or functionally similar amino acid. Conservative

substitution tables providing similar amino acids are well known in the art. By way of example, the groups of amino acids provided in Tables 2-4 are, in some examples, considered conservative substitutions for one another.

Table 2. Selected groups of amino acids that are considered conservative substitutions for one another, in certain examples.

<i>Acidic Residues</i>	D and E
<i>Basic Residues</i>	K, R, and H
<i>Hydrophilic Uncharged Residues</i>	S, T, N, and Q
<i>Aliphatic Uncharged Residues</i>	G, A, V, L, and I
<i>Non-polar Uncharged Residues</i>	C, M, and P
<i>Aromatic Residues</i>	F, Y, and W

Table 3. Additional selected groups of amino acids that are considered conservative substitutions for one another, in certain examples.

<i>Group 1</i>	A, S, and T
<i>Group 2</i>	D and E
<i>Group 3</i>	N and Q
<i>Group 4</i>	R and K
<i>Group 5</i>	I, L, and M
<i>Group 6</i>	F, Y, and W

Table 4. Further selected groups of amino acids that are considered conservative substitutions for one another, in certain examples.

<i>Group A</i>	A and G
<i>Group B</i>	D and E
<i>Group C</i>	N and Q
<i>Group D</i>	R, K, and H
<i>Group E</i>	K, L, M, V
<i>Group F</i>	F, Y, and W
<i>Group G</i>	S and T
<i>Group H</i>	C and M

[0106] Additional conservative substitutions may be found, for example, in Creighton, *Proteins: Structures and Molecular Properties* 2nd ed. (1993) W. H. Freeman & Co., New York, NY. An ABP generated by making one or more conservative substitutions of amino acid residues in a parent ABP is referred to as a "conservatively modified variant."

[0107] The term "amino acid" refers to the twenty common naturally occurring amino acids. Naturally occurring amino acids include alanine (Ala; A), arginine (Arg; R), asparagine (Asn; N), aspartic acid (Asp; D), cysteine (Cys; C), glutamic acid (Glu; E), glutamine (Gln; Q), Glycine

(Gly; G); histidine (His; H), isoleucine (Ile; I), leucine (Leu; L), lysine (Lys; K), methionine (Met; M), phenylalanine (Phe; F), proline (Pro; P), serine (Ser; S), threonine (Thr; T), tryptophan (Trp; W), tyrosine (Tyr; Y), and valine (Val; V).

[0108] The term "vector," as used herein, refers to a nucleic acid molecule capable of propagating another nucleic acid to which it is linked. The term includes the vector as a self-replicating nucleic acid structure as well as the vector incorporated into the genome of a host cell into which it has been introduced. Certain vectors are capable of directing the expression of nucleic acids to which they are operatively linked. Such vectors are referred to herein as "expression vectors."

[0109] The terms "host cell," "host cell line," and "host cell culture" are used interchangeably and refer to cells into which an exogenous nucleic acid has been introduced, and the progeny of such cells. Host cells include "transformants" (or "transformed cells") and "transfectants" (or "transfected cells"), which each include the primary transformed or transfected cell and progeny derived therefrom. Such progeny may not be completely identical in nucleic acid content to a parent cell, and may contain mutations.

[0110] The term "treating" (and variations thereof such as "treat" or "treatment") refers to clinical intervention in an attempt to alter the natural course of a disease or condition in a subject in need thereof. Treatment can be performed both for prophylaxis and during the course of clinical pathology. Desirable effects of treatment include preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, preventing metastasis, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis.

[0111] As used herein, the term "therapeutically effective amount" or "effective amount" refers to an amount of an ABP or pharmaceutical composition provided herein that, when administered to a subject, is effective to treat a disease or disorder.

[0112] As used herein, the term "subject" means a mammalian subject. Exemplary subjects include humans, monkeys, dogs, cats, mice, rats, cows, horses, camels, goats, rabbits, and sheep. In certain embodiments, the subject is a human. In some embodiments the subject has a disease or condition that can be treated with an ABP provided herein. In some aspects, the disease or condition is a cancer. In some aspects, the disease or condition is a viral infection.

[0113] The term "package insert" is used to refer to instructions customarily included in commercial packages of therapeutic or diagnostic products (e.g., kits) that contain information about the indications, usage, dosage, administration, combination therapy, contraindications and/or warnings concerning the use of such therapeutic or diagnostic products.

[0114] The term "cytotoxic agent," as used herein, refers to a substance that inhibits or prevents a cellular function and/or causes cell death or destruction.

[0115] A "chemotherapeutic agent" refers to a chemical compound useful in the treatment of cancer. Chemotherapeutic agents include "anti-hormonal agents" or "endocrine therapeutics" which act to regulate, reduce, block, or inhibit the effects of hormones that can promote the growth of cancer.

[0116] The term "cytostatic agent" refers to a compound or composition which arrests growth of a cell either *in vitro* or *in vivo*. In some embodiments, a cytostatic agent is an agent that reduces the percentage of cells in S phase. In some embodiments, a cytostatic agent reduces the percentage of cells in S phase by at least about 20%, at least about 40%, at least about 60%, or at least about 80%.

[0117] The term "tumor" refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues. The terms "cancer," "cancerous," "cell proliferative disorder," "proliferative disorder" and "tumor" are not mutually exclusive as referred to herein. The terms "cell proliferative disorder" and "proliferative disorder" refer to disorders that are associated with some degree of abnormal cell proliferation. In some embodiments, the cell proliferative disorder is a cancer. In some aspects, the tumor is a solid tumor. In some aspects, the tumor is a hematologic malignancy.

[0118] The term "pharmaceutical composition" refers to a preparation which is in such form as to permit the biological activity of an active ingredient contained therein to be effective in treating a subject, and which contains no additional components which are unacceptably toxic to the subject in the amounts provided in the pharmaceutical composition.

[0119] The terms "modulate" and "modulation" refer to reducing or inhibiting or, alternatively, activating or increasing, a recited variable.

[0120] The terms "increase" and "activate" refer to an increase of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 2-fold, 3-fold, 4-fold, 5-fold, 10-fold, 20-fold, 50-fold, 100-fold, or greater in a recited variable.

[0121] The terms "reduce" and "inhibit" refer to a decrease of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 2-fold, 3-fold, 4-fold, 5-fold, 10-fold, 20-fold, 50-fold, 100-fold, or greater in a recited variable.

[0122] The term "agonize" refers to the activation of receptor signaling to induce a biological response associated with activation of the receptor. An "agonist" is an entity that binds to and agonizes a receptor.

[0123] The term "antagonize" refers to the inhibition of receptor signaling to inhibit a biological response associated with activation of the receptor. An "antagonist" is an entity that binds to and antagonizes a receptor.

[0124] The term "effector T cell" includes T helper (i.e., CD4+) cells and cytotoxic (i.e., CD8+) T cells. CD4+ effector T cells contribute to the development of several immunologic processes, including maturation of B cells into plasma cells and memory B cells, and activation of cytotoxic T cells and macrophages. CD8+ effector T cells destroy virus-infected cells and tumor cells. See Seder and Ahmed, *Nature Immunol.*, 2003, 4:835-842, for additional information on effector T cells.

[0125] The term "regulatory T cell" includes cells that regulate immunological tolerance, for example, by suppressing effector T cells. In some aspects, the regulatory T cell has a CD4+CD25+Foxp3+ phenotype. In some aspects, the regulatory T cell has a CD8+CD25+ phenotype. See Nocentini et al., *Br. J. Pharmacol.*, 2012, 165:2089-2099, for additional information on regulatory T cells expressing TIGIT.

[0126] The term "dendritic cell" refers to a professional antigen-presenting cell capable of activating a naive T cell and stimulating growth and differentiation of a B cell.

2. TIGIT Antigen-Binding Proteins

2.1. TIGIT Binding and Target Cells

[0127] Provided herein are ABPs that specifically bind to TIGIT. In some aspects, the TIGIT is hTIGIT (SEQ ID NO:1). In some aspects, the TIGIT is cTIGIT (SEQ ID NO:2). In some aspects, the TIGIT is mTIGIT with the sequence provided in SEQ ID NO:3. In some aspects, the TIGIT is mTIGIT with the sequence provided in SEQ ID NO: 138.

[0128] In some embodiments, the ABPs provided herein specifically bind to hTIGIT (SEQ ID NO:1), cTIGIT (SEQ ID NO:2), and mTIGIT of SEQ ID NO:3. In some embodiments, the ABPs provided herein specifically bind to hTIGIT (SEQ ID NO:1), cTIGIT (SEQ ID NO:2), and mTIGIT of SEQ ID NO: 138. In some embodiments, the ABPs provided herein specifically bind to hTIGIT (SEQ ID NO:1), and cTIGIT (SEQ ID NO:2). In some embodiments, the ABPs provided herein specifically bind to hTIGIT (SEQ ID NO:1). In some embodiments, the ABPs provided herein do not bind mTIGIT of SEQ ID NO:3. In some embodiments, the ABPs provided herein do not bind mTIGIT of SEQ ID NO:138.

[0129] In some embodiments, the ABPs provided herein specifically bind to the extracellular domain of TIGIT.

[0130] In some embodiments, an ABP provided herein is an antibody. In some embodiments, an ABP provided herein is an antibody fragment. In some embodiments, an ABP provided herein is an alternative scaffold.

[0131] The TIGIT may be expressed on the surface of any suitable target cell. In some embodiments, the target cell is a T cell. In some embodiments, the target cell is an effector T cell. In some embodiments, the target cell is a regulatory T cell. In some embodiments, the target cell is a natural killer (NK) cell. In some embodiments, the target cell is a natural killer T (NKT) cell.

[0132] In some embodiments, the ABPs provided herein comprise an immunoglobulin molecule. In some embodiments, the ABPs provided herein consist of an immunoglobulin molecule. In some embodiments, the ABPs provided herein consist essentially of an immunoglobulin molecule. In some aspects, the immunoglobulin molecule comprises an antibody. In some aspects, the immunoglobulin molecule consists of an antibody. In some aspects, the immunoglobulin molecule consists essentially of an antibody.

[0133] In some embodiments, the ABPs provided herein comprise a light chain. In some aspects, the light chain is a kappa light chain. In some aspects, the light chain is a lambda light chain.

[0134] In some embodiments, the ABPs provided herein comprise a kappa light chain comprising SEQ ID NO: 126.

[0135] In some embodiments, the ABPs provided herein comprise a heavy chain. In some aspects, the heavy chain is an IgA. In some aspects, the heavy chain is an IgD. In some aspects, the heavy chain is an IgE. In some aspects, the heavy chain is an IgG. In some aspects, the heavy chain is an IgM. In some aspects, the heavy chain is an IgG1. In some aspects, the heavy chain is an IgG2. In some aspects, the heavy chain is an IgG3. In some aspects, the heavy chain is an IgG4. In some aspects, the heavy chain is an IgA1. In some aspects, the heavy chain is an IgA2.

[0136] In some embodiments, the ABPs provided herein comprise an IgG4 heavy chain comprising a sequence selected from SEQ ID NO:55 and SEQ ID NO:56. In some embodiments, the ABPs provided herein comprise an IgG1 heavy chain comprising a sequence selected from SEQ ID NO:57 and SEQ ID NO: 125.

[0137] In some embodiments, the ABPs provided herein comprise an antibody fragment. In some embodiments, the ABPs provided herein consist of an antibody fragment. In some embodiments, the ABPs provided herein consist essentially of an antibody fragment. In some aspects, the antibody fragment is an Fv fragment. In some aspects, the antibody fragment is a Fab fragment. In some aspects, the antibody fragment is a F(ab')₂ fragment. In some aspects, the antibody fragment is a Fab' fragment. In some aspects, the antibody fragment is an scFv (sFv) fragment. In some aspects, the antibody fragment is an scFv-Fc fragment. In some aspects, the antibody fragment is a fragment of a single domain antibody.

[0138] In some embodiments, an antibody fragment provided herein is derived from an illustrative antibody provided herein. In some embodiments, an antibody fragments provided

herein is not derived from an illustrative antibody provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining antibody fragments.

[0139] In some embodiments, an antibody fragment provided specifically binds hTIGIT. In some embodiments, an antibody fragment provided herein specifically binds cTIGIT. In some embodiments, an antibody fragment provided herein specifically binds mTIGIT. In some embodiments, an antibody fragment provided herein specifically binds hTIGIT and cTIGIT. In some embodiments, an antibody fragment provided herein specifically binds hTIGIT and mTIGIT. In some embodiments, an antibody fragment provided herein specifically binds cTIGIT and mTIGIT. In some embodiments, an antibody fragment provided herein specifically binds hTIGIT, cTIGIT and mTIGIT.

[0140] In some embodiments, an antibody fragment derived from an antibody provided herein retains affinity, as measured by K_D , for hTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such antibody. In some embodiments, an antibody fragment derived from an antibody provided herein retains affinity, as measured by K_D , for cTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such antibody. In some embodiments, an antibody fragment derived from an antibody provided herein retains affinity, as measured by K_D , for mTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such antibody. In some embodiments, an antibody fragment derived from an antibody provided herein retains affinity, as measured by K_D , for both hTIGIT and cTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such antibody. In some embodiments, an antibody fragment derived from an antibody provided herein retains affinity, as measured by K_D , for both hTIGIT and mTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such antibody. In some embodiments, an antibody fragment derived from an antibody provided herein retains affinity, as measured by K_D , for both cTIGIT and mTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such antibody. In some embodiments, an antibody fragment derived from an antibody provided herein retains affinity, as measured by K_D , for all three of hTIGIT, cTIGIT and mTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such antibody.

[0141] In some embodiments, an antibody fragment provided herein retains the ability to antagonize TIGIT, as measured by one or more assays or biological effects described herein. In some embodiments, an antibody fragment provided herein retains the ability to prevent TIGIT from interacting with one or more of its ligands, as described herein.

[0142] In some embodiments, an antibody fragment provided herein competes for binding to TIGIT with an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB 10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure.

[0143] In some embodiments, an antibody fragment provided herein inhibits binding of CD155 to TIGIT. In some embodiments, an antibody fragment provided herein inhibits binding of CD112 to TIGIT. In some embodiments, an antibody fragment provided herein inhibits association of CD226 with TIGIT.

[0144] In some embodiments, an antibody fragment provided herein activates an effector T cell or a natural killer (NK) cell. In some embodiments, an antibody fragment provided herein decreases the number of regulatory T cells in a tissue or in circulation. In some embodiments, an antibody fragment provided herein inhibits the suppression of an effector T cell by a regulatory T cell.

[0145] In some embodiments, an antibody fragment provided herein does not bind specifically to any of PVRL1, PVRL2, PVRL3, or PVRL4.

[0146] In some embodiments, an antibody fragment provided herein binds murine TIGIT (mTIGIT; SEQ ID NO: 3) with an affinity lower (as indicated by higher K_D) than the affinity of the antibody fragment for hTIGIT, or does not bind mTIGIT.

[0147] In some embodiments, a fragment of an antibody provided herein binds the same epitope of TIGIT as such antibody.

[0148] In some embodiments, the ABPs provided herein are monoclonal antibodies. In some embodiments, the ABPs provided herein are polyclonal antibodies.

[0149] In some embodiments, the ABPs provided herein comprise a chimeric antibody. In some embodiments, the ABPs provided herein consist of a chimeric antibody. In some embodiments, the ABPs provided herein consist essentially of a chimeric antibody. In some embodiments, the ABPs provided herein comprise a humanized antibody. In some embodiments, the ABPs provided herein consist of a humanized antibody. In some embodiments, the ABPs provided herein consist essentially of a humanized antibody. In some embodiments, the ABPs provided herein comprise a human antibody. In some embodiments, the ABPs provided herein consist of a human antibody. In some embodiments, the ABPs provided herein consist essentially of a human antibody.

[0150] In some embodiments, the ABPs provided herein are affinity matured. In some aspects, the affinity matured ABPs are affinity matured ABPs derived from an illustrative ABP provided herein.

[0151] In some embodiments, the ABPs provided herein comprise an alternative scaffold. In

some embodiments, the ABPs provided herein consist of an alternative scaffold. In some embodiments, the ABPs provided herein consist essentially of an alternative scaffold. Any suitable alternative scaffold may be used. In some aspects, the alternative scaffold is selected from an Adnectin[™], an iMab, an Anticalin[®], an EETI-II/AGRP, a Kunitz domain, a thioredoxin peptide aptamer, an Affibody[®], a DARPin, an Affilin, a Tetranectin, a Fynomer, and an Avimer.

[0152] In some embodiments, an ABP provided herein inhibits binding of TIGIT to one or more ligands of TIGIT. In some aspects, the ligand of TIGIT is selected from one or more of poliovirus receptor (PVR; CD155) and nectin-2 (CD112, PVRL2). In some aspects, the ABP inhibits binding of TIGIT to one or more ligands of TIGIT by at least about 50%. In some aspects, the ABP inhibits binding of TIGIT to one or more ligands of TIGIT by at least about 75%. In some aspects, the ABP inhibits binding of TIGIT to one or more ligands of TIGIT by at least about 90%. In some aspects, the ABP inhibits binding of TIGIT to one or more ligands of TIGIT by at least about 95%.

[0153] In some embodiments, an ABP of the invention is an ABP that competes with an illustrative ABP provided herein. In some aspects, the ABP that competes with the illustrative ABP provided herein binds the same epitope as an illustrative ABP provided herein.

[0154] In some embodiments, an ABP provided herein does not bind PVRL4.

[0155] It is known that when an antibody is expressed in cells, the antibody is modified after translation. Examples of the posttranslational modification include cleavage of lysine at the C terminal of the heavy chain by a carboxypeptidase; modification of glutamine or glutamic acid at the N terminal of the heavy chain and the light chain to pyroglutamic acid by pyroglutamylation; glycosylation; oxidation; deamidation; and glycation, and it is known that such posttranslational modifications occur in various antibodies (See Journal of Pharmaceutical Sciences, 2008, Vol. 97, p. 2426-2447). In some embodiments, an ABP of the invention is an antibody or antigen-binding fragment thereof which has undergone posttranslational modification. Examples of an antibody or antigen-binding fragment thereof which have undergone posttranslational modification include an antibody or antigen-binding fragments thereof which have undergone pyroglutamylation at the N terminal of the heavy chain variable region and/or deletion of lysine at the C terminal of the heavy chain. It is known in the art that such posttranslational modification due to pyroglutamylation at the N terminal and deletion of lysine at the C terminal does not have any influence on the activity of the antibody or fragment thereof (Analytical Biochemistry, 2006, Vol. 348, p. 24-39).

2.2. Sequences of TIGIT Antigen-Binding Proteins

2.2.1. V_H Domains

[0156] In some examples, an ABP provided herein comprises a V_H sequence selected from SEQ ID NOs: 4-24. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:4. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:5. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:6. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:7. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:8. In some embodiments an ABP provided herein comprises a V_H sequence of SEQ ID NO:9. In some embodiments an ABP provided herein comprises a V_H sequence of SEQ ID NO:10. In some embodiments an ABP provided herein comprises a V_H sequence of SEQ ID NO: 11. In some embodiments an ABP provided herein comprises a V_H sequence of SEQ ID NO: 12. In some embodiments an ABP provided herein comprises a V_H sequence of SEQ ID NO: 13. In some embodiments an ABP provided herein comprises a V_H sequence of SEQ ID NO: 14. In some embodiments an ABP provided herein comprises a V_H sequence of SEQ ID NO:15. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO: 16. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:17. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:18. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:19. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:20. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:21. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:22. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:23. In some examples an ABP provided herein comprises a V_H sequence of SEQ ID NO:24.

[0157] In some examples, an ABP provided herein comprises a V_H sequence having at least about 50%, 60%, 70%, 80%, 90%, 95%, or 99% identity to an illustrative V_H sequence provided in SEQ ID NOs: 4-24. In some examples, an ABP provided herein comprises a V_H sequence provided in SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

2.2.2. V_L Domains

[0158] In some examples, an ABP provided herein comprises a V_L sequence selected from SEQ ID NOs: 25-28. In some examples an ABP provided herein comprises a V_L sequence of

SEQ ID NO:25. In some embodiments an ABP provided herein comprises a V_L sequence of SEQ ID NO:26. In some examples an ABP provided herein comprises a V_L sequence of SEQ ID NO:27. In some examples an ABP provided herein comprises a V_L sequence of SEQ ID NO:28.

[0159] In some examples, an ABP provided herein comprises a V_L sequence having at least about 50%, 60%, 70%, 80%, 90%, 95%, or 99% identity to an illustrative V_L sequence provided in SEQ ID NOs: 25-28. In some examples, an ABP provided herein comprises a V_L sequence provided in SEQ ID NOs: 25-28, with up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

2.2.3. V_H - V_L Combinations

[0160] In some examples, an ABP provided herein comprises a V_H sequence selected from SEQ ID NOs: 4-24 and a V_L sequence selected from SEQ ID NOs: 25-28.

[0161] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:4 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:5 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:6 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:7 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:8 and a V_L sequence of SEQ ID NO:25. In some embodiments, an ABP provided herein comprises a V_H sequence of SEQ ID NO:9 and a V_L sequence of SEQ ID NO:26. In some embodiments, an ABP provided herein comprises a V_H sequence of SEQ ID NO:10 and a V_L sequence of SEQ ID NO:26. In some embodiments, an ABP provided herein comprises a V_H sequence of SEQ ID NO:11 and a V_L sequence of SEQ ID NO:26. In some embodiments, an ABP provided herein comprises a V_H sequence of SEQ ID NO:12 and a V_L sequence of SEQ ID NO:26. In some embodiments, an ABP provided herein comprises a V_H sequence of SEQ ID NO:13 and a V_L sequence of SEQ ID NO:26. In some embodiments, an ABP provided herein comprises a V_H sequence of SEQ ID NO:14 and a V_L sequence of SEQ ID NO:26. In some embodiments, an ABP provided herein comprises a V_H sequence of SEQ ID

NO:15 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:16 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:17 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:18 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:19 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:20 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:21 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:22 and a V_L sequence of SEQ ID NO:28. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:23 and a V_L sequence of SEQ ID NO:28. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:24 and a V_L sequence of SEQ ID NO:28.

[0162] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:4 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:4 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:4 and a V_L sequence of SEQ ID NO:28.

[0163] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:5 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:5 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:5 and a V_L sequence of SEQ ID NO:28.

[0164] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:6 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:6 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:6 and a V_L sequence of SEQ ID NO:28.

[0165] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:7 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:7 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:7 and a V_L sequence of SEQ ID NO:28.

[0166] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:8

and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:8 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:8 and a V_L sequence of SEQ ID NO:28.

[0167] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:9 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:9 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:9 and a V_L sequence of SEQ ID NO:28.

[0168] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:10 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:10 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:10 and a V_L sequence of SEQ ID NO:28.

[0169] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:11 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:11 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:11 and a V_L sequence of SEQ ID NO:28.

[0170] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:12 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:12 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:12 and a V_L sequence of SEQ ID NO:28.

[0171] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:13 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:13 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:13 and a V_L sequence of SEQ ID NO:28.

[0172] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:14 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:14 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:14 and a V_L sequence of SEQ ID NO:28.

[0173] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:15 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:15 and a V_L sequence of SEQ ID NO:27. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:15 and a V_L sequence of SEQ ID NO:28.

[0174] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:16 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:16 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:16 and a V_L sequence of SEQ ID NO:28.

[0175] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:17 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:17 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:17 and a V_L sequence of SEQ ID NO:28.

[0176] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:18 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:18 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:18 and a V_L sequence of SEQ ID NO:28.

[0177] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:19 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:19 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:19 and a V_L sequence of SEQ ID NO:28.

[0178] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:20 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:20 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:20 and a V_L sequence of SEQ ID NO:28.

[0179] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:21 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:21 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:21 and a V_L sequence of SEQ

ID NO:28.

[0180] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:22 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:22 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:22 and a V_L sequence of SEQ ID NO:27.

[0181] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:23 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:23 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:23 and a V_L sequence of SEQ ID NO:27.

[0182] In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:24 and a V_L sequence of SEQ ID NO:25. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:24 and a V_L sequence of SEQ ID NO:26. In some examples, an ABP provided herein comprises a V_H sequence of SEQ ID NO:24 and a V_L sequence of SEQ ID NO:27.

[0183] In some examples, an ABP provided herein comprises a V_H sequence having at least about 50%, 60%, 70%, 80%, 90%, 95%, or 99% identity to an illustrative V_H sequence provided in SEQ ID NOs: 4-24, and a V_L sequence having at least about 50%, 60%, 70%, 80%, 90%, 95%, or 99% identity to an illustrative V_L sequence provided in SEQ ID NOs: 25-28. In some examples, an ABP provided herein comprises a V_H sequence provided in SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acid substitutions, and a V_L sequence provided in SEQ ID NOs: 25-28, with up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

2.2.4. CDRs

[0184] In some examples, an ABP provided herein comprises one to three CDRs of a V_H domain selected from SEQ ID NOs: 4-24. In some examples, an ABP provided herein

comprises two to three CDRs of a V_H domain selected from SEQ ID NOs: 4-24. In some examples, an ABP provided herein comprises three CDRs of a V_H domain selected from SEQ ID NOs: 4-24. In some examples, the CDRs are Kabat CDRs. In some examples, the CDRs are Chothia CDRs. In some examples, the CDRs are IMGT CDRs.

[0185] In some examples, the CDRs are CDRs having at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H1, CDR-H2, or CDR-H3 of SEQ ID NOs: 4-24. In some examples, the CDR-H1 is a CDR-H1 of a V_H domain selected from SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, or 5 amino acid substitutions. In some examples, the CDR-H2 is a CDR-H2 of a V_H domain selected from SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions. In some examples, the CDR-H3 is a CDR-H3 of a V_H domain selected from SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0186] In some examples, an ABP provided herein comprises one to three CDRs of a V_L domain selected from SEQ ID NOs: 25-28. In some examples, an ABP provided herein comprises two to three CDRs of a V_L domain selected from SEQ ID NOs: 25-28. In some examples, an ABP provided herein comprises three CDRs of a V_L domain selected from SEQ ID NOs: 25-28. In some examples, the CDRs are Kabat CDRs. In some examples, the CDRs are Chothia CDRs. In some examples, the CDRs are IMGT CDRs.

[0187] In some examples, the CDRs are CDRs having at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L1, CDR-L2, or CDR-L3 of SEQ ID NOs: 25-28. In some examples, the CDR-L1 is a CDR-L1 of a V_L domain selected from SEQ ID NOs: 25-28, with up to 1, 2, 3, 4, 5, or 6 amino acid substitutions. In some examples, the CDR-L2 is a CDR-L2 of a V_L domain selected from SEQ ID NOs: 25-28, with up to 1, 2, 3, or 4 amino acid substitutions. In some examples, the CDR-L3 is a CDR-L3 of a V_L domain selected from SEQ ID NOs: 25-28, with up to 1, 2, 3, 4, or 5 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0188] In some examples, an ABP provided herein comprises one to three CDRs of a V_H

domain selected from SEQ ID NOs: 4-24 and one to three CDRs of a V_L domain selected from SEQ ID NOs: 25-28. In some examples, an ABP provided herein comprises two to three CDRs of a V_H domain selected from SEQ ID NOs: 4-24 and two to three CDRs of a V_L domain selected from SEQ ID NOs: 25-28. In some examples, an ABP provided herein comprises three CDRs of a V_H domain selected from SEQ ID NOs: 4-24 and three CDRs of a V_L domain selected from SEQ ID NOs: 25-28. In some examples, the CDRs are Kabat CDRs. In some examples, the CDRs are Chothia CDRs. In some examples, the CDRs are IMGT CDRs.

[0189] In some examples, the CDRs are CDRs having at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H1, CDR-H2, or CDR-H3 of SEQ ID NOs: 4-24 and at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L1, CDR-L2, or CDR-L3 of SEQ ID NOs: 25-28. In some examples, the CDR-H1 is a CDR-H1 of a V_H domain selected from SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, or 5 amino acid substitutions; the CDR-H2 is a CDR-H2 of a V_H domain selected from SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions; the CDR-H3 is a CDR-H3 of a V_H domain selected from SEQ ID NOs: 4-24, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions; the CDR-L1 is a CDR-L1 of a V_L domain selected from SEQ ID NOs: 25-28, with up to 1, 2, 3, 4, 5, or 6 amino acid substitutions; the CDR-L2 is a CDR-L2 of a V_L domain selected from SEQ ID NOs: 25-28, with up to 1, 2, 3, or 4 amino acid substitutions; and the CDR-L3 is a CDR-L3 of a V_L domain selected from SEQ ID NOs: 25-28, with up to 1, 2, 3, 4, or 5 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0190] In some examples, an ABP provided herein comprises a CDR-H3 selected from SEQ ID NOs: 29-35. In some examples, the CDR-H3 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H3 of SEQ ID NOs: 29-35. In some examples, the CDR-H3 is a CDR-H3 according to the IMGT numbering system. In some examples, the CDR-H3 is a CDR-H3 selected from SEQ ID NOs: 29-35, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0191] In some examples, an ABP provided herein comprises a CDR-H2 selected from SEQ ID NOs: 36-47. In some examples, the CDR-H2 has at least about 50%, 75%, 80%, 85%, 90%, or

95% identity with a CDR-H2 of SEQ ID NOs: 36-47. In some examples, the CDR-H2 is a CDR-H2 according to the Kabat numbering system. In some examples, the CDR-H2 is a CDR-H2 selected from SEQ ID NOs: 36-47, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0192] In some examples, an ABP provided herein comprises a CDR-H1 selected from SEQ ID NOs: 48-54 or 58-62. In some examples, the CDR-H1 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H1 of SEQ ID NOs: 48-54 or 58-62. In some examples, the CDR-H1 is a CDR-H1 that spans the CDR-H1 as defined by both the Chothia and Kabat numbering systems. In some examples, the CDR-H1 is a CDR-H1 selected from SEQ ID NOs: 48-54 or 58-62, with up to 1, 2, 3, 4, or 5 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0193] In some examples, an ABP provided herein comprises a CDR-H3 selected from SEQ ID NOs: 29-35 and a CDR-H2 selected from SEQ ID NOs: 36-47. In some examples, an ABP provided herein comprises a CDR-H3 selected from SEQ ID NOs: 29-35, a CDR-H2 selected from SEQ ID NOs: 36-47, and a CDR-H1 selected from SEQ ID NOs: 48-54 or 58-62. In some examples, the CDR-H3 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H3 of SEQ ID NOs: 29-35, the CDR-H2 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H2 of SEQ ID NOs: 36-47, and the CDR-H1 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H1 of SEQ ID NOs: 48-54 or 58-62. In some examples, the CDR-H3 is a CDR-H3 selected from SEQ ID NOs: 29-35, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions; the CDR-H2 is a CDR-H2 selected from SEQ ID NOs: 36-47, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions; and the CDR-H1 is a CDR-H1 selected from SEQ ID NOs: 48-54 or 58-62, with up to 1, 2, 3, 4, or 5 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0194] In some examples, an ABP provided herein comprises a CDR-L3 selected from SEQ ID NOs: 63-66. In some examples, the CDR-L3 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L3 of SEQ ID NOs: 63-66. In some examples, the CDR-L3 is a CDR-L3 according to the Kabat, Chothia, and IMGT numbering systems. In some examples, the CDR-L3 is a CDR-L3 selected from SEQ ID NOs: 63-66, with up to 1, 2, 3, 4, or 5 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0195] In some examples, an ABP provided herein comprises a CDR-L2 selected from SEQ ID NOs: 67-69. In some examples, the CDR-L2 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L2 of SEQ ID NOs: 67-69. In some examples, the CDR-L2 is a CDR-L2 according to the Kabat and Chothia numbering systems. In some examples, the CDR-L2 is a CDR-L2 selected from SEQ ID NOs: 67-69, with up to 1, 2, 3, or 4 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0196] In some examples, an ABP provided herein comprises a CDR-L1 selected from SEQ ID NOs: 70-72. In some examples, the CDR-L1 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L1 of SEQ ID NOs: 70-72. In some examples, the CDR-L1 is a CDR-L1 according to the Kabat and Chothia numbering systems. In some examples, the CDR-L1 is a CDR-L1 selected from SEQ ID NOs: 70-72, with up to 1, 2, 3, 4, 5, or 6 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0197] In some examples, an ABP provided herein comprises a CDR-L3 selected from SEQ ID NOs: 63-66 and a CDR-L2 selected from SEQ ID NOs: 67-69. In some examples, an ABP provided herein comprises a CDR-L3 selected from SEQ ID NOs: 63-66, a CDR-L2 selected from SEQ ID NOs: 67-69, and a CDR-L1 selected from SEQ ID NOs: 70-72. In some

examples, the CDR-L3 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L3 of SEQ ID NOs: 63-66, the CDR-L2 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L2 of SEQ ID NOs: 67-69, and the CDR-L1 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L1 of SEQ ID NOs: 70-72. In some examples, the CDR-L3 is a CDR-L3 selected from SEQ ID NOs: 63-66, with up to 1, 2, 3, 4, or 5 amino acid substitutions; the CDR-L2 is a CDR-L2 selected from SEQ ID NOs: 67-69, with up to 1, 2, 3, or 4 amino acid substitutions; and the CDR-L1 is a CDR-L1 selected from SEQ ID NOs: 70-72, with up to 1, 2, 3, 4, 5, or 6 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0198] In some examples, an ABP provided herein comprises a CDR-H3 selected from SEQ ID NOs: 29-35, a CDR-H2 selected from SEQ ID NOs: 36-47, a CDR-H1 selected from SEQ ID NOs: 48-54 or 58-62, a CDR-L3 selected from SEQ ID NOs: 63-66, a CDR-L2 selected from SEQ ID NOs: 67-69, and a CDR-L1 selected from SEQ ID NOs: 70-72. In some examples, the CDR-H3 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H3 of SEQ ID NOs: 29-35, the CDR-H2 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H2 of SEQ ID NOs: 36-47, the CDR-H1 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-H1 of SEQ ID NOs: 48-54 or 58-62, the CDR-L3 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L3 of SEQ ID NOs: 63-66, the CDR-L2 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L2 of SEQ ID NOs: 67-69, and the CDR-L1 has at least about 50%, 75%, 80%, 85%, 90%, or 95% identity with a CDR-L1 of SEQ ID NOs: 70-72. In some examples, the CDR-H3 is a CDR-H3 selected from SEQ ID NOs: 29-35, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions; the CDR-H2 is a CDR-H2 selected from SEQ ID NOs: 36-47, with up to 1, 2, 3, 4, 5, 6, 7, or 8 amino acid substitutions; the CDR-H1 is a CDR-H1 selected from SEQ ID NOs: 48-54 or 58-62, with up to 1, 2, 3, 4, or 5 amino acid substitutions; the CDR-L3 is a CDR-L3 selected from SEQ ID NOs: 63-66, with up to 1, 2, 3, 4, or 5 amino acid substitutions; the CDR-L2 is a CDR-L2 selected from SEQ ID NOs: 67-69, with up to 1, 2, 3, or 4 amino acid substitutions; and the CDR-L1 is a CDR-L1 selected from SEQ ID NOs: 70-72, with up to 1, 2, 3, 4, 5, or 6 amino acid substitutions. In some examples, the amino acid substitutions are conservative amino acid substitutions. In some examples, the ABPs described in this paragraph are referred to herein as "variants." In some examples, such variants are derived from a sequence provided herein, for example, by affinity maturation, site directed mutagenesis, random mutagenesis, or any other method known in the art or described herein. In some examples, such variants are not derived from a sequence provided herein and may, for example, be isolated *de novo* according to the methods provided herein for obtaining ABPs.

[0199] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:29, a

CDR-H2 of SEQ ID NO:36, a CDR-H1 of SEQ ID NO:48, a CDR-L3 of SEQ ID NO:63, a CDR-L2 of SEQ ID NO:67, and a CDR-L1 of SEQ ID NO:70.

[0200] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:29, a CDR-H2 of SEQ ID NO:37, a CDR-H1 of SEQ ID NO:49, a CDR-L3 of SEQ ID NO:63, a CDR-L2 of SEQ ID NO:67, and a CDR-L1 of SEQ ID NO:70.

[0201] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:29, a CDR-H2 of SEQ ID NO:37, a CDR-H1 of SEQ ID NO:50, a CDR-L3 of SEQ ID NO:63, a CDR-L2 of SEQ ID NO:67, and a CDR-L1 of SEQ ID NO:70.

[0202] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:30, a CDR-H2 of SEQ ID NO:37, a CDR-H1 of SEQ ID NO:50, a CDR-L3 of SEQ ID NO:63, a CDR-L2 of SEQ ID NO:67, and a CDR-L1 of SEQ ID NO:70.

[0203] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:29, a CDR-H2 of SEQ ID NO:38, a CDR-H1 of SEQ ID NO:50, a CDR-L3 of SEQ ID NO:63, a CDR-L2 of SEQ ID NO:67, and a CDR-L1 of SEQ ID NO:70.

[0204] In some embodiments, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:31, a CDR-H2 of SEQ ID NO:39, a CDR-H1 of SEQ ID NO:51, a CDR-L3 of SEQ ID NO:64, a CDR-L2 of SEQ ID NO:68, and a CDR-L1 of SEQ ID NO:71.

[0205] In some embodiments, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:31, a CDR-H2 of SEQ ID NO:40, a CDR-H1 of SEQ ID NO:52, a CDR-L3 of SEQ ID NO:64, a CDR-L2 of SEQ ID NO:68, and a CDR-L1 of SEQ ID NO:71.

[0206] In some embodiments, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:31, a CDR-H2 of SEQ ID NO:41, a CDR-H1 of SEQ ID NO:53, a CDR-L3 of SEQ ID NO:64, a CDR-L2 of SEQ ID NO:68, and a CDR-L1 of SEQ ID NO:71.

[0207] In some embodiments, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:31, a CDR-H2 of SEQ ID NO:40, a CDR-H1 of SEQ ID NO:54, a CDR-L3 of SEQ ID NO:64, a CDR-L2 of SEQ ID NO:68, and a CDR-L1 of SEQ ID NO:71.

[0208] In some embodiments, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:32, a CDR-H2 of SEQ ID NO:40, a CDR-H1 of SEQ ID NO:54, a CDR-L3 of SEQ ID NO:64, a CDR-L2 of SEQ ID NO:68, and a CDR-L1 of SEQ ID NO:71.

[0209] In some embodiments, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:32, a CDR-H2 of SEQ ID NO:40, a CDR-H1 of SEQ ID NO:54, a CDR-L3 of SEQ ID NO:64, a CDR-L2 of SEQ ID NO:68, and a CDR-L1 of SEQ ID NO:71.

[0210] In some embodiments, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:32,

a CDR-H2 of SEQ ID NO:40, a CDR-H1 of SEQ ID NO:54, a CDR-L3 of SEQ ID NO:64, a CDR-L2 of SEQ ID NO:68, and a CDR-L1 of SEQ ID NO:71.

[0211] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:33, a CDR-H2 of SEQ ID NO:42, a CDR-H1 of SEQ ID NO:58, a CDR-L3 of SEQ ID NO:65, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0212] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:33, a CDR-H2 of SEQ ID NO:42, a CDR-H1 of SEQ ID NO:59, a CDR-L3 of SEQ ID NO:65, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0213] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:33, a CDR-H2 of SEQ ID NO:43, a CDR-H1 of SEQ ID NO:60, a CDR-L3 of SEQ ID NO:65, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0214] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:34, a CDR-H2 of SEQ ID NO:43, a CDR-H1 of SEQ ID NO:60, a CDR-L3 of SEQ ID NO:65, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0215] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:34, a CDR-H2 of SEQ ID NO:44, a CDR-H1 of SEQ ID NO:61, a CDR-L3 of SEQ ID NO:65, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0216] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:33, a CDR-H2 of SEQ ID NO:44, a CDR-H1 of SEQ ID NO:59, a CDR-L3 of SEQ ID NO:65, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0217] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:35, a CDR-H2 of SEQ ID NO:45, a CDR-H1 of SEQ ID NO:62, a CDR-L3 of SEQ ID NO:66, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0218] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:35, a CDR-H2 of SEQ ID NO:46, a CDR-H1 of SEQ ID NO:62, a CDR-L3 of SEQ ID NO:66, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

[0219] In some examples, an ABP provided herein comprises a CDR-H3 of SEQ ID NO:35, a CDR-H2 of SEQ ID NO:47, a CDR-H1 of SEQ ID NO:62, a CDR-L3 of SEQ ID NO:66, a CDR-L2 of SEQ ID NO:69, and a CDR-L1 of SEQ ID NO:72.

2.2.5. Heavy Chains and Light Chains

[0220] In some examples, an ABP provided herein comprises a V_H selected from a V_H of SEQ ID NO:4-24 (or a variant described herein) and a constant region selected from SEQ ID NOs:

55-57 or 125. In some examples, an ABP provided herein comprises a V_L selected from a V_L of SEQ ID NO:25-28 (or a variant described herein) and a constant region of SEQ ID NO:126.

[0221] In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:79. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:80. In some examples, an ABP provided herein comprises a light chain of SEQ ID NO:81. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:79 and a light chain of SEQ ID NO: 81. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:80 and a light chain of SEQ ID NO: 81.

[0222] In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:82. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:83. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:82 and a light chain of SEQ ID NO: 81. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:83 and a light chain of SEQ ID NO: 81.

[0223] In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:84. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:85. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:84 and a light chain of SEQ ID NO: 81. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:85 and a light chain of SEQ ID NO: 81.

[0224] In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:86. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:87. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:86 and a light chain of SEQ ID NO: 81. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:87 and a light chain of SEQ ID NO: 81.

[0225] In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:88. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:89. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:88 and a light chain of SEQ ID NO: 81. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:89 and a light chain of SEQ ID NO: 81.

[0226] In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:90. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:91. In some embodiments, an ABP provided herein comprises a light chain of SEQ ID NO:92. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:90 and a light chain of SEQ ID NO:92. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:91 and a light chain of SEQ ID NO:92.

[0227] In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:93. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:94. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID

NO:93 and a light chain of SEQ ID NO:92. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:94 and a light chain of SEQ ID NO:92.

[0228] In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:95. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:96. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:95 and a light chain of SEQ ID NO:92. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:96 and a light chain of SEQ ID NO:92.

[0229] In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:97. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:98. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:97 and a light chain of SEQ ID NO:92. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:98 and a light chain of SEQ ID NO:92.

[0230] In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:99. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:100. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:99 and a light chain of SEQ ID NO:92. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:100 and a light chain of SEQ ID NO:92.

[0231] In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:101. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:102. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:101 and a light chain of SEQ ID NO:92. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:102 and a light chain of SEQ ID NO:92.

[0232] In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:103. In some embodiments, an ABP provided herein comprises a heavy chain of SEQ ID NO:104. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:103 and a light chain of SEQ ID NO:92. In some embodiments, an APB provided herein comprises a heavy chain of SEQ ID NO:104 and a light chain of SEQ ID NO:92.

[0233] In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:105. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:106. In some examples, an ABP provided herein comprises a light chain of SEQ ID NO:107. In some examples, an APB provided herein comprises a heavy chain of SEQ ID NO:105 and a light chain of SEQ ID NO:107. In some examples, an APB provided herein comprises a heavy chain of SEQ ID NO:106 and a light chain of SEQ ID NO:107.

[0234] In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:108. In some examples, an ABP provided herein comprises a heavy chain of SEQ ID NO:109. In some examples, an APB provided herein comprises a heavy chain of SEQ ID NO:108 and a light chain of SEQ ID NO:107. In some examples, an APB provided herein

2.2.6. Consensus Sequences

[0242] In some examples, provided herein is a first family of ABPs, wherein an ABP of such family comprises the following six CDR sequences: (a) a CDR-H3 having the sequence A-R-D-G-V-L-X₁-L-N-K-R-S-F-D-I, wherein X₁ is A or T (SEQ ID NO: 128); (b) a CDR-H2 having the sequence S-I-Y-Y-S-G-X₂-T-Y-Y-N-P-S-L-K-S, wherein X₂ is S, Q or G (SEQ ID NO: 129); (c) a CDR-H1 having the sequence G-S-I-X₃-S-G-X₄-Y-Y-W-G, wherein X₃ is E or A, and X₄ is L, V or S (SEQ ID NO: 130); (d) a CDR-L3 having the sequence QQHTVRPPLT (SEQ ID NO: 64); (e) a CDR-L2 having the sequence GASSRAT (SEQ ID NO: 68); and (f) a CDR-L1 having the sequence RASQSVSSSYLA (SEQ ID NO: 71). In some examples, provided herein is an ABP within such first family.

[0243] In some examples, provided herein is a second family of ABPs, wherein an ABP of such family comprises the following six CDR sequences: (a) a CDR-H3 having the sequence A-R-D-A-N-Y-Y-G-X₁-A-W-A-F-D-P, wherein X₁ is S or G (SEQ ID NO: 131); (b) a CDR-H2 having the sequence S-I-Y-Y-S-G-X₂-T-F-Y-N-P-S-L-K-X₃, wherein X₂ is S or A, and X₃ is S or G (SEQ ID NO: 132); (c) a CDR-H1 having the sequence G-S-I-X₄-S-X₅-X₆-X₇-Y-W-G, wherein X₄ is S or T, X₅ is S or T, X₆ is S or K, and X₇ is H or Y (SEQ ID NO: 133); (d) a CDR-L3 having the sequence QQHFNLP (SEQ ID NO: 63); (e) a CDR-L2 having the sequence DASNRAT (SEQ ID NO: 67); and (f) a CDR-L1 having the sequence RASQSVSSSYLA (SEQ ID NO: 70). In some examples, provided herein is an ABP within such second family.

[0244] In some examples, provided herein is a third family of ABPs, wherein an ABP of such family comprises the following six CDR sequences: (a) a CDR-H3 having the sequence A-R-G-G-R-T-T-W-I-G-A-X₁-D-I, wherein X₁ is F or L (SEQ ID NO: 134); (b) a CDR-H2 having the sequence I-I-N-P-S-X₂-G-L-T-S-Y-A-X₃-K-F-Q-G, wherein X₂ is L or I, and X₃ is Q or R (SEQ ID NO: 135); (c) a CDR-H1 having the sequence Y-T-F-X₄-X₅-Y-Y-X₆-H, wherein X₄ is G, P or R, X₅ is N, A or E, and X₆ is M or I (SEQ ID NO: 136); (d) a CDR-L3 having the sequence QQYVWPPLT (SEQ ID NO: 65); (e) a CDR-L2 having the sequence GASTRAT (SEQ ID NO: 69); and (f) a CDR-L1 having the sequence RASQSVSSNLA (SEQ ID NO: 72). In some examples, provided herein is an ABP within such third family.

[0245] In some examples, provided herein is a fourth family of ABPs, wherein an ABP of such family comprises the following six CDR sequences: (a) a CDR-H3 having the sequence ARLHVSGSYYPAYLDY (SEQ ID NO: 35); (b) a CDR-H2 having the sequence X₁-I-N-P-S-M-G-A-T-S-Y-X₂-Q-K-F-X₃-G, wherein X₁ is V or I, X₂ is A or T, and X₃ is Q or R (SEQ ID NO: 137); (c) a CDR-H1 having the sequence YTFTSHYMG (SEQ ID NO: 62); (d) a CDR-L3 having the sequence QQYIVFPWT (SEQ ID NO: 66); (e) a CDR-L2 having the sequence GASTRAT (SEQ ID NO: 69); and (f) a CDR-L1 having the sequence RASQSVSSNLA, (SEQ ID NO: 72). In some examples, provided herein is an ABP within such fourth family.

2.2.7. Functional Properties of ABP Variants

[0246] As described above, and elsewhere in this disclosure, provided herein are ABP variants defined based on percent identity to an illustrative ABP sequence provided herein, or substitution of amino acid residues in comparison to an illustrative ABP sequence provided herein.

[0247] In some embodiments, a variant of an ABP provided herein has specificity for hTIGIT. In some embodiments, a variant of an ABP provided herein has specificity for cTIGIT. In some embodiments, a variant of an ABP provided herein has specificity for mTIGIT. In some embodiments, a variant of an ABP provided herein has specificity for hTIGIT and cTIGIT. In some embodiments, a variant of an ABP provided herein has specificity for hTIGIT and mTIGIT. In some embodiments, a variant of an ABP provided herein has specificity for cTIGIT and mTIGIT. In some embodiments, a variant of an ABP provided herein has specificity for hTIGIT, cTIGIT and mTIGIT.

[0248] In some embodiments, a variant of an ABP that is derived from an illustrative ABP sequence provided herein retains affinity, as measured by K_D , for hTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such illustrative ABP. In some embodiments, a variant of an ABP that is derived from an illustrative ABP sequence provided herein retains affinity, as measured by K_D , for cTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such illustrative ABP. In some embodiments, a variant of an ABP that is derived from an illustrative ABP sequence provided herein retains affinity, as measured by K_D , for mTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such illustrative ABP. In some embodiments, a variant of an ABP that is derived from an illustrative ABP sequence provided herein retains affinity, as measured by K_D , for both hTIGIT and cTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such illustrative ABP. In some embodiments, a variant of an ABP that is derived from an illustrative ABP sequence provided herein retains affinity, as measured by K_D , for both hTIGIT and mTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such illustrative ABP. In some embodiments, a variant of an ABP that is derived from an illustrative ABP sequence provided herein retains affinity, as measured by K_D , for both cTIGIT and mTIGIT that is within about 1.5-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such illustrative ABP. In some embodiments, a variant of an ABP that is derived from an illustrative ABP sequence provided herein retains affinity, as measured by K_D , for all three of hTIGIT, cTIGIT and mTIGIT that is within about 1.5-

fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 6-fold, about 7-fold, about 8-fold, about 9-fold or about 10-fold the affinity of such illustrative ABP.

[0249] In some embodiments, a variant of an ABP provided herein retains the ability to antagonize TIGIT, as measured by one or more assays or biological effects described herein. In some embodiments, a variant of an ABP provided herein retains the ability to prevent TIGIT from interacting with one or more of its ligands, as described herein.

[0250] In some embodiments, a variant of an ABP provided herein competes for binding to TIGIT with an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure.

[0251] In some embodiments, a variant of an ABP provided herein inhibits binding of CD155 to TIGIT. In some embodiments, a variant of an ABP provided herein inhibits binding of CD112 to TIGIT. In some embodiments, a variant of an ABP provided herein inhibits association of CD226 with TIGIT.

[0252] In some embodiments, a variant of an ABP provided herein activates an effector T cell or a natural killer (NK) cell. In some embodiments, a variant of an ABP provided herein decreases the number of regulatory T cells in a tissue or in circulation. In some embodiments, a variant of an ABP provided herein inhibits the suppression of an effector T cell by a regulatory T cell.

[0253] In some embodiments, a variant of an ABP provided herein does not bind specifically to any of PVRL1, PVRL2, PVRL3, or PVRL4.

[0254] In some embodiments, a variant of an ABP provided herein binds murine TIGIT (SEQ ID NO: 3) with an affinity lower (as indicated by higher K_D) than the affinity of the ABP for hTIGIT, or does not bind mTIGIT. In some embodiments, a variant of an ABP provided herein binds murine TIGIT (SEQ ID NO: 138) with an affinity lower (as indicated by higher K_D) than the affinity of the ABP for hTIGIT, or does not bind mTIGIT.

[0255] In some embodiments, a variant of an ABP provided herein binds the same epitope of TIGIT as such ABP.

2.2.8. Other Functional Properties of ABPs

[0256] In some embodiments, an ABP provided herein has one or more of the characteristics listed in the following (a)-(j): (a) competes for binding to TIGIT with an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as

provided in Table 5 of this disclosure; (b) inhibits binding of CD155 to TIGIT; (c) inhibits binding of CD112 to TIGIT; (d) inhibits association of CD226 with TIGIT; (e) activates an effector T cell or a natural killer (NK) cell; (f) decreases the number of regulatory T cells in a tissue or in circulation; (g) inhibits the suppression of an effector T cell by a regulatory T cell; (h) does not bind specifically to any of PVRL1, PVRL2, PVRL3, or PVRL4; (i) specifically binds cynomolgus monkey TIGIT (cTIGIT; SEQ ID NO: 2); or (j) binds murine TIGIT (mTIGIT; SEQ ID NO: 3) with an affinity lower (as indicated by higher K_D) than the affinity of the ABP for hTIGIT, or does not bind mTIGIT. In some embodiments, an ABP provided herein has two or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has three or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has four or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has five or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has six or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has seven or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has eight or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has nine or more of the characteristics listed in the foregoing (a)-(j). In some embodiments, an ABP provided herein has all ten of the characteristics listed in the foregoing (a)-(j).

[0257] In some embodiments, an ABP provided herein exhibits a combination of the characteristics listed in the following (a)-(j): (a) competes for binding to TIGIT with an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure; (b) inhibits binding of CD155 to TIGIT; (c) inhibits binding of CD112 to TIGIT; (d) inhibits association of CD226 with TIGIT; (e) activates an effector T cell or a natural killer (NK) cell; (f) decreases the number of regulatory T cells in a tissue or in circulation; (g) inhibits the suppression of an effector T cell by a regulatory T cell; (h) does not bind specifically to any of PVRL1, PVRL2, PVRL3, or PVRL4; (i) specifically binds cynomolgus monkey TIGIT (cTIGIT; SEQ ID NO: 2); or (j) binds murine TIGIT (mTIGIT; SEQ ID NO: 3) with an affinity lower (as indicated by higher K_D) than the affinity of the ABP for hTIGIT, or does not bind mTIGIT. In some embodiments, such ABP exhibits a combination of the characteristics selected from (a and b), (a and c), (a and d), (a and e), (a and f), (a and g), (a and h), (a and i), (a and j), (b and a), (b and c), (b and d), (b and e), (b and f), (b and g), (b and h), (b and i), (b and j), (c and a), (c and b), (c and d), (c and e), (c and f), (c and g), (c and h), (c and i), (c and j), (d and a), (d and b), (d and c), (d and e), (d and f), (d and g), (d and h), (d and i), (d and j), (e and a), (e and b), (e and c), (e and d), (e and f), (e and g), (e and h), (e and i), (e and j), (f and a), (f and b), (f and c), (f and d), (f and e), (f and g), (f and h), (f and i), (f and j), (g and a), (g and b), (g and c), (g and d), (g and e), (g and f), (g and h), (g and i), (g and j), (h and a), (h and b), (h and c), (h and d), (h and e), (h and f), (h and g), (h and i), (h and j), (i and a), (i and b), (i and c), (i and d), (i and e), (i and f), (i and g), (i and h), (i and j), (j and a), (j and b), (j and c), (j and d), (j and e), (j and f), (j and g), (j and h), and (j and i). In some embodiments, such ABP exhibits a combination of the characteristics selected from (a and b and c), (a and b and d), (a and b and e), (a and b and f), (a and b and g), (a and b and

[illegible]

[illegible]

and b and j), (h and b and a), (h and c and b), (h and c and d), (h and c and e), (h and c and f), (h and c and g), (h and c and i), (h and c and j), (h and d and a), (h and d and b), (h and d and c), (h and d and e), (h and d and f), (h and d and g), (h and d and i), (h and d and j), (h and e and a), (h and e and b), (h and e and c), (h and e and d), (h and e and f), (h and e and g), (h and e and i), (h and e and j), (h and f and a), (h and f and b), (h and f and c), (h and f and d), (h and f and e), (h and f and g), (h and f and i), (h and f and j), (h and g and a), (h and g and b), (h and g and c), (h and g and d), (h and g and e), (h and g and f), (h and g and i), (h and g and j), (h and i and a), (h and i and b), (h and i and c), (h and i and d), (h and i and e), (h and i and f), (h and i and g), (h and i and j), (h and j and a), (h and j and b), (h and j and c), (h and j and d), (h and j and e), (h and j and f), (h and j and g), (h and j and i), (h and j and a), (i and a and b), (i and a and c), (i and a and d), (i and a and e), (i and a and f), (i and a and g), (i and a and h), (i and a and j), (i and b and a), (i and b and c), (i and b and d), (i and b and e), (i and b and f), (i and b and g), (i and b and h), (i and b and j), (i and c and a), (i and c and b), (i and c and d), (i and c and e), (i and c and f), (i and c and g), (i and c and h), (i and c and j), (i and d and a), (i and d and b), (i and d and c), (i and d and e), (i and d and f), (i and d and g), (i and d and h), (i and d and j), (i and e and a), (i and e and b), (i and e and c), (i and e and d), (i and e and f), (i and e and g), (i and e and h), (i and e and j), (i and f and a), (i and f and b), (i and f and c), (i and f and d), (i and f and e), (i and f and g), (i and f and h), (i and f and j), (i and g and a), (i and g and b), (i and g and c), (i and g and d), (i and g and e), (i and g and f), (i and g and h), (i and g and j), (i and h and a), (i and h and b), (i and h and c), (i and h and d), (i and h and e), (i and h and f), (i and h and g), (i and h and j), (i and j and a), (i and j and b), (i and j and c), (i and j and d), (i and j and e), (i and j and f), (i and j and g), (i and j and h), (j and a and i), (j and a and b), (j and a and c), (j and a and d), (j and a and e), (j and a and f), (j and a and g), (j and a and h), (j and b and i), (j and b and a), (j and b and c), (j and b and d), (j and b and e), (j and b and f), (j and b and g), (j and b and h), (j and c and i), (j and c and a), (j and c and b), (j and c and d), (j and c and e), (j and c and f), (j and c and g), (j and c and h), (j and d and i), (j and d and a), (j and d and b), (j and d and c), (j and d and e), (j and d and f), (j and d and g), (j and d and h), (j and e and i), (j and e and a), (j and e and b), (j and e and c), (j and e and d), (j and e and f), (j and e and g), (j and e and h), (j and f and i), (j and f and a), (j and f and b), (j and f and c), (j and f and d), (j and f and e), (j and f and g), (j and f and h), (j and g and i), (j and g and a), (j and g and b), (j and g and c), (j and g and d), (j and g and e), (j and g and f), (j and g and h), (j and h and i), (j and h and a), (j and h and b), (j and h and c), (j and h and d), (j and h and e), (j and h and f), (j and h and g), (j and i and h), (j and i and a), (j and i and b), (j and i and c), (j and i and d), (j and i and e), (j and i and f), and (j and i and g).

2.3. Germlines

[0258] The ABPs provided herein may comprise any suitable V_H and V_L germline sequences.

[0259] In some examples, the V_H region of an ABP provided herein is from the VH4 germline.

In some examples, the V_H region of an ABP provided herein is from the VH1 germline.

[0260] In some embodiments, the V_H region of an ABP provided herein is from the VH4-39 germline. In some embodiments, the V_H region of an ABP provided herein is from the VH4-31 germline. In some examples, the V_H region of an ABP provided herein is from the VH1-46 germline.

[0261] In some examples, the V_L region of an ABP provided herein is from the VK3 germline.

[0262] In some examples, the V_L region of an ABP provided herein is from the VK3-11 germline. In some embodiments, the V_L region of an ABP provided herein is from the VK3-20 germline. In some examples, the V_L region of an ABP provided herein is from the VK3-15 germline.

2.4. Monospecific and Multispecific TIGIT Antigen-Binding Proteins

[0263] In some embodiments, the ABPs provided herein are monospecific ABPs.

[0264] In some embodiments, the ABPs provided herein are multispecific ABPs.

[0265] In some embodiments, a multispecific ABP provided herein binds more than one antigen. In some embodiments, a multispecific antibody binds 2 antigens. In some embodiments, a multispecific antibody binds 3 antigens. In some embodiments, a multispecific antibody binds 4 antigens. In some embodiments, a multispecific antibody binds 5 antigens.

[0266] In some embodiments, a multispecific antibody provided herein binds more than one epitope on a TIGIT antigen. In some embodiments, a multispecific antibody binds 2 epitopes on a TIGIT antigen. In some embodiments, a multispecific antibody binds 3 epitopes on a TIGIT antigen.

[0267] Many multispecific ABP constructs are known in the art, and the ABPs provided herein may be provided in the form of any suitable multispecific suitable construct.

[0268] In some embodiments, the multispecific ABP comprises an immunoglobulin comprising at least two different heavy chain variable regions each paired with a common light chain variable region (i.e., a "common light chain antibody"). The common light chain variable region forms a distinct antigen-binding domain with each of the two different heavy chain variable regions. See Merchant et al., Nature Biotechnol., 1998, 16:677-681.

[0269] In some embodiments, the multispecific ABP comprises an immunoglobulin comprising an antibody or fragment thereof attached to one or more of the N- or C-termini of the heavy or light chains of such immunoglobulin. See Coloma and Morrison, Nature Biotechnol., 1997, 15:159-163. In some aspects, such ABP comprises a tetravalent bispecific antibody.

[0270] In some embodiments, the multispecific ABP comprises a hybrid immunoglobulin comprising at least two different heavy chain variable regions and at least two different light chain variable regions. See Milstein and Cuello, *Nature*, 1983, 305:537-540; and Staerz and Bevan, *Proc. Natl. Acad. Sci. USA*, 1986, 83:1453-1457.

[0271] In some embodiments, the multispecific ABP comprises immunoglobulin chains with alterations to reduce the formation of side products that do not have multispecificity. In some aspects, the ABPs comprise one or more "knobs-into-holes" modifications as described in U.S. Pat. No. 5,731,168.

[0272] In some embodiments, the multispecific ABP comprises immunoglobulin chains with one or more electrostatic modifications to promote the assembly of Fc hetero-multimers. See WO 2009/089004.

[0273] In some embodiments, the multispecific ABP comprises a bispecific single chain molecule. See Traunecker et al., *EMBO J.*, 1991, 10:3655-3659; and Gruber et al., *J. Immunol.*, 1994, 152:5368-5374.

[0274] In some embodiments, the multispecific ABP comprises a heavy chain variable domain and a light chain variable domain connected by a polypeptide linker, where the length of the linker is selected to promote assembly of multispecific ABPs with the desired multispecificity. For example, monospecific scFvs generally form when a heavy chain variable domain and light chain variable domain are connected by a polypeptide linker of more than 12 amino acid residues. See U.S. Pat. Nos. 4,946,778 and 5,132,405. In some embodiments, reduction of the polypeptide linker length to less than 12 amino acid residues prevents pairing of heavy and light chain variable domains on the same polypeptide chain, thereby allowing pairing of heavy and light chain variable domains from one chain with the complementary domains on another chain. The resulting ABPs therefore have multispecificity, with the specificity of each binding site contributed by more than one polypeptide chain. Polypeptide chains comprising heavy and light chain variable domains that are joined by linkers between 3 and 12 amino acid residues form predominantly dimers (termed diabodies). With linkers between 0 and 2 amino acid residues, trimers (termed triabodies) and tetramers (termed tetrabodies) are favored. However, the exact type of oligomerization appears to depend on the amino acid residue composition and the order of the variable domain in each polypeptide chain (e.g., V_H-linker-V_L vs. V_L-linker-V_H), in addition to the linker length. A skilled person can select the appropriate linker length based on the desired multispecificity.

[0275] In some embodiments, the multispecific ABP comprises a diabody. See Hollinger et al., *Proc. Natl. Acad. Sci. USA*, 1993, 90:6444-6448. In some embodiments, the multispecific ABP comprises a triabody. See Todorovska et al., *J. Immunol. Methods*, 2001, 248:47-66. In some embodiments, the multispecific ABP comprises a tetrabody. See *id.*.

[0276] In some embodiments, the multispecific ABP comprises a trispecific F(ab')₃ derivative. See Tutt et al. *J. Immunol.*, 1991, 147:60-69.

[0277] In some embodiments, the multispecific ABP comprises a cross-linked antibody. See U.S. Patent No. 4,676,980; Brennan et al., *Science*, 1985, 229:81-83; Staerz, et al. *Nature*, 1985, 314:628-631; and EP 0453082.

[0278] In some embodiments, the multispecific ABP comprises antigen-binding domains assembled by leucine zippers. See Kostelny et al., *J. Immunol.*, 1992, 148:1547-1553.

[0279] In some embodiments, the multispecific ABP comprises complementary protein domains. In some aspects, the complementary protein domains comprise an anchoring domain (AD) and a dimerization and docking domain (DDD). In some embodiments, the AD and DDD bind to each other and thereby enable assembly of multispecific ABP structures via the "dock and lock" (DNL) approach. ABPs of many specificities may be assembled, including bispecific ABPs, trispecific ABPs, tetraspecific ABPs, quintspecific ABPs, and hexaspecific ABPs. Multispecific ABPs comprising complementary protein domains are described, for example, in U.S. Pat. Nos. 7,521,056; 7,550,143; 7,534,866; and 7,527,787.

[0280] In some embodiments, the multispecific ABP comprises a dual action Fab (DAF) antibody as described in U.S. Pat. Pub. No. 2008/0069820.

[0281] In some embodiments, the multispecific ABP comprises an antibody formed by reduction of two parental molecules followed by mixing of the two parental molecules and reoxidation to assembly a hybrid structure. See Carling et al., *PLoS One*, 2011, 6:e22533.

[0282] In some embodiments, the multispecific ABP comprises a DVD-Ig[™]. A DVD-Ig[™] is a dual variable domain immunoglobulin that can bind to two or more antigens. DVD-Igs[™] are described in U.S. Pat. No. 7,612,181.

[0283] In some embodiments, the multispecific ABP comprises a DART[™]. DARTs[™] are described in Moore et al., *Blood*, 2011, 117:454-451.

[0284] In some embodiments, the multispecific ABP comprises a DuoBody[®]. DuoBodies[®] are described in Labrijn et al., *Proc. Natl. Acad. Sci. USA*, 2013, 110:5145-5150; Gramer et al., *mAbs*, 2013, 5:962-972; and Labrijn et al., *Nature Protocols*, 2014, 9:2450-2463.

[0285] In some embodiments, the multispecific ABP comprises an antibody fragment attached to another antibody or fragment. The attachment can be covalent or non-covalent. When the attachment is covalent, it may be in the form of a fusion protein or via a chemical linker. Illustrative examples of multispecific ABPs comprising antibody fragments attached to other antibodies include tetravalent bispecific antibodies, where an scFv is fused to the C-terminus of the C_H3 from an IgG. See Coloma and Morrison, *Nature Biotechnol.*, 1997, 15:159-163. Other examples include antibodies in which a Fab molecule is attached to the constant region of an immunoglobulin. See Miler et al., *J. Immunol.*, 2003, 170:4854-4861. Any suitable fragment

may be used, including any of the fragments described herein or known in the art.

[0286] In some embodiments, the multispecific ABP comprises a CovX-Body. CovX-Bodies are described, for example, in Doppalapudi et al., Proc. Natl. Acad. Sci. USA, 2010, 107:22611-22616.

[0287] In some embodiments, the multispecific ABP comprises an Fcab antibody, where one or more antigen-binding domains are introduced into an Fc region. Fcab antibodies are described in Wozniak-Knopp et al., Protein Eng. Des. Sel., 2010, 23:289-297.

[0288] In some embodiments, the multispecific ABP comprises an TandAb[®] antibody. TandAb[®] antibodies are described in Kipriyanov et al., J. Mol. Biol., 1999, 293:41-56 and Zhukovsky et al., Blood, 2013, 122:5116.

[0289] In some embodiments, the multispecific ABP comprises a tandem Fab. Tandem Fabs are described in WO 2015/103072.

[0290] In some embodiments, the multispecific ABP comprises a Zyboby[™]. Zybodies[™] are described in LaFleur et al., mAbs, 2013, 5:208-218.

2.5. TIGIT Antagonism

[0291] In some embodiments, the ABPs provided herein antagonize TIGIT upon binding.

[0292] In some embodiments, antagonism of TIGIT by an ABP provided herein results in dimerization and/or activation of CD226 (also known as DNAM-1), a co-stimulatory receptor whose dimerization and function is impaired by direct interaction with TIGIT. See Grogan et al., J. Immunol., 2014, 192 (1 Supplement) 2013.15. Figure 2 provides an illustration of the CD226-TIGIT pathway in comparison to the CD28/CTLA4 pathway, which has similar costimulation/coinhibition biology.

[0293] In some embodiments, antagonism of TIGIT by an ABP provided herein increases the amount of CD226 and CD155 that interact in comparison to the amount that interact in the absence of the ABP.

[0294] In some embodiments, antagonism of TIGIT by an ABP provided herein results in activation of an effector T cell. In some aspects, the effector T cell is a CD8+ T cell. In some aspects, the effector T cell is a CD4+ T cell.

[0295] In some embodiments, antagonism of TIGIT by an ABP provided herein results in activation of an NK cell. In some embodiments, antagonism of TIGIT by an ABP provided herein results in activation of an NKT cell.

[0296] In some embodiments, antagonism of TIGIT by an ABP provided herein results in a reduction of the inhibitory activity of a regulatory T cell toward an effector T cell.

[0297] In some embodiments, antagonism of TIGIT by an ABP provided herein results in increased secretion of IL-2, IL-6, GM-CSF, TNF, LT- α , and/or IFN- γ by a target cell.

[0298] In some embodiments, antagonism of TIGIT by an ABP provided herein increases the proliferation, survival, and/or function of an effector T cell. In some aspects the effector T cell is a CD4⁺ effector T cell. In some aspects, the effector T cell is a CD8⁺ effector T cell.

[0299] In some embodiments, antagonism of TIGIT by an ABP provided herein abrogates suppression of an effector T cell by a regulatory T cell. In some aspects, the regulatory T cell is a CD4⁺CD25⁺Foxp3⁺ regulator T cell. In some aspects, the regulatory T cell is a CD8⁺CD25⁺ regulatory T cell.

[0300] In some embodiments, antagonism of TIGIT by an ABP provided herein results in an enhancement of an immune response.

[0301] In some embodiments, antagonism of TIGIT by an ABP provided herein results in the prevention of a tumor. In some embodiments, antagonism of TIGIT by an ABP provided herein results in the delay of onset of a tumor. In some embodiments, antagonism of TIGIT by an ABP provided herein results in a reduction of the size of a tumor. In some embodiments, antagonism of TIGIT by an ABP provided herein results in elimination of a tumor. In some embodiments, antagonism of TIGIT by an ABP provided herein results in a reduction in the number of metastases.

[0302] In some embodiments, antagonism of TIGIT by an ABP provided herein results in the prevention of a viral disease. In some embodiments, antagonism of TIGIT by an ABP provided herein results in the delay of onset of a viral disease. In some embodiments, antagonism of TIGIT by an ABP provided herein results in a reduction of the viral load in a subject. In some embodiments, antagonism of TIGIT by an ABP provided herein results in the elimination of a viral infection.

2.6. Affinity and Kinetics of Antigen-Binding Proteins for TIGIT; Potency

[0303] In some embodiments, the affinity of an ABP provided herein for TIGIT as indicated by K_D , is less than about 10^{-5} M, less than about 10^{-6} M, less than about 10^{-7} M, less than about 10^{-8} M, less than about 10^{-9} M, less than about 10^{-10} M, less than about 10^{-11} M, or less than about 10^{-12} M. In some embodiments, the affinity of the ABP is between about 10^{-7} M and 10^{-12} M. In some embodiments, the affinity of the ABP is between about 10^{-7} M and 10^{-11} M. In some embodiments, the affinity of the ABP is between about 10^{-7} M and 10^{-10} M. In some

embodiments, the affinity of the ABP is between about 10^{-7} M and 10^{-9} M. In some embodiments, the affinity of the ABP is between about 10^{-7} M and 10^{-8} M. In some embodiments, the affinity of the ABP is between about 10^{-8} M and 10^{-12} M. In some embodiments, the affinity of the ABP is between about 10^{-8} M and 10^{-11} M. In some embodiments, the affinity of the ABP is between about 10^{-9} M and 10^{-11} M. In some embodiments, the affinity of the ABP is between about 10^{-10} M and 10^{-11} M.

[0304] In some embodiments, the affinity of an ABP provided herein for hTIGIT as indicated by K_D measured by ForteBio, as set forth in Example 4 is selected from about 5.24×10^{-10} M, about 4.57×10^{-10} M, about 3.32×10^{-10} M, about 2.46×10^{-10} M, about 1.96×10^{-10} M, about 3.11×10^{-9} M, about 2.54×10^{-9} M, about 3.13×10^{-9} M, about 2.83×10^{-9} M, about 1.71×10^{-9} M, about 2.47×10^{-9} M, about 2.35×10^{-9} M, about 1.44×10^{-9} M, about 1.23×10^{-9} M, about 5.26×10^{-10} M, about 3.78×10^{-10} M, about 4.29×10^{-10} M, or about 4.48×10^{-10} M. In some embodiments, such affinity ranges from about 3.13×10^{-9} M to about 1.96×10^{-10} M. In some embodiments, such K_D is about 3.13×10^{-9} M or less.

[0305] In some embodiments, the affinity of an ABP provided herein for cTIGIT as indicated by K_D measured by ForteBio, as set forth in Example 4 is selected from about 2.64×10^{-9} M, about 6.55×10^{-9} M, about 8.14×10^{-9} M, about 6.57×10^{-9} M, about 7.94×10^{-8} M, about 7.04×10^{-8} M, about 1.10×10^{-7} M, about 7.20×10^{-8} M, about 1.57×10^{-9} M, about 8.02×10^{-10} M, about 3.67×10^{-10} M, about 8.98×10^{-10} M, about 1.75×10^{-8} M, or about 2.58×10^{-8} M, about 9.35×10^{-9} M. In some embodiments, such affinity ranges from about 1.10×10^{-7} M to about 3.69×10^{-10} M. In some embodiments, such K_D is about 1.10×10^{-7} M or less.

[0306] In some embodiments, the affinity of an ABP provided herein for hTIGIT as indicated by K_D measured by solution equilibrium methods (MSD-SET), as set forth in Example 4 is selected from about 5.40×10^{-11} M, about 1.10×10^{-10} M, about 1.50×10^{-10} M, about 5.60×10^{-11} M, about 4.00×10^{-10} M, about 3.80×10^{-10} M, about 2.10×10^{-10} M, about 7.00×10^{-11} M, about 4.10×10^{-11} M, about 2.50×10^{-11} M, about 3.00×10^{-11} M, about 8.00×10^{-11} M, about 8.10×10^{-12} M, about 5.00×10^{-12} M, or about 4.90×10^{-12} M. In some embodiments, such affinity ranges from about 4.00×10^{-10} M to about 4.90×10^{-12} M. In some embodiments, such K_D is about 4.00×10^{-10} M or less.

[0307] In some embodiments, the affinity of an ABP provided herein for cTIGIT as indicated by K_D measured by MSD-SET, as set forth in Example 4 is selected from about 3.20×10^{-10} M, about 2.30×10^{-10} M, about 3.50×10^{-11} M, about 1.50×10^{-11} M, or about 4.60×10^{-11} M. In

some embodiments, such affinity ranges from about 3.20×10^{-10} M to about 1.50×10^{-11} M. In some embodiments, such K_D is about 3.20×10^{-10} M or less.

[0308] In some embodiments, the affinity of an ABP provided herein for hTIGIT as indicated by K_D measured by ForteBio, as set forth in Example 6 is selected from about 7.1×10^{-10} M, about 8.1×10^{-11} M, about 1.9×10^{-10} M, about 5.6×10^{-10} M, about 2.4×10^{-10} M, about 2.8×10^{-10} M, about 1.6×10^{-10} M, about 5.8×10^{-10} M, about 1.1×10^{-9} M, about 8.1×10^{-10} M, about 4.6×10^{-10} M, or about 3.6×10^{-10} M. In some embodiments, such affinity ranges from about 1.1×10^{-9} M to about 8.1×10^{-11} M. In some embodiments, such K_D is about 1.1×10^{-9} M or less.

[0309] In some embodiments, the affinity of an ABP provided herein for hTIGIT as indicated by K_D measured by ForteBio, as set forth in Example 6, is about 2.4×10^{-10} M. In some embodiments, the affinity of an ABP provided herein for cTIGIT as indicated by K_D measured by ForteBio, as set forth in Example 6, is about 6.2×10^{-9} M. In some embodiments, such K_D is about 6.2×10^{-9} M or less.

[0310] In some embodiments, the affinity of an ABP provided herein for hTIGIT expressed on the surface of a Jurkat cell, as indicated by K_D , described in Example 6 is about 5.1×10^{-10} M. In some embodiments, such K_D is about 5.1×10^{-10} M or less.

[0311] In some embodiments, the affinity of an ABP provided herein for cTIGIT expressed on the surface of a Jurkat cell, as indicated by K_D , described in Example 6 is about 4.0×10^{-10} M. In some embodiments, such K_D is about 4.0×10^{-10} M or less.

[0312] In some embodiments, the affinity of an ABP provided herein for mTIGIT (SEQ ID NO: 3) expressed on the surface of a Jurkat cell, as indicated by K_D , described in Example 6 is about 9.8×10^{-9} M. In some embodiments, such K_D is about 9.8×10^{-9} M or less. In some embodiments, such K_D is about 9.8×10^{-9} M or greater.

[0313] In some embodiments, the affinity of an ABP provided herein for hTIGIT expressed on the surface of a human CD8+ T cell, as indicated by K_D , described in Example 6 is about 1.3×10^{-9} M. In some embodiments, such K_D is about 1.3×10^{-9} M or less.

[0314] In some embodiments, the affinity of an ABP provided herein for cTIGIT expressed on the surface of a cynomolgus monkey CD8+ T cell, as indicated by K_D , described in Example 6 is about 2.8×10^{-9} M. In some embodiments, such K_D is about 2.8×10^{-9} M or less.

[0315] In some embodiments, the affinity of an ABP provided herein for mTIGIT expressed on the surface of a murine T regulatory cell (i.e., mTIGIT as it naturally occurs on such cells, whether or not such mTIGIT is of SEQ ID NOs: 3 or 138, but inclusive of such SEQ ID NOs), as indicated by K_D , described in Example 6 is about 2.5×10^{-8} M. In some embodiments, such K_D is about 2.5×10^{-8} M or less.

[0316] In some embodiments, the ABPs provided herein specifically bind to hTIGIT (SEQ ID NO:1) with a K_D of X and to cTIGIT (SEQ ID NO:2) or mTIGIT (SEQ ID NO:3 or 138) with a K_D of $\leq 10X$. In some embodiments, the ABPs provided herein specifically bind to hTIGIT (SEQ ID NO:1) with a K_D of X and to cTIGIT (SEQ ID NO:2) or mTIGIT (SEQ ID NO:3 or 138) with a K_D of $\leq 5X$. In some embodiments, the ABPs provided herein specifically bind to hTIGIT (SEQ ID NO:1) with a K_D of X and to cTIGIT (SEQ ID NO:2) or mTIGIT (SEQ ID NO:3 or 138) with a K_D of $\leq 2X$. In some aspects, X is any K_D described in this disclosure. In some aspects, X is 0.01 nM, 0.1 nM, 1 nM, 10 nM, 20 nM, 50 nM, or 100 nM.

[0317] In some embodiments, the ratio of $K_{D(hTIGIT)} : K_{D(cTIGIT)}$ for an ABP provided herein, as measured by ForteBio as set forth in Example 4, is selected from about 1.98×10^{-1} , about 2.61×10^{-1} , about 3.03×10^{-1} , about 3.58×10^{-1} , about 6.62×10^{-3} , about 1.98×10^{-1} , about 5.37×10^{-3} , about 3.90×10^{-3} , about 6.22×10^{-3} , about 2.91×10^{-1} , about 4.14×10^{-1} , about 6.67×10^{-1} , about 2.18×10^{-1} , about 1.78×10^{-1} , about 1.21×10^{-1} , or about 3.03×10^{-1} . In some embodiments, such ratio ranges from about 3.90×10^{-3} to about 6.67×10^{-1} .

[0318] In some embodiments, the ratio of $K_{D(hTIGIT)} : K_{D(cTIGIT)}$ for an ABP provided herein, as measured by ForteBio as set forth in Example , is about 3.87×10^{-2} .

[0319] In some embodiments, the ratio of $K_{D(hTIGIT)} : K_{D(cTIGIT)}$ for an ABP provided herein, as measured by MSD-SET as set forth in Example 4, is selected from about 3.33×10^{-1} , about 2.31×10^{-1} , about 1.09×10^{-1} , about 1.07×10^{-1} , or about 1.69×10^{-1} . In some embodiments, such ratio ranges from about 1.07×10^{-1} M to about 3.33×10^{-1} M.

[0320] In some embodiments an ABP provided herein has a k_a of at least about $10^4 \text{ M}^{-1} \times \text{sec}^{-1}$. In some embodiments the ABP has a k_a of at least about $10^5 \text{ M}^{-1} \times \text{sec}^{-1}$. In some embodiments the ABP has a k_a of at least about $10^6 \text{ M}^{-1} \times \text{sec}^{-1}$. In some embodiments the ABP has a k_a of between about $10^4 \text{ M}^{-1} \times \text{sec}^{-1}$ and about $10^5 \text{ M}^{-1} \times \text{sec}^{-1}$. In some embodiments the ABP has a k_a of between about $10^5 \text{ M}^{-1} \times \text{sec}^{-1}$ and about $10^6 \text{ M}^{-1} \times \text{sec}^{-1}$. In some embodiments, such k_a is at least about $10^5 \text{ M}^{-1} \times \text{sec}^{-1}$.

[0321] In some embodiments, an ABP provided herein has a k_a for hTIGIT, as measured by

ForteBio as set forth in Example 6, selected from about $3.2 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, about $7.0 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, about $7.7 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, about $1.6 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, about $2.0 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, about $1.3 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, about $1.5 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, about $1.1 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, about $4.5 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, about $7.5 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, about $8.9 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, or about $1.4 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$. In some embodiments, such k_a ranges from about $3.2 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$ to about $2.0 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$. In some embodiments, such k_d is about $2.0 \times 10^6 \text{ M}$ or less.

[0322] In some embodiments, an ABP provided herein has a k_a for hTIGIT, as measured by ForteBio as set forth in Example 6, of about $2.0 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$. In some embodiments, such k_a is at least about $2.0 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$.

[0323] In some embodiments, an ABP provided herein has a k_a for cTIGIT, as measured by ForteBio as set forth in Example 6, of about $7.9 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$. In some embodiments, such k_a is at least about $7.9 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$.

[0324] In some embodiments an ABP provided herein has a k_d of about 10^{-5} sec^{-1} or less. In some embodiments the ABP has a k_d of about 10^{-4} sec^{-1} or less. In some embodiments the ABP has a k_d of about 10^{-3} sec^{-1} or less. In some embodiments the ABP has a k_d of between about 10^{-2} sec^{-1} and about 10^{-5} sec^{-1} . In some embodiments the ABP has a k_d of between about 10^{-2} sec^{-1} and about 10^{-4} sec^{-1} . In some embodiments the ABP has a k_d of between about 10^{-3} sec^{-1} and about 10^{-5} sec^{-1} .

[0325] In some embodiments, an ABP provided herein has a k_d , for hTIGIT, as measured by ForteBio as set forth in Example 6, selected from about $2.3 \times 10^{-4} \text{ sec}^{-1}$, about $6.3 \times 10^{-5} \text{ sec}^{-1}$, about $1.4 \times 10^{-4} \text{ sec}^{-1}$, about $8.5 \times 10^{-4} \text{ sec}^{-1}$, about $3.8 \times 10^{-4} \text{ sec}^{-1}$, about $3.5 \times 10^{-4} \text{ sec}^{-1}$, about $2.4 \times 10^{-4} \text{ sec}^{-1}$, about $6.6 \times 10^{-4} \text{ sec}^{-1}$, about $5.9 \times 10^{-4} \text{ sec}^{-1}$, or about $5.0 \times 10^{-4} \text{ sec}^{-1}$. In some embodiments, such k_d ranges from about $6.3 \times 10^{-5} \text{ sec}^{-1}$ to about $8.5 \times 10^{-4} \text{ sec}^{-1}$. In some embodiments, such k_d is less than about $8.5 \times 10^{-4} \text{ sec}^{-1}$.

[0326] In some embodiments, an ABP provided herein has a k_d for hTIGIT, as measured by ForteBio as set forth in Example 6, of about $3.8 \times 10^{-4} \text{ sec}^{-1}$. In some embodiments, such k_d is less than about $3.8 \times 10^{-4} \text{ sec}^{-1}$.

[0327] In some embodiments, an ABP provided herein has a k_d for cTIGIT, as measured by ForteBio as set forth in Example 6, of about $4.6 \times 10^{-3} \text{ sec}^{-1}$. In some embodiments, such k_d is less than about $4.6 \times 10^{-3} \text{ sec}^{-1}$.

[0328] In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $3.2 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $2.3 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $7.1 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $7.0 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $6.3 \times 10^5 \text{ sec}^{-1}$, and a K_D for hTIGIT of about $8.1 \times 10^{-11} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $7.7 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $1.4 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $1.9 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $1.6 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $8.5 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $5.6 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $2.0 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $3.8 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $2.4 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $1.3 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $3.5 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $2.8 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $1.5 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $2.4 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $1.6 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $1.1 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $6.6 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $5.8 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $4.5 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $3.5 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $1.1 \times 10^{-9} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $7.5 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $5.9 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $8.1 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $8.9 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $3.8 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $4.6 \times 10^{-10} \text{ M}$. In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $1.4 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $5.0 \times 10^{-4} \text{ sec}^{-1}$, and a K_D for hTIGIT of about $3.6 \times 10^{-10} \text{ M}$. In some embodiments, such k_a , k_d and K_D are determined according to the methods provided in Example 6.

[0329] In some embodiments, an ABP provided herein has a k_a for hTIGIT of about $2.0 \times 10^6 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for hTIGIT of about $3.8 \times 10^{-4} \text{ sec}^{-1}$, a K_D for hTIGIT of about $2.4 \times 10^{-10} \text{ M}$, a k_a for cTIGIT of about $7.9 \times 10^5 \text{ M}^{-1}\text{sec}^{-1}$, a k_d for cTIGIT of about $4.6 \times 10^{-3} \text{ sec}^{-1}$, a K_D for cTIGIT of about $6.2 \times 10^{-9} \text{ M}$, and a K_D for mTIGIT (SEQ ID NO: 3) of greater than about $7.0 \times 10^{-7} \text{ M}$. In some embodiments, such k_a , k_d and K_D are determined according to the methods

provided in Example 6.

[0330] In some embodiments, K_D , k_a , and k_d are determined using surface plasmon resonance (SPR). In some aspects, the SPR analysis utilizes a BIACORE[®] instrument. In some aspects, the antigen is immobilized on a carboxymethylated dextran biosensor chip (CM4 or CM5) and contacted with an ABP provided herein. Association and dissociation rate constants may be calculated using the BIAevaluation[®] software and a one-to-one Langmuir binding model. In some aspects, the assay is performed at 25°C. In some aspects, the assay is performed at 37°C.

[0331] In some embodiments, K_D , k_a , and k_d are determined using biolayer interferometry (BLI). Any suitable BLI method may be used. In some aspects, the BLI analysis utilizes a FORTEBIO[®] instrument. In some aspects, an anti-human IgG Fc capture (AHC) biosensor is used to capture ABPs onto the surface of a sensor. Subsequently, association of the ABP and antigen is monitored by contacting the immobilized ABP with different concentrations of TIGIT. Dissociation of the antigen and ABP is then measured in a buffer without TIGIT. Association and dissociation rate constants are calculated using the kinetic modules of the FORTEBIO[®] Analysis Software. In some aspects, the assay is performed at 30°C.

[0332] In other embodiments, K_D may be determined by a radiolabeled antigen-binding assay, as described in Chen et al. J. Mol. Biol., 1999, 293:865-881.

[0333] In other embodiments, K_D may be determined by using MSD-SET, as described in Example 4.

[0334] In some embodiments, an ABP provided herein has an EC_{50} , as measured by IL-2 production in a human TIGIT Jurkat co-culture assay as described in Example 7, of about 0.22 nM, about 0.31 nM, about 0.33 nM, about 0.34 nM, about 0.25 nM, about 0.24 nM, about 0.11 nM, about 0.06 nM, about 0.14 nM, about 0.16 nM, about 1.40 nM, about 0.71 nM, about 0.21 nM, about 1.11 nM, about 0.13 nM, about 0.20 nM, about 0.68 nM, or about 0.61 nM. In some embodiments, such EC_{50} ranges from about 0.06 nM to about 1.40 nM. In some embodiments, such EC_{50} is about 1.40 nM or less.

[0335] In some embodiments, an ABP provided herein has an EC_{50} , as measured by IL-2 production in a cynomolgus monkey TIGIT Jurkat co-culture assay as described in Example 7, of about 2.87 nM. In some embodiments, such EC_{50} is about 2.87 nM or less. In some embodiments, the ratio of $EC_{50(cTIGIT)} : EC_{50(hTIGIT)}$ in such assay ranges from about 2.05 to about 47.8.

[0336] In some embodiments, an ABP provided herein has an EC_{10} , as measured by TNF production in PBMCs isolated from a human donor and treated as described in Example 9, in a

range of about 5.02 nM to about 18.86 nM. In some embodiments, such EC₁₀ is about 18.86 nM or less.

[0337] In some embodiments, an ABP provided herein has an EC₅₀, as measured by TNF production in PBMCs isolated from a human donor and treated as described in Example 9, in a range of about 12.60 nM to about 20.60 nM. In some embodiments, such EC₅₀ is about 20.60 nM or less.

[0338] In some embodiments, an ABP provided herein has an EC₉₀, as measured by TNF production in PBMCs isolated from a human donor and treated as described in Example 9, in a range of about 22.49 nM to about 31.59 nM. In some embodiments, such EC₉₀ is about 31.59 nM or less.

[0339] In some embodiments, an ABP provided herein has an EC₁₀ in a range of about 5.02 nM to about 18.86 nM, an EC₅₀ in a range of about 12.60 nM to about 20.60 nM, and EC₉₀ in a range of about 22.49 nM to about 31.59 nM, in each cases as measured by TNF production in PBMCs isolated from a human donor and treated as described in Example 9.

[0340] In some embodiments, an ABP provided herein has an EC₁₀ of about 11.94 nM or less, an EC₅₀ of about 16.60 nM or less, and EC₉₀ of about 27.04 nM or less, in each cases as measured by TNF production in PBMCs isolated from a human donor and treated as described in Example 9.

[0341] In some embodiments, an ABP provided herein has an EC₁₀ of about 18.86 nM or less, an EC₅₀ of about 20.06 nM or less, and EC₉₀ of about 31.59 nM or less, in each cases as measured by TNF production in PBMCs isolated from a human donor and treated as described in Example 9.

[0342] In some embodiments, an ABP provided herein has an EC₁₀ of about 5.02 nM or less, an EC₅₀ of about 12.60 nM or less, and EC₉₀ of about 22.49 nM or less, in each cases as measured by TNF production in PBMCs isolated from a human donor and treated as described in Example 9.

[0343] In some embodiments, an ABP provided herein has an EC₁₀, as measured by IFN- γ production in CD4+ T cells isolated from a human donor and treated as described in Example 9, in a range of about 0.37 nM to about 1.05 nM. In some embodiments, such EC₁₀ is about 1.05 nM or less.

[0344] In some embodiments, an ABP provided herein has an EC₅₀, as measured by IFN- γ production in CD4+ T cells isolated from a human donor and treated as described in Example 9, in a range of about 0.94 nM to about 1.12 nM. In some embodiments, such EC₅₀ is about 1.12 nM or less.

[0345] In some embodiments, an ABP provided herein has an EC₉₀, as measured by IFN- γ production in CD4+ T cells isolated from a human donor and treated as described in Example 9, in a range of about 1.04 nM to about 2.72 nM. In some embodiments, such EC₉₀ is about 2.72 nM or less.

[0346] In some embodiments, an ABP provided herein has an EC₁₀ in a range of about 0.37 nM to about 1.05 nM, an EC₅₀ in a range of about 0.94 nM to about 1.12 nM, and EC₉₀ in a range of about 1.04 nM to about 2.72 nM, in each cases as measured by IFN- γ production in PBMCs isolated from a human donor and treated as described in Example 9.

[0347] In some embodiments, an ABP provided herein has an EC₁₀ of about 0.37 nM or less, an EC₅₀ of about 1.00 nM or less, and EC₉₀ of about 2.72 nM or less, in each cases as measured by IFN- γ production in PBMCs isolated from a human donor and treated as described in Example 9.

[0348] In some embodiments, an ABP provided herein has an EC₁₀ of about 0.85 nM or less, an EC₅₀ of about 0.94 nM or less, and EC₉₀ of about 1.04 nM or less, in each cases as measured by IFN- γ production in PBMCs isolated from a human donor and treated as described in Example 9.

[0349] In some embodiments, an ABP provided herein has an EC₁₀ of about 1.05 nM or less, an EC₅₀ of about 1.12 nM or less, and EC₉₀ of about 1.19 nM or less, in each cases as measured by IFN- γ production in PBMCs isolated from a human donor and treated as described in Example 9.

[0350] In some embodiments, an ABP provided herein has an EC₁₀ of about 0.75 nM or less, an EC₅₀ of about 1.02 nM or less, and EC₉₀ of about 1.65 nM or less, in each cases as measured by IFN- γ production in PBMCs isolated from a human donor and treated as described in Example 9.

[0351] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 5.24×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 2.64×10^{-9} M (as determined by ForteBio), hTIGIT with a K_D of about 5.40×10^{-11} M (as determined by MSD-SET), and cTIGIT with a K_D of about 3.20×10^{-10} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0352] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 4.57×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 1.57×10^{-9} M (as determined by ForteBio), hTIGIT with a K_D of about 2.50×10^{-11} M (as determined by MSD-SET), and

cTIGIT with a K_D of about 2.30×10^{-10} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0353] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 3.32×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 8.02×10^{-10} M (as determined by ForteBio), hTIGIT with a K_D of about 8.10×10^{-12} M (as determined by MSD-SET), and cTIGIT with a K_D of about 3.50×10^{-11} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0354] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 2.46×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 3.69×10^{-10} M (as determined by ForteBio), hTIGIT with a K_D of about 5.00×10^{-12} M (as determined by MSD-SET), and cTIGIT with a K_D of about 1.50×10^{-11} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0355] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 1.96×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 8.98×10^{-10} M (as determined by ForteBio), hTIGIT with a K_D of about 4.90×10^{-12} M (as determined by MSD-SET), and cTIGIT with a K_D of about 4.60×10^{-11} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0356] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 3.11×10^{-9} M (as determined by ForteBio) and cTIGIT with a K_D of about 1.75×10^{-8} M (as determined by ForteBio), in each case determined according to the methods provided in Example 4.

[0357] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 2.54×10^{-9} M, as determined by ForteBio according to the methods provided in Example 4.

[0358] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 3.13×10^{-9} M (as determined by ForteBio) and cTIGIT with a K_D of about 2.58×10^{-8} M (as determined by ForteBio), in each case determined according to the methods provided in Example 4.

[0359] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 2.83×10^{-9} M (as determined by ForteBio) and cTIGIT with a K_D of about 9.35×10^{-9} M (as determined by ForteBio), in each case determined according to the methods provided in Example 4.

[0360] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 1.71×10^{-9} M (as determined by ForteBio), cTIGIT with a K_D of about 6.55×10^{-9} M (as determined by ForteBio), and hTIGIT with a K_D of about 1.10×10^{-10} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0361] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 2.47×10^{-9} M (as determined by ForteBio), cTIGIT with a K_D of about 8.14×10^{-9} M (as determined by ForteBio), and hTIGIT with a K_D of about 1.50×10^{-10} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0362] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 2.35×10^{-9} M (as determined by ForteBio), cTIGIT with a K_D of about 6.57×10^{-9} M (as determined by ForteBio), and hTIGIT with a K_D of about 5.60×10^{-11} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0363] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 1.44×10^{-9} M (as determined by ForteBio) and hTIGIT with a K_D of about 4.00×10^{-10} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0364] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 1.23×10^{-9} M (as determined by ForteBio) and hTIGIT with a K_D of about 3.80×10^{-10} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0365] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 5.26×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 7.94×10^{-8} M (as determined by ForteBio), and hTIGIT with a K_D of about 2.10×10^{-10} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0366] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 3.78×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 7.04×10^{-8} M (as determined by ForteBio), and hTIGIT with a K_D of about 7.00×10^{-11} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0367] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 4.29×10^{-10} M (as determined by ForteBio), cTIGIT with a K_D of about 1.10×10^{-7} M (as determined

by ForteBio), and hTIGIT with a K_D of about 4.10×10^{-11} M (as determined by MSD-SET), in each case determined according to the methods provided in Example 4.

[0368] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 4.48×10^{-10} M (as determined by ForteBio) and cTIGIT with a K_D of about 7.20×10^{-8} M (as determined by ForteBio), in each case determined according to the methods provided in Example 4.

[0369] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 3.00×10^{-11} M, as determined by MSD-SET according to the methods provided in Example 4.

[0370] In some embodiments, an ABP provided herein binds hTIGIT with a K_D of about 8.00×10^{-11} M, as determined by MSD-SET according to the methods provided in Example 4.

[0371] In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.2 nM, about 2.3 nM, about 1.6 nM, about 1.9 nM, about 1.7 nM, about 3.2 nM, about 2.6 nM, about 2.9 nM, about 3.3 nM, about 2 nM, about 2.2 nM, about 2.1 nM, about 1.8 nM, about 6.4 nM, or about 1 nM. In some embodiments, such IC_{50} ranges from about 1 nM to about 6.4 nM. In some embodiments, such IC_{50} is about 6.4 nM or less. In some embodiments, such IC_{50} is determined as described in Example 5.

[0372] In some embodiments, an ABP provided herein inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.4 nM, about 1.3 nM, about 1.2 nM, about 1.6 nM, about 2 nM, about 1.2 nM, about 1.1 nM, about 1 nM, about 1.8 nM, about 1.9 nM, about 2 nM, or about 0.8 nM. In some embodiments, such IC_{50} ranges from about 0.8 nM to about 2 nM. In some embodiments, such IC_{50} is about 2 nM or less. In some embodiments, such IC_{50} is determined as described in Example 5.

[0373] In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.2 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.4 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.3 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.3 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 1.6 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.2 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 1.9 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.6 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 1.7 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.4 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 3.2 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.4 nM. In some

embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.6 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 2 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.9 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.2 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 1.9 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.1 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 3.3 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.2 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 1.7 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.2 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.1 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.8 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.6 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.6 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.2 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.1 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.1 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.3 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.6 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.9 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 1.8 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.9 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 6.4 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 2 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 2.3 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 1.9 nM. In some embodiments, an ABP provided herein inhibits binding of PVR to TIGIT with an IC_{50} of about 1 nM and inhibits binding of PVRL2 to TIGIT with an IC_{50} of about 0.8 nM. In some embodiments, such IC_{50} is about 2 nM or less. In some embodiments, such IC_{50} is determined as described in Example 5.

2.6.1. Glycosylation Variants

[0374] In certain embodiments, an ABP provided herein may be altered to increase, decrease or eliminate the extent to which it is glycosylated. Glycosylation of polypeptides is typically either "N-linked" or "O-linked."

[0375] "N-linked" glycosylation refers to the attachment of a carbohydrate moiety to the side chain of an asparagine residue. The tripeptide sequences asparagine-X-serine and asparagine-X-threonine, where X is any amino acid except proline, are the recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain. Thus, the presence of either of these tripeptide sequences in a polypeptide creates a potential glycosylation site.

[0376] "O-linked" glycosylation refers to the attachment of one of the sugars N-acetylgalactosamine, galactose, or xylose to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be used.

[0377] Addition or deletion of N-linked glycosylation sites to or from an ABP provided herein may be accomplished by altering the amino acid sequence such that one or more of the above-described tripeptide sequences is created or removed. Addition or deletion of O-linked glycosylation sites may be accomplished by addition, deletion, or substitution of one or more serine or threonine residues in or to (as the case may be) the sequence of an ABP.

[0378] In some embodiments, an ABP provided herein comprises a glycosylation motif that is different from a naturally occurring ABP. Any suitable naturally occurring glycosylation motif can be modified in the ABPs provided herein. The structural and glycosylation properties of immunoglobulins, for example, are known in the art and summarized, for example, in Schroeder and Cavacini, *J. Allergy Clin. Immunol.*, 2010, 125:S41-52.

[0379] In some embodiments, an ABP provided herein comprises an IgG1 Fc region with modification to the oligosaccharide attached to asparagine 297 (Asn 297). Naturally occurring IgG1 antibodies produced by mammalian cells typically comprise a branched, biantennary oligosaccharide that is generally attached by an N-linkage to Asn 297 of the C_{H2} domain of the Fc region. See Wright et al., *TIBTECH*, 1997, 15:26-32. The oligosaccharide attached to Asn 297 may include various carbohydrates such as mannose, N-acetyl glucosamine (GlcNAc), galactose, and sialic acid, as well as a fucose attached to a GlcNAc in the "stem" of the biantennary oligosaccharide structure.

[0380] In some embodiments, the oligosaccharide attached to Asn 297 is modified to create ABPs having altered ADCC. In some embodiments, the oligosaccharide is altered to improve ADCC. In some embodiments, the oligosaccharide is altered to reduce ADCC.

[0381] In some aspects, an ABP provided herein comprises an IgG1 domain with reduced fucose content at position Asn 297 compared to a naturally occurring IgG1 domain. Such Fc domains are known to have improved ADCC. See Shields et al., *J. Biol. Chem.*, 2002, 277:26733-26740. In some aspects, such ABPs do not comprise any fucose at position Asn 297. The amount of fucose may be determined using any suitable method, for example as described in WO 2008/077546.

[0382] In some embodiments, an ABP provided herein comprises a bisected oligosaccharide, such as a biantennary oligosaccharide attached to the Fc region of the ABP that is bisected by GlcNAc. Such ABP variants may have reduced fucosylation and/or improved ADCC function. Examples of such ABP variants are described, for example, in WO 2003/011878; U.S. Pat. No. 6,602,684; and U.S. Pat. Pub. No. 2005/0123546.

[0383] Other illustrative glycosylation variants which may be incorporated into the ABPs provided herein are described, for example, in U.S. Pat. Pub. Nos. 2003/0157108, 2004/0093621, 2003/0157108, 2003/0115614, 2002/0164328, 2004/0093621, 2004/0132140, 2004/0110704, 2004/0110282, 2004/0109865; International Pat. Pub. Nos. 2000/61739, 2001/29246, 2003/085119, 2003/084570, 2005/035586, 2005/035778; 2005/053742, 2002/031140; Okazaki et al., J. Mol. Biol., 2004, 336:1239-1249; and Yamane-Ohnuki et al., Biotech. Bioeng., 2004, 87: 614-622.

[0384] In some embodiments, an ABP provided herein comprises an Fc region with at least one galactose residue in the oligosaccharide attached to the Fc region. Such ABP variants may have improved CDC function. Examples of such ABP variants are described, for example, in WO 1997/30087; WO 1998/58964; and WO 1999/22764.

[0385] Examples of cell lines capable of producing defucosylated ABPs include Lec13 CHO cells, which are deficient in protein fucosylation (see Ripka et al., Arch. Biochem. Biophys., 1986, 249:533-545; U.S. Pat. Pub. No. 2003/0157108; WO 2004/056312), and knockout cell lines, such as alpha-1,6-fucosyltransferase gene or FUT8 knockout CHO cells (see Yamane-Ohnuki et al., Biotech. Bioeng., 2004, 87: 614-622; Kanda et al., Biotechnol. Bioeng., 2006, 94:680-688; and WO 2003/085107).

[0386] In some embodiments, an ABP provided herein is an aglycosylated ABP. An aglycosylated ABP can be produced using any method known in the art or described herein. In some aspects, an aglycosylated ABP is produced by modifying the ABP to remove all glycosylation sites. In some aspects, the glycosylation sites are removed only from the Fc region of the ABP. In some aspects, an aglycosylated ABP is produced by expressing the ABP in an organism that is not capable of glycosylation, such as *E. coli*, or by expressing the ABP in a cell-free reaction mixture.

[0387] In some embodiments, an ABP provided herein has a constant region with reduced effector function compared to a native IgG1 antibody. In some embodiments, the affinity of a constant region of an Fc region of an ABP provided herein for Fc receptor is less than the affinity of a native IgG1 constant region for such Fc receptor.

2.7. Fc Region Amino Acid Sequence Variants

[0388] In certain embodiments, an ABP provided herein comprises an Fc region with one or more amino acid substitutions, insertions, or deletions in comparison to a naturally occurring

Fc region. In some aspects, such substitutions, insertions, or deletions yield ABPs with altered stability, glycosylation, or other characteristics. In some aspects, such substitutions, insertions, or deletions yield aglycosylated ABPs.

[0389] In some aspects, the Fc region of an ABP provided herein is modified to yield an ABP with altered affinity for an Fc receptor, or an ABP that is more immunologically inert. In some embodiments, the ABP variants provided herein possess some, but not all, effector functions. Such ABPs may be useful, for example, when the half-life of the ABP is important *in vivo*, but when certain effector functions (e.g., complement activation and ADCC) are unnecessary or deleterious.

[0390] In some embodiments, the Fc region of an ABP provided herein is a human IgG4 Fc region comprising one or more of the hinge stabilizing mutations S228P and L235E. See Aalberse et al., *Immunology*, 2002, 105:9-19. In some embodiments, the IgG4 Fc region comprises one or more of the following mutations: E233P, F234V, and L235A. See Armour et al., *Mol. Immunol.*, 2003, 40:585-593. In some embodiments, the IgG4 Fc region comprises a deletion at position G236.

[0391] In some embodiments, the Fc region of an ABP provided herein is a human IgG1 Fc region comprising one or more mutations to reduce Fc receptor binding. In some aspects, the one or more mutations are in residues selected from S228 (e.g., S228A), L234 (e.g., L234A), L235 (e.g., L235A), D265 (e.g., D265A), and N297 (e.g., N297A). In some aspects, the ABP comprises a PVA236 mutation. PVA236 means that the amino acid sequence ELLG, from amino acid position 233 to 236 of IgG1 or EFLG of IgG4, is replaced by PVA. See U.S. Pat. No. 9,150,641.

[0392] In some embodiments, the Fc region of an ABP provided herein is modified as described in Armour et al., *Eur. J. Immunol.*, 1999, 29:2613-2624; WO 1999/058572; and/or U.K. Pat. App. No. 98099518.

[0393] In some embodiments, the Fc region of an ABP provided herein is a human IgG2 Fc region comprising one or more of mutations A330S and P331S.

[0394] In some embodiments, the Fc region of an ABP provided herein has an amino acid substitution at one or more positions selected from 238, 265, 269, 270, 297, 327 and 329. See U.S. Pat. No. 6,737,056. Such Fc mutants include Fc mutants with substitutions at two or more of amino acid positions 265, 269, 270, 297 and 327, including the so-called "DANA" Fc mutant with substitution of residues 265 and 297 with alanine. See U.S. Pat. No. 7,332,581. In some embodiments, the ABP comprises an alanine at amino acid position 265. In some embodiments, the ABP comprises an alanine at amino acid position 297.

[0395] In certain embodiments, an ABP provided herein comprises an Fc region with one or more amino acid substitutions which improve ADCC, such as a substitution at one or more of positions 298, 333, and 334 of the Fc region. In some embodiments, an ABP provided herein

comprises an Fc region with one or more amino acid substitutions at positions 239, 332, and 330, as described in Lazar et al., Proc. Natl. Acad. Sci. USA, 2006, 103:4005-4010.

[0396] In some embodiments, an ABP provided herein comprises one or more alterations that improves or diminishes C1q binding and/or CDC. See U.S. Pat. No. 6,194,551; WO 99/51642; and Idusogie et al., J. Immunol., 2000, 164:4178-4184.

[0397] In some embodiments, an ABP provided herein comprises one or more alterations to increase half-life. ABPs with increased half-lives and improved binding to the neonatal Fc receptor (FcRn) are described, for example, in Hinton et al., J. Immunol., 2006, 176:346-356; and U.S. Pat. Pub. No. 2005/0014934. Such Fc variants include those with substitutions at one or more of Fc region residues: 238, 250, 256, 265, 272, 286, 303, 305, 307, 311, 312, 314, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424, 428, and 434 of an IgG.

[0398] In some embodiments, an ABP provided herein comprises one or more Fc region variants as described in U.S. Pat. Nos. 7,371,826 5,648,260, and 5,624,821; Duncan and Winter, Nature, 1988, 322:738-740; and WO 94/29351.

2.8. Pyroglutamate

[0399] As is known in the art, both glutamate (E) and glutamine (Q) at the N-termini of recombinant proteins can cyclize spontaneously to form pyroglutamate (pE) *in vitro* and *in vivo*. See Liu et al., J. Biol. Chem., 2011, 286:11211-11217.

[0400] In some embodiments, provided herein are ABPs comprising a polypeptide sequence having a pE residue at the N-terminal position. In some embodiments, provided herein are ABPs comprising a polypeptide sequence in which the N-terminal residue has been converted from Q to pE. In some embodiments, provided herein are ABPs comprising a polypeptide sequence in which the N-terminal residue has been converted from E to pE.

[0401] In some embodiments, provided herein are ABPs comprising V_H sequences having a pE residue at the N-terminal position. In some embodiments, provided herein are ABPs comprising a V_H sequence in which the N-terminal residue has been converted from Q to pE. In some embodiments, provided herein is an ABP comprising a V_H sequence selected from SEQ ID NOs: 4-24, wherein the N-terminal Q residue has been converted to pE. In some embodiments, provided herein is a composition comprising an ABP, wherein the ABP comprises a V_H selected from SEQ ID NOs: 4-24, in which at least about 20%, at least about 40%, at least about 60%, at least about 80%, at least about 90%, at least about 95%, or at least about 99% of the N-terminal residues of such V_H in such composition have been converted from Q to pE.

[0402] In some embodiments, provided herein are ABPs comprising V_L sequences having a pE

residue at the N-terminal position. In some embodiments, provided herein are ABPs comprising a V_L sequence in which the N-terminal residue has been converted from E to pE. In some embodiments, provided herein is an ABP comprising a V_L sequence selected from SEQ ID NOs: 25-28, wherein the N-terminal E residue has been converted to pE. In some embodiments, provided herein is a composition comprising an ABP, wherein the ABP comprises a V_L selected from SEQ ID NOs: 25-28, in which at least about 20%, at least about 40%, at least about 60%, at least about 80%, at least about 90%, at least about 95%, or at least about 99% of the N-terminal residues of such V_L in such composition have been converted from E to pE.

[0403] In some embodiments, provided herein are ABPs comprising heavy chain sequences having a pE residue at the N-terminal position. In some embodiments, provided herein are ABPs comprising a heavy chain sequence in which the N-terminal residue has been converted from Q to pE. In some embodiments, provided herein is an ABP comprising a heavy chain sequence selected from SEQ ID NOs: 79, 80, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 121, 122, 123 or 124, wherein the N-terminal Q residue has been converted to pE. In some embodiments, provided herein is a composition comprising an ABP, wherein the ABP comprises a heavy chain selected from SEQ ID NOs: 79, 80, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 121, 122, 123 or 124, in which at least about 20%, at least about 40%, at least about 60%, at least about 80%, at least about 90%, at least about 95%, or at least about 99% of the N-terminal residues of such heavy chain in such composition have been converted from Q to pE.

[0404] In some embodiments, provided herein are ABPs comprising light chain sequences having a pE residue at the N-terminal position. In some embodiments, provided herein are ABPs comprising a light chain sequence in which the N-terminal residue has been converted from E to pE. In some embodiments, provided herein is an ABP comprising a light chain sequence selected from SEQ ID NOs: 81, 92, 107 or 120, wherein the N-terminal E residue has been converted to pE. In some embodiments, provided herein is a composition comprising an ABP, wherein the ABP comprises a light chain selected from SEQ ID NOs: 81, 92, 107 or 120, in which at least about 20%, at least about 40%, at least about 60%, at least about 80%, at least about 90%, at least about 95%, or at least about 99% of the N-terminal residues of such light chain in such composition have been converted from E to pE.

2.9. Cysteine Engineered Antigen-Binding Protein Variants

[0405] In certain embodiments, provided herein are cysteine engineered ABPs, also known as "thioMAbs," in which one or more residues of the ABP are substituted with cysteine residues. In particular embodiments, the substituted residues occur at solvent accessible sites of the ABP. By substituting such residues with cysteine, reactive thiol groups are introduced at solvent

accessible sites of the ABP and may be used to conjugate the ABP to other moieties, such as drug moieties or linker-drug moieties, for example, to create an immunoconjugate.

[0406] In certain embodiments, any one or more of the following residues may be substituted with cysteine: V205 of the light chain; A118 of the heavy chain Fc region; and S400 of the heavy chain Fc region. Cysteine engineered ABPs may be generated as described, for example, in U.S. Pat. No. 7,521,541.

2.9.1. Immunoconjugates

2.9.1.1. Antigen-Binding Protein-Polymer Conjugates

[0407] In some embodiments, an ABP provided herein is derivatized by conjugation with a polymer. Any suitable polymer may be conjugated to the ABP.

[0408] In some embodiments, the polymer is a water soluble polymer. Illustrative examples of water soluble polymers include polyethylene glycol (PEG), copolymers of ethylene glycol/propylene glycol, carboxymethylcellulose, dextran, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1,3-dioxolane, poly-1,3,6-trioxane, ethylene/maleic anhydride copolymer, polyaminoacids (either homopolymers or random copolymers), poly(n-vinyl pyrrolidone)-co-polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols (e.g., glycerol), polyvinyl alcohol, and mixtures thereof. In some aspects, polyethylene glycol propionaldehyde may be useful for manufacturing purposes due to its stability in water.

[0409] The polymer may be of any molecular weight, and may be branched or unbranched. The number of polymers attached to each ABP may vary, and if more than one polymer is attached, they may be the same polymer or different polymers. In general, the number and/or type of polymers used for derivatization can be determined based on considerations including the particular properties or functions of the ABP to be improved and the intended use of the ABP.

2.9.1.2. Antigen-Binding Protein-Drug Conjugates

[0410] In some embodiments, the ABPs provided herein are conjugated to one or more therapeutic agents. Any suitable therapeutic agent may be conjugated to the ABP. Exemplary therapeutic agents include cytokines, chemokines, and other agents that induce a desired T cell activity, such as OX40L, 4-1BBL, TNF-alpha (as used herein, "TNF"), IL-2, IL-15 fusion, CXCL9, CXCL10, IL-10 trap, IL-27 trap, and IL-35 trap. Cytokine traps and their use are known in the art and described, for example, in Economides et al., Nature Medicine, 2003, 9:47-52.

3. Methods of Making TIGIT Antigen-Binding Proteins

3.1. TIGIT Antigen Preparation

[0411] The TIGIT antigen used for isolation of the ABPs provided herein may be intact TIGIT or a fragment of TIGIT. The TIGIT antigen may be, for example, in the form of an isolated protein or a protein expressed on the surface of a cell.

[0412] In some embodiments, the TIGIT antigen is a non-naturally occurring variant of TIGIT, such as a TIGIT protein having an amino acid sequence or post-translational modification that does not occur in nature.

[0413] In some embodiments, the TIGIT antigen is truncated by removal of, for example, intracellular or membrane-spanning sequences, or signal sequences. In some embodiments, the TIGIT antigen is fused at its C-terminus to a human IgG1 Fc domain or a polyhistidine tag.

3.2. Methods of Making Monoclonal Antibodies

[0414] Monoclonal antibodies may be obtained, for example, using the hybridoma method first described by Kohler et al., *Nature*, 1975, 256:495-497, and/or by recombinant DNA methods (see e.g., U.S. Patent No. 4,816,567). Monoclonal antibodies may also be obtained, for example, using phage or yeast-based libraries. See e.g., U.S. Patent Nos. 8,258,082 and 8,691,730.

[0415] In the hybridoma method, a mouse or other appropriate host animal is immunized to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the protein used for immunization. Alternatively, lymphocytes may be immunized *in vitro*. Lymphocytes are then fused with myeloma cells using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell. See Goding J.W., *Monoclonal Antibodies: Principles and Practice* 3rd ed. (1986) Academic Press, San Diego, CA.

[0416] The hybridoma cells are seeded and grown in a suitable culture medium that contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells. For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine (HAT medium), which substances prevent the growth of HGPRT-deficient cells.

[0417] Useful myeloma cells are those that fuse efficiently, support stable high-level production

of antibody by the selected antibody-producing cells, and are sensitive media conditions, such as the presence or absence of HAT medium. Among these, preferred myeloma cell lines are murine myeloma lines, such as those derived from MOP-21 and MC-11 mouse tumors (available from the Salk Institute Cell Distribution Center, San Diego, CA), and SP-2 or X63-Ag8-653 cells (available from the American Type Culture Collection, Rockville, MD). Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies. See e.g., Kozbor, J. Immunol., 1984, 133:3001.

[0418] After the identification of hybridoma cells that produce antibodies of the desired specificity, affinity, and/or biological activity, selected clones may be subcloned by limiting dilution procedures and grown by standard methods. See Goding, *supra*. Suitable culture media for this purpose include, for example, D-MEM or RPMI-1640 medium. In addition, the hybridoma cells may be grown *in vivo* as ascites tumors in an animal.

[0419] DNA encoding the monoclonal antibodies may be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of the monoclonal antibodies). Thus, the hybridoma cells can serve as a useful source of DNA encoding antibodies with the desired properties. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as bacteria (e.g., *E. coli*), yeast (e.g., *Saccharomyces* or *Pichia sp.*), COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce antibody, to produce the monoclonal antibodies.

3.3. Methods of Making Chimeric Antibodies

[0420] Illustrative methods of making chimeric antibodies are described, for example, in U.S. Pat. No. 4,816,567; and Morrison et al., Proc. Natl. Acad. Sci. USA, 1984, 81:6851-6855. In some embodiments, a chimeric antibody is made by using recombinant techniques to combine a non-human variable region (e.g., a variable region derived from a mouse, rat, hamster, rabbit, or non-human primate, such as a monkey) with a human constant region.

3.4. Methods of Making Humanized Antibodies

[0421] Humanized antibodies may be generated by replacing most, or all, of the structural portions of a non-human monoclonal antibody with corresponding human antibody sequences. Consequently, a hybrid molecule is generated in which only the antigen-specific variable, or CDR, is composed of non-human sequence. Methods to obtain humanized antibodies include those described in, for example, Winter and Milstein, Nature, 1991, 349:293-299; Rader et al., Proc. Nat. Acad. Sci. U.S.A., 1998, 95:8910-8915; Steinberger et al., J. Biol. Chem., 2000, 275:36073-36078; Queen et al., Proc. Natl. Acad. Sci. U.S.A., 1989, 86:10029-10033; and U.S. Patent Nos. 5,585,089, 5,693,761, 5,693,762, and 6,180,370.

3.5. Methods of making Human Antibodies

[0422] Human antibodies can be generated by a variety of techniques known in the art, for example by using transgenic animals (e.g., humanized mice). See, e.g., Jakobovits et al., Proc. Natl. Acad. Sci. U.S.A., 1993, 90:2551; Jakobovits et al., Nature, 1993, 362:255-258; Bruggermann et al., Year in Immuno., 1993, 7:33; and U.S. Patent Nos. 5,591,669, 5,589,369 and 5,545,807. Human antibodies can also be derived from phage-display libraries (see e.g., Hoogenboom et al., J. Mol. Biol., 1991, 227:381-388; Marks et al., J. Mol. Biol., 1991, 222:581-597; and U.S. Pat. Nos. 5,565,332 and 5,573,905). Human antibodies may also be generated by *in vitro* activated B cells (see e.g., U.S. Patent. Nos. 5,567,610 and 5,229,275). Human antibodies may also be derived from yeast-based libraries (see e.g., U.S. Patent No. 8,691,730).

3.6. Methods of Making Antibody Fragments

[0423] The antibody fragments provided herein may be made by any suitable method, including the illustrative methods described herein or those known in the art. Suitable methods include recombinant techniques and proteolytic digestion of whole antibodies. Illustrative methods of making antibody fragments are described, for example, in Hudson et al., Nat. Med., 2003, 9:129-134. Methods of making scFv antibodies are described, for example, in Plückthun, in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994); WO 93/16185; and U.S. Pat. Nos. 5,571,894 and 5,587,458.

3.7. Methods of Making Alternative Scaffolds

[0424] The alternative scaffolds provided herein may be made by any suitable method, including the illustrative methods described herein or those known in the art. For example, methods of preparing Adnectins[™] are described in Emanuel et al., mAbs, 2011, 3:38-48. Methods of preparing iMabs are described in U.S. Pat. Pub. No. 2003/0215914. Methods of preparing Anticalins[®] are described in Vogt and Skerra, Chem. Biochem., 2004, 5:191-199. Methods of preparing Kunitz domains are described in Wagner et al., Biochem. & Biophys. Res. Comm., 1992, 186:118-1145. Methods of preparing thioredoxin peptide aptamers are provided in Geyer and Brent, Meth. Enzymol., 2000, 328:171-208. Methods of preparing Affibodies are provided in Fernandez, Curr. Opinion in Biotech., 2004, 15:364-373. Methods of preparing DARPins are provided in Zahnd et al., J. Mol. Biol., 2007, 369:1015-1028. Methods of preparing Affilins are provided in Ebersbach et al., J. Mol. Biol., 2007, 372:172-185. Methods of preparing Tetranectins are provided in Graversen et al., J. Biol. Chem., 2000, 275:37390-37396. Methods of preparing Avimers are provided in Silverman et al., Nature Biotech., 2005,

23:1556-1561. Methods of preparing Fynomers are provided in Silacci et al., J. Biol. Chem., 2014, 289:14392-14398.

[0425] Further information on alternative scaffolds is provided in Binz et al., Nat. Biotechnol., 2005 23:1257-1268; and Skerra, Current Opin. in Biotech., 2007 18:295-304.

3.8. Methods of Making Multispecific ABPs

[0426] The multispecific ABPs provided herein may be made by any suitable method, including the illustrative methods described herein or those known in the art. Methods of making common light chain antibodies are described in Merchant et al., Nature Biotechnol., 1998, 16:677-681. Methods of making tetravalent bispecific antibodies are described in Coloma and Morrison, Nature Biotechnol., 1997, 15:159-163. Methods of making hybrid immunoglobulins are described in Milstein and Cuello, Nature, 1983, 305:537-540; and Staerz and Bevan, Proc. Natl. Acad. Sci. USA, 1986, 83:1453-1457. Methods of making immunoglobulins with knobs-into-holes modification are described in U.S. Pat. No. 5,731,168. Methods of making immunoglobulins with electrostatic modifications are provided in WO 2009/089004. Methods of making bispecific single chain antibodies are described in Traunecker et al., EMBO J., 1991, 10:3655-3659; and Gruber et al., J. Immunol., 1994, 152:5368-5374. Methods of making single-chain antibodies, whose linker length may be varied, are described in U.S. Pat. Nos. 4,946,778 and 5,132,405. Methods of making diabodies are described in Hollinger et al., Proc. Natl. Acad. Sci. USA, 1993, 90:6444-6448. Methods of making triabodies and tetrabodies are described in Todorovska et al., J. Immunol. Methods, 2001, 248:47-66. Methods of making trispecific F(ab')₃ derivatives are described in Tutt et al. J. Immunol., 1991, 147:60-69. Methods of making cross-linked antibodies are described in U.S. Patent No. 4,676,980; Brennan et al., Science, 1985, 229:81-83; Staerz, et al. Nature, 1985, 314:628-631; and EP 0453082. Methods of making antigen-binding domains assembled by leucine zippers are described in Kostelny et al., J. Immunol., 1992, 148:1547-1553. Methods of making ABPs via the DNL approach are described in U.S. Pat. Nos. 7,521,056; 7,550,143; 7,534,866; and 7,527,787. Methods of making hybrids of antibody and non-antibody molecules are described in WO 93/08829, for examples of such ABPs. Methods of making DAF antibodies are described in U.S. Pat. Pub. No. 2008/0069820. Methods of making ABPs via reduction and oxidation are described in Carlring et al., PLoS One, 2011, 6:e22533. Methods of making DVD-Igs[™] are described in U.S. Pat. No. 7,612,181. Methods of making DARTs[™] are described in Moore et al., Blood, 2011, 117:454-451. Methods of making DuoBodies[®] are described in Labrijn et al., Proc. Natl. Acad. Sci. USA, 2013, 110:5145-5150; Gramer et al., mAbs, 2013, 5:962-972; and Labrijn et al., Nature Protocols, 2014, 9:2450-2463. Methods of making antibodies comprising scFvs fused to the C-terminus of the C_H3 from an IgG are described in Coloma and Morrison, Nature Biotechnol., 1997, 15:159-163. Methods of making antibodies in which a Fab molecule is attached to the constant region of an immunoglobulin are described in Miler et al., J. Immunol., 2003, 170:4854-4861. Methods of making CovX-Bodies are described in Doppalapudi et al., Proc. Natl. Acad. Sci. USA, 2010, 107:22611-22616. Methods of making

Fcab antibodies are described in Wozniak-Knopp et al., Protein Eng. Des. Sel., 2010, 23:289-297. Methods of making TandAb[®] antibodies are described in Kipriyanov et al., J. Mol. Biol., 1999, 293:41-56 and Zhukovsky et al., Blood, 2013, 122:5116. Methods of making tandem Fabs are described in WO 2015/103072. Methods of making Zybodies[™] are described in LaFleur et al., mAbs, 2013, 5:208-218.

3.9. Methods of Making Variants

[0427] In some embodiments, an ABP provided herein is an affinity matured variant of a parent ABP, which may be generated, for example, using phage display-based affinity maturation techniques. Briefly, one or more CDR residues may be mutated and the variant ABPs, or portions thereof, displayed on phage and screened for affinity. Such alterations may be made in CDR "hotspots," or residues encoded by codons that undergo mutation at high frequency during the somatic maturation process (see Chowdhury, Methods Mol. Biol., 2008, 207:179-196,), and/or residues that contact the antigen.

[0428] Any suitable method can be used to introduce variability into a polynucleotide sequence(s) encoding an ABP, including error-prone PCR, chain shuffling, and oligonucleotide-directed mutagenesis such as trinucleotide-directed mutagenesis (TRIM). In some aspects, several CDR residues (e.g., 4-6 residues at a time) are randomized. CDR residues involved in antigen binding may be specifically identified, for example, using alanine scanning mutagenesis or modeling. CDR-H3 and CDR-L3 in particular are often targeted for mutation.

[0429] The introduction of diversity into the variable regions and/or CDRs can be used to produce a secondary library. The secondary library is then screened to identify ABP variants with improved affinity. Affinity maturation by constructing and reselecting from secondary libraries has been described, for example, in Hoogenboom et al., Methods in Molecular Biology, 2001, 178:1-37.

3.10. Vectors, Host Cells, and Recombinant Methods

[0430] Also provided are isolated nucleic acids encoding TIGIT ABPs, vectors comprising the nucleic acids, and host cells comprising the vectors and nucleic acids, as well as recombinant techniques for the production of the ABPs.

[0431] For recombinant production of an ABP, the nucleic acid(s) encoding it may be isolated and inserted into a replicable vector for further cloning (i.e., amplification of the DNA) or expression. In some aspects, the nucleic acid may be produced by homologous recombination, for example as described in U.S. Patent No. 5,204,244.

[0432] Many different vectors are known in the art. The vector components generally include

one or more of the following: a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence, for example as described in U.S. Patent No. 5,534,615.

[0433] Illustrative examples of suitable host cells are provided below. These host cells are not meant to be limiting, and any suitable host cell may be used to produce the ABPs provided herein.

[0434] Suitable host cells include any prokaryotic (e.g., bacterial), lower eukaryotic (e.g., yeast), or higher eukaryotic (e.g., mammalian) cells. Suitable prokaryotes include eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *Escherichia* (*E. coli*), *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella* (*S. typhimurium*), *Serratia* (*S. marcescans*), *Shigella*, *Bacilli* (*B. subtilis* and *B. licheniformis*), *Pseudomonas* (*P. aeruginosa*), and *Streptomyces*. One useful *E. coli* cloning host is *E. coli* 294, although other strains such as *E. coli* B, *E. coli* X1776, and *E. coli* W3110 are also suitable.

[0435] In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are also suitable cloning or expression hosts for TIGIT ABP -encoding vectors. *Saccharomyces cerevisiae*, or common baker's yeast, is a commonly used lower eukaryotic host microorganism. However, a number of other genera, species, and strains are available and useful, such as *Schizosaccharomyces pombe*, *Kluyveromyces* (*K. lactis*, *K. fragilis*, *K. bulgaricus*, *K. wickerhamii*, *K. waltii*, *K. drosophilum*, *K. thermotolerans*, and *K. marxianus*), *Yarrowia*, *Pichia pastoris*, *Candida* (*C. albicans*), *Trichoderma reesia*, *Neurospora crassa*, *Schwanniomyces* (*S. occidentalis*), and filamentous fungi such as, for example *Penicillium*, *Tolypocladium*, and *Aspergillus* (*A. nidulans* and *A. niger*).

[0436] Useful mammalian host cells include COS-7 cells, HEK293 cells; baby hamster kidney (BHK) cells; Chinese hamster ovary (CHO); mouse sertoli cells; African green monkey kidney cells (VERO-76), and the like.

[0437] The host cells used to produce the TIGIT ABP of this invention may be cultured in a variety of media. Commercially available media such as, for example, Ham's F10, Minimal Essential Medium (MEM), RPMI-1640, and Dulbecco's Modified Eagle's Medium (DMEM) are suitable for culturing the host cells. In addition, any of the media described in Ham et al., Meth. Enz., 1979, 58:44; Barnes et al., Anal. Biochem., 1980, 102:255; and U.S. Patent Nos. 4,767,704, 4,657,866, 4,927,762, 4,560,655, and 5,122,469; or WO 90/03430 and WO 87/00195 may be used.

[0438] Any of these media may be supplemented as necessary with hormones and/or other growth factors (such as insulin, transferrin, or epidermal growth factor), salts (such as sodium chloride, calcium, magnesium, and phosphate), buffers (such as HEPES), nucleotides (such as adenosine and thymidine), antibiotics, trace elements (defined as inorganic compounds usually present at final concentrations in the micromolar range), and glucose or an equivalent energy source. Any other necessary supplements may also be included at appropriate concentrations

that would be known to those skilled in the art.

[0439] The culture conditions, such as temperature, pH, and the like, are those previously used with the host cell selected for expression, and will be apparent to the ordinarily skilled artisan.

[0440] When using recombinant techniques, the ABP can be produced intracellularly, in the periplasmic space, or directly secreted into the medium. If the ABP is produced intracellularly, as a first step, the particulate debris, either host cells or lysed fragments, is removed, for example, by centrifugation or ultrafiltration. For example, Carter et al. (Bio/Technology, 1992, 10:163-167) describes a procedure for isolating ABPs which are secreted to the periplasmic space of *E. coli*. Briefly, cell paste is thawed in the presence of sodium acetate (pH 3.5), EDTA, and phenylmethylsulfonylfluoride (PMSF) over about 30 min. Cell debris can be removed by centrifugation.

[0441] In some embodiments, the ABP is produced in a cell-free system. In some aspects, the cell-free system is an *in vitro* transcription and translation system as described in Yin et al., mAbs, 2012, 4:217-225. In some aspects, the cell-free system utilizes a cell-free extract from a eukaryotic cell or from a prokaryotic cell. In some aspects, the prokaryotic cell is *E. coli*. Cell-free expression of the ABP may be useful, for example, where the ABP accumulates in a cell as an insoluble aggregate, or where yields from periplasmic expression are low.

[0442] Where the ABP is secreted into the medium, supernatants from such expression systems are generally first concentrated using a commercially available protein concentration filter, for example, an Amicon® or Millipore® Pellicon® ultrafiltration unit. A protease inhibitor such as PMSF may be included in any of the foregoing steps to inhibit proteolysis and antibiotics may be included to prevent the growth of adventitious contaminants.

[0443] The ABP composition prepared from the cells can be purified using, for example, hydroxylapatite chromatography, gel electrophoresis, dialysis, and affinity chromatography, with affinity chromatography being a particularly useful purification technique. The suitability of protein A as an affinity ligand depends on the species and isotype of any immunoglobulin Fc domain that is present in the ABP. Protein A can be used to purify ABPs that comprise human $\gamma 1$, $\gamma 2$, or $\gamma 4$ heavy chains (Lindmark et al., J. Immunol. Meth., 1983, 62:1-13). Protein G is useful for all mouse isotypes and for human $\gamma 3$ (Guss et al., EMBO J., 1986, 5:1567-1575).

[0444] The matrix to which the affinity ligand is attached is most often agarose, but other matrices are available. Mechanically stable matrices such as controlled pore glass or poly(styrenedivinyl)benzene allow for faster flow rates and shorter processing times than can be achieved with agarose. Where the ABP comprises a C_{H3} domain, the BakerBond ABX® resin is useful for purification.

[0445] Other techniques for protein purification, such as fractionation on an ion-exchange

column, ethanol precipitation, Reverse Phase HPLC, chromatography on silica, chromatography on heparin Sepharose®, chromatofocusing, SDS-PAGE, and ammonium sulfate precipitation are also available, and can be applied by one of skill in the art.

[0446] Following any preliminary purification step(s), the mixture comprising the ABP of interest and contaminants may be subjected to low pH hydrophobic interaction chromatography using an elution buffer at a pH between about 2.5 to about 4.5, generally performed at low salt concentrations (e.g., from about 0 to about 0.25 M salt).

4. Assays

[0447] A variety of assays known in the art may be used to identify and characterize the TIGIT ABPs provided herein.

4.1. Binding, Competition, and Epitope Mapping Assays

[0448] Specific antigen-binding activity of the ABPs provided herein may be evaluated by any suitable method, including using SPR, BLI, RIA and MSD-SET, as described elsewhere in this disclosure. Additionally, antigen-binding activity may be evaluated by ELISA assays and Western blot assays.

[0449] Assays for measuring competition between two ABPs, or an ABP and another molecule (e.g., one or more ligands of TIGIT) are described elsewhere in this disclosure and, for example, in Harlow and Lane, *Antibodies: A Laboratory Manual* ch.14, 1988, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.

[0450] Assays for mapping the epitopes to which the ABPs provided herein bind are described, for example, in Morris "Epitope Mapping Protocols," in *Methods in Molecular Biology* vol. 66, 1996, Humana Press, Totowa, N.J.. In some examples, the epitope is determined by peptide competition. In some examples, the epitope is determined by mass spectrometry. In some examples, the epitope is determined by crystallography.

4.2. TIGIT Antagonism Assays

[0451] In some examples, the ABPs provided herein are screened to identify or characterize ABPs with antagonistic activity against TIGIT. Any suitable assay may be used to identify or characterize such ABPs. In some examples, the assay measures the amount of a cytokine secreted by an effector T cell after contacting the effector T cell with an ABP provided herein. In some examples, the cytokine is selected from IL-2, IL-6, LT- α , TNF, GM-CSF, IFN γ , and combinations thereof. In some examples, the cytokine is selected from sCD40L, VEGF, TGF- α ,

RANTES, PDGF-AB/BB, PDGF-AA, MIP-1 β , MIP-1 α , MDC (CCL22), MCP-3, MCP-1, IP-10, IL-17A, IL-2R α , IL-15, IL-13, IL-12 (p70), IL-12 (p40), IL-10, IL-9, IL-8, IL-7, IL-5, IL-4, IL-3, IL-2, IL-2R α , IL-1RA, IL-1 β , IL-1 α , IFN γ , IFN α 2, GRO, GM-CSF, G-CSF, fractalkine, Flt-3 ligand, FGF-2, eotaxin, EGF, and combinations thereof.

[0452] In some examples, the effector cells are co-stimulated with an agonist of CD3, to promote the secretion of cytokines by the effector cell. In some examples, the CD3 agonist is provided at a submaximal level.

[0453] In some examples, such assays may measure the proliferation of an effector T cell after contacting the effector T cell with an ABP provided herein. In some examples, proliferation of the effector T cell is measured by dilution of a dye (e.g., carboxyfluorescein diacetate succinimidyl ester; CFSE), by tritiated thymidine uptake, by luminescent cell viability assays, or by other assays known in the art.

[0454] In some examples, such assays may measure the differentiation, cytokine production, viability (e.g., survival), proliferation, or suppressive activity of a regulatory T cell after contacting the regulatory T cell with an ABP provided herein.

[0455] In some examples, such assays may measure the cytotoxic activity of an NK cell after contacting the NK cell with an ABP provided herein. In some examples, the cytotoxic activity of the NK cell is measured using a cytotoxicity assay that quantifies NK-mediated killing of target cells (e.g., a K562 cell line). See Jang et al., *Ann. Clin. Lab. Sci.*, 2012, 42:42-49.

[0456] In some examples, such assays may measure the amount of granzyme B. In some examples, such assays may measure the amount of perforin.

4.3. Assays for Effector Functions

[0457] Effector function following treatment with the ABPs provided herein may be evaluated using a variety of *in vitro* and *in vivo* assays known in the art, including those described in Ravetch and Kinet, *Annu. Rev. Immunol.*, 1991, 9:457-492; U.S. Pat. Nos. 5,500,362, 5,821,337; Hellstrom et al., *Proc. Nat'l Acad. Sci. USA*, 1986, 83:7059-7063; Hellstrom et al., *Proc. Nat'l Acad. Sci. USA*, 1985, 82:1499-1502; Bruggemann et al., *J. Exp. Med.*, 1987, 166:1351-1361; Clynes et al., *Proc. Nat'l Acad. Sci. USA*, 1998, 95:652-656; WO 2006/029879; WO 2005/100402; Gazzano-Santoro et al., *J. Immunol. Methods*, 1996, 202:163-171; Cragg et al., *Blood*, 2003, 101:1045-1052; Cragg et al. *Blood*, 2004, 103:2738-2743; and Petkova et al., *Int'l. Immunol.*, 2006, 18:1759-1769.

5. Pharmaceutical Compositions

[0458] The ABPs provided herein can be formulated in any appropriate pharmaceutical composition and administered by any suitable route of administration. Suitable routes of administration include, but are not limited to, the intraarterial, intradermal, intramuscular, intraperitoneal, intravenous, nasal, parenteral, pulmonary, and subcutaneous routes.

[0459] The pharmaceutical composition may comprise one or more pharmaceutical excipients. Any suitable pharmaceutical excipient may be used, and one of ordinary skill in the art is capable of selecting suitable pharmaceutical excipients. Accordingly, the pharmaceutical excipients provided below are intended to be illustrative, and not limiting. Additional pharmaceutical excipients include, for example, those described in the Handbook of Pharmaceutical Excipients, Rowe et al. (Eds.) 6th Ed. (2009).

[0460] In some embodiments, the pharmaceutical composition comprises an anti-foaming agent. Any suitable anti-foaming agent may be used. In some aspects, the anti-foaming agent is selected from an alcohol, an ether, an oil, a wax, a silicone, a surfactant, and combinations thereof. In some aspects, the anti-foaming agent is selected from a mineral oil, a vegetable oil, ethylene bis stearamide, a paraffin wax, an ester wax, a fatty alcohol wax, a long chain fatty alcohol, a fatty acid soap, a fatty acid ester, a silicon glycol, a fluorosilicone, a polyethylene glycol-polypropylene glycol copolymer, polydimethylsiloxane-silicon dioxide, ether, octyl alcohol, capryl alcohol, sorbitan trioleate, ethyl alcohol, 2-ethyl-hexanol, dimethicone, oleyl alcohol, simethicone, and combinations thereof.

[0461] In some embodiments, the pharmaceutical composition comprises a cosolvent. Illustrative examples of cosolvents include ethanol, poly(ethylene) glycol, butylene glycol, dimethylacetamide, glycerin, propylene glycol, and combinations thereof.

[0462] In some embodiments, the pharmaceutical composition comprises a buffer. Illustrative examples of buffers include acetate, borate, carbonate, lactate, malate, phosphate, citrate, hydroxide, diethanolamine, monoethanolamine, glycine, methionine, guar gum, monosodium glutamate, and combinations thereof.

[0463] In some embodiments, the pharmaceutical composition comprises a carrier or filler. Illustrative examples of carriers or fillers include lactose, maltodextrin, mannitol, sorbitol, chitosan, stearic acid, xanthan gum, guar gum, and combinations thereof.

[0464] In some embodiments, the pharmaceutical composition comprises a surfactant. Illustrative examples of surfactants include d-alpha tocopherol, benzalkonium chloride, benzethonium chloride, cetrimide, cetylpyridinium chloride, docusate sodium, glyceryl behenate, glyceryl monooleate, lauric acid, macrogol 15 hydroxystearate, myristyl alcohol, phospholipids, polyoxyethylene alkyl ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene stearates, polyoxylglycerides, sodium lauryl sulfate, sorbitan esters, vitamin E polyethylene(glycol) succinate, and combinations thereof.

[0465] In some embodiments, the pharmaceutical composition comprises an anti-caking

agent. Illustrative examples of anti-caking agents include calcium phosphate (tribasic), hydroxymethyl cellulose, hydroxypropyl cellulose, magnesium oxide, and combinations thereof.

[0466] Other excipients that may be used with the pharmaceutical compositions include, for example, albumin, antioxidants, antibacterial agents, antifungal agents, bioabsorbable polymers, chelating agents, controlled release agents, diluents, dispersing agents, dissolution enhancers, emulsifying agents, gelling agents, ointment bases, penetration enhancers, preservatives, solubilizing agents, solvents, stabilizing agents, sugars, and combinations thereof. Specific examples of each of these agents are described, for example, in the Handbook of Pharmaceutical Excipients, Rowe et al. (Eds.) 6th Ed. (2009), The Pharmaceutical Press.

[0467] In some embodiments, the pharmaceutical composition comprises a solvent. In some aspects, the solvent is saline solution, such as a sterile isotonic saline solution or dextrose solution. In some aspects, the solvent is water for injection.

[0468] In some embodiments, the pharmaceutical compositions are in a particulate form, such as a microparticle or a nanoparticle. Microparticles and nanoparticles may be formed from any suitable material, such as a polymer or a lipid. In some aspects, the microparticles or nanoparticles are micelles, liposomes, or polymersomes.

[0469] Further provided herein are anhydrous pharmaceutical compositions and dosage forms comprising an ABP, since water can facilitate the degradation of some ABPs.

[0470] Anhydrous pharmaceutical compositions and dosage forms provided herein can be prepared using anhydrous or low moisture containing ingredients and low moisture or low humidity conditions. Pharmaceutical compositions and dosage forms that comprise lactose and at least one active ingredient that comprises a primary or secondary amine can be anhydrous if substantial contact with moisture and/or humidity during manufacturing, packaging, and/or storage is expected.

[0471] An anhydrous pharmaceutical composition should be prepared and stored such that its anhydrous nature is maintained. Accordingly, anhydrous compositions can be packaged using materials known to prevent exposure to water such that they can be included in suitable formulary kits. Examples of suitable packaging include, but are not limited to, hermetically sealed foils, plastics, unit dose containers (e.g., vials), blister packs, and strip packs.

5.1. Parenteral Dosage Forms

[0472] In certain embodiments, the ABPs provided herein are formulated as parenteral dosage forms. Parenteral dosage forms can be administered to subjects by various routes including, but not limited to, subcutaneous, intravenous (including infusions and bolus injections), intramuscular, and intraarterial. Because their administration typically bypasses subjects'

natural defenses against contaminants, parenteral dosage forms are typically, sterile or capable of being sterilized prior to administration to a subject. Examples of parenteral dosage forms include, but are not limited to, solutions ready for injection, dry (e.g., lyophilized) products ready to be dissolved or suspended in a pharmaceutically acceptable vehicle for injection, suspensions ready for injection, and emulsions.

[0473] Suitable vehicles that can be used to provide parenteral dosage forms are well known to those skilled in the art. Examples include, but are not limited to: Water for Injection USP; aqueous vehicles such as, but not limited to, Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, and Lactated Ringer's Injection; water miscible vehicles such as, but not limited to, ethyl alcohol, polyethylene glycol, and polypropylene glycol; and nonaqueous vehicles such as, but not limited to, corn oil, cottonseed oil, peanut oil, sesame oil, ethyl oleate, isopropyl myristate, and benzyl benzoate.

[0474] Excipients that increase the solubility of one or more of the ABPs disclosed herein can also be incorporated into the parenteral dosage forms.

[0475] In some embodiments, the parenteral dosage form is lyophilized. Exemplary lyophilized formulations are described, for example, in U.S. Pat. Nos. 6,267,958 and 6,171,586; and WO 2006/044908.

6. Dosage and Unit Dosage Forms

[0476] In human therapeutics, the doctor will determine the posology which he considers most appropriate according to a preventive or curative treatment and according to the age, weight, condition and other factors specific to the subject to be treated.

[0477] In certain embodiments, a composition provided herein is a pharmaceutical composition or a single unit dosage form. Pharmaceutical compositions and single unit dosage forms provided herein comprise a prophylactically or therapeutically effective amount of one or more prophylactic or therapeutic ABPs.

[0478] The amount of the ABP or composition which will be effective in the prevention or treatment of a disorder or one or more symptoms thereof will vary with the nature and severity of the disease or condition, and the route by which the ABP is administered. The frequency and dosage will also vary according to factors specific for each subject depending on the specific therapy (e.g., therapeutic or prophylactic agents) administered, the severity of the disorder, disease, or condition, the route of administration, as well as age, body, weight, response, and the past medical history of the subject. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

[0479] In certain embodiments, exemplary doses of a composition include milligram or microgram amounts of the ABP per kilogram of subject or sample weight (e.g., about 10

micrograms per kilogram to about 50 milligrams per kilogram, about 100 micrograms per kilogram to about 25 milligrams per kilogram, or about 100 microgram per kilogram to about 10 milligrams per kilogram). In certain embodiment, the dosage of the ABP provided herein, based on weight of the ABP, administered to prevent, treat, manage, or ameliorate a disorder, or one or more symptoms thereof in a subject is 0.1 mg/kg, 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 10 mg/kg, or 15 mg/kg or more of a subject's body weight. It may be necessary to use dosages of the ABP outside the ranges disclosed herein in some cases, as will be apparent to those of ordinary skill in the art. Furthermore, it is noted that the clinician or treating physician will know how and when to interrupt, adjust, or terminate therapy in conjunction with subject response.

[0480] Different therapeutically effective amounts may be applicable for different diseases and conditions, as will be readily known by those of ordinary skill in the art. Similarly, amounts sufficient to prevent, manage, treat or ameliorate such disorders, but insufficient to cause, or sufficient to reduce, adverse effects associated with the ABPs provided herein are also encompassed by the dosage amounts and dose frequency schedules provided herein. Further, when a subject is administered multiple dosages of a composition provided herein, not all of the dosages need be the same. For example, the dosage administered to the subject may be increased to improve the prophylactic or therapeutic effect of the composition or it may be decreased to reduce one or more side effects that a particular subject is experiencing.

[0481] In certain examples, treatment or prevention can be initiated with one or more loading doses of an ABP or composition provided herein followed by one or more maintenance doses.

[0482] In certain examples, a dose of an ABP or composition provided herein can be administered to achieve a steady-state concentration of the ABP in blood or serum of the subject. The steady-state concentration can be determined by measurement according to techniques available to those of skill or can be based on the physical characteristics of the subject such as height, weight and age.

[0483] In certain examples, administration of the same composition may be repeated and the administrations may be separated by at least 1 day, 2 days, 3 days, 5 days, 10 days, 15 days, 30 days, 45 days, 2 months, 75 days, 3 months, or 6 months.

[0484] As discussed in more detail elsewhere in this disclosure, an ABP provided herein may optionally be administered with one or more additional agents useful to prevent or treat a disease or disorder. The effective amount of such additional agents may depend on the amount of ABP present in the formulation, the type of disorder or treatment, and the other factors known in the art or described herein.

7. Therapeutic Applications

[0485] For therapeutic applications, the ABPs of the disclosure are administered to a mammal,

generally a human, in a pharmaceutically acceptable dosage form such as those known in the art and those discussed above. For example, the ABPs of the disclosure may be administered to a human intravenously as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intra-cerebrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, or intratumoral routes. The ABPs also are suitably administered by peritumoral, intralesional, or perilesional routes, to exert local as well as systemic therapeutic effects. The intraperitoneal route may be particularly useful, for example, in the treatment of ovarian tumors.

[0486] The ABPs provided herein may be useful for the treatment of any disease or condition involving TIGIT. In some examples, the disease or condition is a disease or condition that can benefit from treatment with an anti-TIGIT ABP. In some examples, the disease or condition is a tumor. In some examples, the disease or condition is a cell proliferative disorder. In some examples, the disease or condition is a cancer. In some examples, the disease or condition is a viral infection.

[0487] In some embodiments, the ABPs provided herein are provided for use as a medicament. In some embodiments, the ABPs provided herein are provided for use in the manufacture or preparation of a medicament. In some embodiments, the medicament is for the treatment of a disease or condition that can benefit from an anti-TIGIT ABP. In some embodiments, the disease or condition is a tumor. In some embodiments, the disease or condition is a cell proliferative disorder. In some embodiments, the disease or condition is a cancer. In some embodiments, the disease or condition is a viral infection.

[0488] Any suitable cancer may be treated with the ABPs provided herein. Illustrative suitable cancers include, for example, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, anal cancer, appendix cancer, astrocytoma, basal cell carcinoma, brain tumor, bile duct cancer, bladder cancer, bone cancer, breast cancer, bronchial tumor, carcinoma of unknown primary origin, cardiac tumor, cervical cancer, chordoma, colon cancer, colorectal cancer, craniopharyngioma, ductal carcinoma, embryonal tumor, endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, fibrous histiocytoma, Ewing sarcoma, eye cancer, germ cell tumor, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, gestational trophoblastic disease, glioma, head and neck cancer, hepatocellular cancer, histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, Kaposi sarcoma, kidney cancer, Langerhans cell histiocytosis, laryngeal cancer, lip and oral cavity cancer, liver cancer, lobular carcinoma in situ, lung cancer, macroglobulinemia, malignant fibrous histiocytoma, melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary, midline tract carcinoma involving *NUT* gene, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma, mycosis fungoides, myelodysplastic syndrome, myelodysplastic/myeloproliferative neoplasm, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-small cell lung cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, papillomatosis, paraganglioma, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytomas, pituitary tumor,

pleuropulmonary blastoma, primary central nervous system lymphoma, prostate cancer, rectal cancer, renal cell cancer, renal pelvis and ureter cancer, retinoblastoma, rhabdoid tumor, salivary gland cancer, Sezary syndrome, skin cancer, small cell lung cancer, small intestine cancer, soft tissue sarcoma, spinal cord tumor, stomach cancer, T-cell lymphoma, teratoid tumor, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, vulvar cancer, and Wilms tumor.

[0489] Any suitable virus may be treated with the ABPs provided herein. Illustrative suitable viruses include, for example, adeno-associated virus, Aichi virus, Australian bat lyssavirus, BK polyomavirus, Banna virus, Barmah forest virus, Bunyamwera virus, Bunyavirus La Crosse, Bunyavirus snowshoe hare, Cercopithecine herpesvirus, Chandipura virus, Chikungunya virus, Cosavirus A, cowpox virus, Coxsackievirus, Crimean-Congo hemorrhagic fever virus, Dengue virus, Dhori virus, Dugbe virus, Duvenhage virus, eastern equine encephalitis virus, ebolavirus, echovirus, encephalomyocarditis virus, Epstein-Barr virus, European bat lyssavirus, GB virus C/Hepatitis G virus, Hantaan virus, Hendra virus, hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis E virus, hepatitis delta virus, horsepox virus, human adenovirus, human astrovirus, human coronavirus, human cytomegalovirus, human enterovirus, human herpesvirus 1, human herpesvirus 2, human herpesvirus 6, human herpesvirus 7, human herpesvirus 8, human immunodeficiency virus, human papillomavirus 1, human papillomavirus 2, human papillomavirus, human parainfluenza, human parvovirus B19, human respiratory syncytial virus, human rhinovirus, human SARS coronavirus, human spumaretrovirus, human T-lymphotropic virus, human torovirus, influenza A virus, influenza B virus, influenza C virus, Isfahan virus, JC polyomavirus, Japanese encephalitis virus, Junin arenavirus, KI polyomavirus, Kunjin virus, Lagos bat virus, Lake Victoria marburgvirus, Langat virus, Lassa virus, Lordsdale virus, Louping ill virus, lymphocytic choriomeningitis virus, Machupo virus, Mayaro virus, MERS coronavirus, measles virus, Mengo encephalomyocarditis virus, Merkel cell polyomavirus, Mokola virus, molluscum contagiosum virus, monkeypox virus, mumps virus, Murray valley encephalitis virus, New York virus, Nipah virus, Norwalk virus, O'nyong-nyong virus, Orf virus, Oropouche virus, Pichinde virus, poliovirus, Punta toro phlebovirus, Puumala virus, rabies virus, Rift Valley fever virus, Rosavirus A, Ross River virus, rotavirus A, rotavirus B, rotavirus C, rubella virus, Sagiyama virus, salivirus A, sandfly fever Sicilian virus, Sapporo virus, Semliki Forest virus, Seoul virus, simian foamy virus, simian virus 5, Sindbis virus, Southampton virus, St. Louis encephalitis virus, tick-borne powassan virus, torque teno virus, Toscana virus, Uukuniemi virus, vaccinia virus, varicella-zoster virus, variola virus, Venezuelan equine encephalitis virus, vesicular stomatitis virus, western equine encephalitis virus, WU polyomavirus, West Nile virus, Yaba monkey tumor virus, Yaba-like disease virus, yellow fever virus, and Zika virus.

[0490] In some examples, provided herein is a method of antagonizing TIGIT in a target cell of a subject in need thereof by administering an effective amount of an ABP provided herein to the subject. In some examples, antagonism of TIGIT by an ABP provided herein results in increased secretion of IL-2, LT- α , IL-6, TNF, GM-CSF, IFN γ or combinations thereof by a target cell.

[0491] In some examples, provided herein is a method of increasing the proliferation, survival, and/or function of an effector T cell in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject. In some examples the effector T cell is a CD4⁺ effector T cell. In some examples, the effector T cell is a CD8⁺ effector T cell.

[0492] In some examples, provided herein is a method of abrogating suppression of an effector T cell by a regulatory T cell in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject. In some examples, the regulatory T cell is a CD4⁺CD25⁺Foxp3⁺ regulator T cell. In some examples, the regulatory T cell is a CD8⁺CD25⁺ regulatory T cell.

[0493] In some examples, provided herein is a method of increasing the activity of a natural killer (NK) or natural killer T (NKT) cell in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0494] In some examples, provided herein is a method of enhancing an immune response in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0495] In some examples, provided herein is a method delaying the onset of a tumor in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0496] In some examples, provided herein is a method preventing the onset of a tumor in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0497] In some examples, provided herein is a method of delaying the onset of a cancer in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0498] In some examples, provided herein is a method of preventing the onset of a cancer in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0499] In some examples, provided herein is a method of reducing the size of a tumor in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0500] In some examples, provided herein is a method of reducing the number of metastases in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0501] In some examples, provided herein is a method of delaying the onset of a viral infection

in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0502] In some examples, provided herein is a method of preventing the onset of a viral infection in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0503] In some examples, provided herein is a method of reducing viral titer a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0504] In some examples, provided herein is a method of eliminating a virus from subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0505] In some examples, provided herein is a method for extending the period of overall survival, median survival time, or progression-free survival in a subject in need thereof by administering an effective amount of an ABP provided herein to the subject.

[0506] In some examples, provided herein is a method for treating a subject who has become resistant to a standard of care therapeutic by administering an effective amount of an ABP provided herein to the subject. In some examples, the standard-of-care therapeutic to which the subject has become resistant is a PD-1 inhibitor. In other examples, the standard-of-care therapeutic to which the subject has become resistant is a PD-L1 inhibitor. In other examples, the standard-of-care therapeutic to which the subject has become resistant is a CTLA-4 inhibitor.

8. Combination Therapies

[0507] In some embodiments, an ABP provided herein is for use with at least one additional therapeutic agent. Any suitable additional therapeutic agent may be administered with an ABP provided herein. In some aspects, the additional therapeutic agent is selected from radiation, a cytotoxic agent, a chemotherapeutic agent, a cytostatic agent, an anti-hormonal agent, an EGFR inhibitor, an immunostimulatory agent, an anti-angiogenic agent, and combinations thereof.

[0508] In some embodiments, the additional therapeutic agent comprises an immunostimulatory agent.

[0509] In some embodiments, the immunostimulatory agent is an agent that blocks signaling of an inhibitory receptor of an immune cell, or a ligand thereof. In some aspects, the inhibitory receptor or ligand is selected from CTLA-4, PD-1, PD-L1, LAG-3, Tim3, TIGIT, neuritin, BTLA, KIR, and combinations thereof. In some aspects, the agent is selected from an anti-PD-1 antibody (e.g., pembrolizumab or nivolumab), and anti-PD-L1 antibody (e.g., atezolizumab), an anti-CTLA-4 antibody (e.g., ipilimumab), and combinations thereof. In some aspects, the agent

is pembrolizumab. In some aspects, the agent is nivolumab. In some aspects, the agent is atezolizumab.

[0510] In some embodiments, the additional therapeutic agent is an agent that inhibits the interaction between PD-1 and PD-L1. In some aspects, the additional therapeutic agent that inhibits the interaction between PD-1 and PD-L1 is selected from an antibody, a peptidomimetic and a small molecule. In some aspects, the additional therapeutic agent that inhibits the interaction between PD-1 and PD-L1 is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, BMS-936559, sulfamonomethoxine 1, and sulfamethizole 2. In some embodiments, the additional therapeutic agent that inhibits the interaction between PD-1 and PD-L1 is any therapeutic known in the art to have such activity, for example as described in Weinmann et al., Chem Med Chem, 2016, 14:1576 (DOI: 10.1002/cmdc.201500566). In some embodiments, the agent that inhibits the interaction between PD-1 and PD-L1 is formulated in the same pharmaceutical composition as an ABP provided herein. In some embodiments, the agent that inhibits the interaction between PD-1 and PD-L1 is formulated in a different pharmaceutical composition from an ABP provided herein. In some embodiments, the agent that inhibits the interaction between PD-1 and PD-L1 is administered prior to administration of an ABP provided herein. In some embodiments, the agent that inhibits the interaction between PD-1 and PD-L1 is administered after administration of an ABP provided herein. In some embodiments, the agent that inhibits the interaction between PD-1 and PD-L1 is administered contemporaneously with an ABP provided herein, but the agent and ABP are administered in separate pharmaceutical compositions.

[0511] In some embodiments, the immunostimulatory agent is an agonist of a co-stimulatory receptor of an immune cell. In some aspects, the co-stimulatory receptor is selected from OX40, ICOS, CD27, CD28, 4-1BB, or CD40. In some embodiments, the agonist is an antibody.

[0512] In some embodiments, the immunostimulatory agent is a cytokine. In some aspects, the cytokine is selected from IL-2, IL-5, IL-7, IL-12, IL-15, IL-21, and combinations thereof.

[0513] In some embodiments, the immunostimulatory agent is an oncolytic virus. In some aspects, the oncolytic virus is selected from a herpes simplex virus, a vesicular stomatitis virus, an adenovirus, a Newcastle disease virus, a vaccinia virus, and a maraba virus.

[0514] In some embodiments, the immunostimulatory agent is a T cell with a chimeric antigen receptor (CAR-T cell). In some embodiments, the immunostimulatory agent is a bi- or multi-specific T cell directed antibody. In some embodiments, the immunostimulatory agent is an anti-TGF- β antibody. In some embodiments, the immunostimulatory agent is a TGF- β trap.

[0515] In some embodiments, the additional therapeutic agent is a vaccine to a tumor antigen. Any suitable antigen may be targeted by the vaccine, provided that it is present in a tumor treated by the methods provided herein. In some aspects, the tumor antigen is a tumor antigen that is overexpressed in comparison its expression levels in normal tissue. In some aspects, the tumor antigen is selected from cancer testis antigen, differentiation antigen, NY-ESO-1,

MAGE-A1, MART, and combinations thereof.

[0516] Further examples of additional therapeutic agents include a taxane (e.g., paclitaxel or docetaxel); a platinum agent (e.g., carboplatin, oxaliplatin, and/or cisplatin); a topoisomerase inhibitor (e.g., irinotecan, topotecan, etoposide, and/or mitoxantrone); folinic acid (e.g., leucovorin); or a nucleoside metabolic inhibitor (e.g., fluorouracil, capecitabine, and/or gemcitabine). In some embodiments, the additional therapeutic agent is folinic acid, 5-fluorouracil, and/or oxaliplatin. In some embodiments, the additional therapeutic agent is 5-fluorouracil and irinotecan. In some embodiments, the additional therapeutic agent is a taxane and a platinum agent. In some embodiments, the additional therapeutic agent is paclitaxel and carboplatin. In some embodiments, the additional therapeutic agent is pemetrexate. In some embodiments, the additional therapeutic agent is a targeted therapeutic such as an EGFR, RAF or MEK-targeted agent.

[0517] The additional therapeutic agent may be administered by any suitable means. In some embodiments, an ABP provided herein and the additional therapeutic agent are included in the same pharmaceutical composition. In some embodiments, an ABP provided herein and the additional therapeutic agent are included in different pharmaceutical compositions.

[0518] In embodiments where an ABP provided herein and the additional therapeutic agent are included in different pharmaceutical compositions, administration of the ABP can occur prior to, simultaneously, and/or following, administration of the additional therapeutic agent. In some examples, administration of an ABP provided herein and the additional therapeutic agent occur within about one month of each other. In some examples, administration of an ABP provided herein and the additional therapeutic agent occur within about one week of each other. In some examples, administration of an ABP provided herein and the additional therapeutic agent occur within about one day of each other. In some examples, administration of an ABP provided herein and the additional therapeutic agent occur within about twelve hours of each other. In some examples, administration of an ABP provided herein and the additional therapeutic agent occur within about one hour of each other.

9. Diagnostic Methods

[0519] Also provided are methods for detecting the presence of TIGIT on cells from a subject. Such methods may be used, for example, to predict and evaluate responsiveness to treatment with an ABP provided herein.

[0520] In some examples, a blood sample is obtained from a subject and the fraction of cells expressing TIGIT is determined. In some examples, the relative amount of TIGIT expressed by such cells is determined. The fraction of cells expressing TIGIT and the relative amount of TIGIT expressed by such cells can be determined by any suitable method. In some examples, flow cytometry is used to make such measurements. In some examples, fluorescence assisted cell sorting (FACS) is used to make such measurement. See Li et al., J. Autoimmunity, 2003,

21:83-92 for methods of evaluating expression of TIGIT in peripheral blood.

10. Kits

[0521] Also provided are kits comprising the ABPs provided herein. The kits may be used for the treatment, prevention, and/or diagnosis of a disease or disorder, as described herein.

[0522] In some embodiments, the kit comprises a container and a label or package insert on or associated with the container. Suitable containers include, for example, bottles, vials, syringes, and IV solution bags. The containers may be formed from a variety of materials, such as glass or plastic. The container holds a composition that is by itself, or when combined with another composition, effective for treating, preventing and/or diagnosing a disease or disorder. The container may have a sterile access port. For example, if the container is an intravenous solution bag or a vial, it may have a port that can be pierced by a needle. At least one active agent in the composition is an ABP provided herein. The label or package insert indicates that the composition is used for treating the selected condition.

[0523] In some embodiments, the kit comprises (a) a first container with a first composition contained therein, wherein the first composition comprises an ABP provided herein; and (b) a second container with a second composition contained therein, wherein the second composition comprises a further therapeutic agent. The kit in this embodiment of the invention may further comprise a package insert indicating that the compositions can be used to treat a particular condition.

[0524] Alternatively, or additionally, the kit may further comprise a second (or third) container comprising a pharmaceutically-acceptable excipient. In some aspects, the excipient is a buffer. The kit may further include other materials desirable from a commercial and user standpoint, including filters, needles, and syringes.

11. Other Illustrative Examples

[0525] The examples provided below are non-limiting and provided by way of illustration of certain examples of the disclosure, in addition to those described throughout this disclosure.

[0526] Example 1: An antigen binding protein that binds specifically to a human TIGIT (hTIGIT) and is capable of at least one of the following: a) inhibits binding of hTIGIT to CD155 and CD112; b) increases a T effector cell function; c) increases a natural killer (NK) cell function; d) decreases the number of regulatory T cells in tissues or in circulation; e) suppresses a regulatory T cell or a regulatory T cell activity; f) inhibits association of TIGIT and CD226; and does not bind specifically to Nectin-4 (also known as poliovirus-receptor-like 4, PVRL4).

[0527] Example 2: The antigen binding protein of Example 1, wherein the antigen binding protein has one or more of the following characteristics: a) is a monoclonal antibody; b) is a human antibody, a humanized antibody, or a chimeric antibody; c) is a bispecific antibody, a multispecific antibody, a diabody, or a multivalent antibody; d) is of the IgG1, IgG2, IgG3, the IgG4 type, or the IgG4 isotype with a S228P substitution; e) is an antigen-binding antibody fragment; f) is a Fab fragment, a Fab' fragment, a F(ab')₂ fragment, or an Fv fragment; g) is a single chain antibody, a single domain antibody, or a nanobody.

[0528] Example 3: A pharmaceutical composition comprising an effective amount of an antibody which binds to hTIGIT and: (a) increases cell-mediated immunity; (b) increases T-cell activity; (c) increases cytolytic T-cell (CTL) activity; (d) increases natural killer (NK) cell activity; (e) is an antagonist of TIGIT-mediated signaling; (f) inhibits TIGIT signaling; (g) inhibits or blocks the interaction between PVR and TIGIT; (h) inhibits or blocks the interaction of TIGIT and CD155 ligand and/or CD112; but does not inhibit the interaction between PVR and CD226.

[0529] Example 4: A pharmaceutical composition comprising the antigen-binding protein of Example 1 or Example 2.

[0530] Example 5: The pharmaceutical composition of Example 4, further comprising an effective amount of an anti-PD-1 antibody.

[0531] Example 6: The antigen binding protein of Example 1, wherein the antigen binding protein has one or more of the following characteristics: a) binds to a human TIGIT polypeptide or a variant thereof, or as otherwise provided herein with a K_D of less than about 20 nM; or b) binds to a cynomolgus monkey (also "cynomolgus" or "cyno") TIGIT polypeptide or a variant thereof, or as otherwise provided herein, with a K_D of less than about 200 nM; c) binds to a murine TIGIT polypeptide or a variant thereof, or as otherwise provided herein, with a K_D of less than about 200 nM; or d) a combination of at least 2 of a), b), and c).

[0532] Example 7: An antigen binding protein that competes or is capable of competing for binding to human TIGIT with a reference antigen binding protein, wherein the reference antigen binding protein is the antigen binding protein of Example 1.

[0533] Example 8: The antigen binding protein of Example 7, wherein the antigen binding protein and the reference antibody cross-compete or are capable of cross-competing for binding to a human TIGIT.

[0534] Example 9: The antigen binding protein of Example 1, comprising a heavy chain constant region comprising a human heavy chain constant region or fragment or a variant thereof, wherein the constant region variant comprises up to 20 conservatively modified amino acid substitutions.

[0535] Example 10: The antigen binding protein of Example 1, that competes or is capable of

competing for binding to human TIGIT with a CD155 protein and/or a CD112 protein.

[0536] Example 11: The antigen binding protein of Example 1, that is capable of antagonizing TIGIT signaling in a T cell-specific manner.

[0537] Example 12: An isolated antibody molecule capable of binding to human TIGIT (hTIGIT), comprising a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NOs: 48-62, a VHCDR2 amino acid sequence of SEQ ID NO:36-47, and a VHCDR3 amino acid sequence of SEQ ID NO:29-35; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO:70-72, a VLCDR2 amino acid sequence of SEQ ID NO:67-69, and a VLCDR3 amino acid sequence of SEQ ID NO:63-66.

[0538] Example 13: An isolated nucleic acid encoding an antigen binding protein according to Example 1.

[0539] Example 14: An expression vector comprising the nucleic acid according to Example 13.

[0540] Example 15: A prokaryotic or eukaryotic host cell comprising a vector of Example 14.

[0541] Example 16: A method for the production of a recombinant protein comprising the steps of expressing a nucleic acid according to Example 13 in a prokaryotic or eukaryotic host cell and recovering said protein from said cell or the cell culture supernatant.

[0542] Example 17: A method for treatment of a subject suffering from cancer or from an inflammatory disease, comprising the step of administering to the subject a pharmaceutical composition comprising an effective amount of the antigen binding protein of Example 1.

[0543] Example 18: The method of Example 17, wherein the cancer is a solid cancer.

[0544] Example 19: The method of Example 17, wherein the cancer is a hematological cancer.

[0545] Example 20: A method for modulating immune system function in a human subject in need thereof, comprising the step of contacting a population of T cells of the human subject with a pharmaceutical composition comprising an effective amount of the antigen binding protein of Example 1, under conditions such that the immune system is modulated.

[0546] Example 21: A method for inducing or enhancing an immune response in a subject, comprising the step of administering to the subject a pharmaceutical composition comprising an antigen binding protein or a bispecific antibody or a complexing antigen binding protein, of any of the preceding examples, wherein the immune response is generated against a tumor antigen.

[0547] Example 22: The method of Example 21, wherein the antigen binding protein, bispecific antibody or the complexing antigen binding protein is administered in an amount sufficient to achieve one or more of the following in the subject: a) reduce regulatory T cells suppression of activity of effector T cells; b) decrease levels of regulatory T cells; c) activation of effector T cells; d) induce or enhance effector T cell proliferation; e) inhibit tumor growth; and f) induce tumor regression.

[0548] Example 23: The method of Example 22, wherein the method further comprises one or more of the following a) administering chemotherapy; b) administering radiation therapy; or c) administering one or more additional therapeutic agents.

[0549] Example 24: The method of Example 23, wherein the additional therapeutic agent comprises an immunostimulatory agent.

[0550] Example 25: The method of Example 24, wherein the immunostimulatory agent comprises an antagonist to an inhibitory receptor of an immune cell.

[0551] Example 26: The method of Example 25, wherein the inhibitory receptor is CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5, VISTA, LAIR1, CD160, 2B4, TGF-R, or a KIR.

[0552] Example 27: The method of Example 24, wherein the immunostimulatory agent comprises an agonist of co-stimulatory receptor of an immune cell.

[0553] Example 28: The method of Example 27, wherein the co-stimulatory receptor is OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD28, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3 or CD83 ligand.

[0554] Example 29: The method of Example 24, wherein the immunostimulatory agent comprises a cytokine.

[0555] Example 30: The method of Example 29, wherein the cytokine is IL-2, IL-5, IL-7, IL-12, IL-15 or IL-21.

[0556] Example 31: The method of Example 24, wherein the immunostimulatory agent comprises an oncolytic virus.

[0557] Example 32: The method of Example 31, wherein the oncolytic virus is a Herpes simplex virus, a Vesicular stomatitis virus, an adenovirus, a Newcastle disease virus, a vaccinia virus, or a maraba virus.

[0558] Example 33: The method of Example 24, wherein the immunostimulatory agent comprises a chimeric antigen engineered T cell.

[0559] Example 34: The method of Example 24, wherein the immunostimulatory agent comprises a bi- or multispecific T cell directed antibody.

[0560] Example 35: The method of Example 23, wherein the additional therapeutic agent comprises an anti-TGF-beta antibody or a TGF β receptor trap.

[0561] Example 36: The method of any one of Example 20-35, wherein administration of the pharmaceutical composition results in induction or enhancement of proliferation of a T-effector cell, or modulation of I- κ B and/or NF- κ B in the T cell, or modulation of TIGIT activity in the T cell, or T cell receptor induced signaling in a T-effector cell, or a combination thereof.

[0562] Example 37: A method of screening for test compounds comprising an antigen binding protein of Example 1 that are capable of inhibiting the interaction of a TIGIT ligand with TIGIT, comprising the steps of: contacting a sample containing a TIGIT ligand and TIGIT with the compound; and determining whether the interaction of a TIGIT ligand with TIGIT in the sample is decreased relative to the interaction of a TIGIT ligand with TIGIT in a sample not contacted with the compound, whereby a decrease in the interaction of a TIGIT ligand with TIGIT in the sample contacted with the compound identifies the compound as one that inhibits the interaction of a TIGIT ligand with TIGIT.

[0563] Example 38: The antigen binding protein of Example 1, that is capable of inhibiting phosphorylation of the ITIM domain of the TIGIT polypeptide.

[0564] Example 1A: An isolated antigen-binding protein (ABP) that specifically binds to TIGIT, wherein the antibody: (a) competes for binding to TIGIT with an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure; (b) inhibits binding of CD155 to TIGIT; (c) inhibits binding of CD112 to TIGIT; (d) inhibits association of CD226 with TIGIT; (e) activates an effector T cell or an NK cell; (f) decreases the number of regulatory T cells in a tissue or in circulation; (g) inhibits the suppression of an effector T cell by a regulatory T cell; (h) does not bind specifically to any of PVRL1, PVRL2, PVRL3, or PVRL4; or (i) is capable of any combination of (a) - (h).

[0565] Example 2A: The ABP of Example 1A, wherein the ABP comprises a CDR-H3 of a V_H region selected from SEQ ID NOs: 4-24, or a CDR-H3 having at least about 80% identity to a CDR-H3 of a V_H region selected from SEQ ID NOs: 4-24.

[0566] Example 3A: The ABP of Example 2A, wherein the CDR-H3 is identified according to the Kabat, Chothia, or IMGT numbering schemes.

[0567] Example 4A: The ABP of any of Example 2A-3A, wherein the CDR-H3 is selected from SEQ ID NOs: 29-35.

[0568] Example 5A: The ABP of any of Examples 1A-4A, wherein the ABP comprises a CDR-H2 of a V_H region selected from SEQ ID NOs: 4-24, or a CDR-H2 having at least about 80% identity to a CDR-H2 of a V_H region selected from SEQ ID NOs: 4-24

[0569] Example 6A: The ABP of Example 5A, wherein the CDR-H2 is identified according to the Kabat, Chothia, or IMGT numbering schemes.

[0570] Example 7A: The ABP of any of Examples 5A-6A, wherein the CDR-H2 is selected from SEQ ID NOs: 36-47.

[0571] Example 8A: The ABP of any of Examples 1A-7A, wherein the ABP comprises a CDR-H1 of a V_H region selected from SEQ ID NOs: 4-24, or a CDR-H1 having at least about 80% identity to a CDR-H1 of a V_H region selected from SEQ ID NOs: 4-24

[0572] Example 9A: The ABP of Example 8A, wherein the CDR-H1 is identified according to the Kabat, Chothia, Kabat plus Chothia, or IMGT numbering schemes.

[0573] Example 10A: The ABP of any of Examples 8A-9A, wherein the CDR-H1 is selected from SEQ ID NOs: 48-54 and 58-62.

[0574] Example 11A: The ABP of any of Examples 1A-10A, wherein the ABP comprises a CDR-L3 of a V_L region selected from SEQ ID NOs: 25-28, or a CDR-L3 having at least about 80% identity to a CDR-L3 of a V_L region selected from SEQ ID NOs: 25-28.

[0575] Example 12A: The ABP of Example 11A, wherein the CDR-L3 is identified according to the Kabat, Chothia, or IMGT numbering schemes.

[0576] Example 13A: The ABP of any of Examples 11A-12A, wherein the CDR-L3 is selected from SEQ ID NOs: 63-66.

[0577] Example 14A: The ABP of any of Examples 1A-13A, wherein the ABP comprises a CDR-L2 of a V_L region selected from SEQ ID NOs: 25-28, or a CDR-L2 having at least about 80% identity to a CDR-L2 of a V_L region selected from SEQ ID NOs: 25-28.

[0578] Example 15A: The ABP of Example 14A, wherein the CDR-L2 is identified according to the Kabat, Chothia, or IMGT numbering schemes.

[0579] Example 16A: The ABP of any of Examples 14A-15A, wherein the CDR-L2 is selected from SEQ ID NOs: 67-69.

[0580] Example 17A: The ABP of any of Examples 1A-16A, wherein the ABP comprises a CDR-L1 of a V_L region selected from SEQ ID NOs: 25-28, or a CDR-L1 having at least about 80% identity to a CDR-L1 of a V_L region selected from SEQ ID NOs: 25-28.

[0581] Example 18A: The ABP of Example 17A, wherein the CDR-L1 is identified according to the Kabat, Chothia, or IMGT numbering schemes.

[0582] Example 19A: The ABP of any of Examples 17A-18A, wherein the CDR-L1 is selected from SEQ ID NOs: 70-72.

[0583] Example 20A: The ABP of any of Examples 1A-19A, wherein the ABP comprises a V_H region selected from SEQ ID NOs: 4-24.

[0584] Example 21A: The ABP of any of Examples 1A-20A, wherein the ABP comprises a V_L region selected from SEQ ID NOs: 25-28.

[0585] Example 22A: The ABP of any of Examples 1A-21A, wherein the TIGIT is selected from hTIGIT (SEQ ID NO: 1), cTIGIT (SEQ ID NO: 2), and mTIGIT (SEQ ID NOs: 3 or 138).

[0586] Example 23A: The ABP of any of Examples 1A-22A, wherein the ABP comprises an antibody.

[0587] Example 24A: The ABP of Example 23A, wherein the antibody comprises a V_H and V_L paired as provided for an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure.

[0588] Example 25A: The ABP of Example 24A, wherein the ABP is an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure.

[0589] Example 26A: The ABP of any of Examples 23A-25A, wherein the antibody is a monoclonal antibody.

[0590] Example 27A: The ABP of any of Examples 23A-26A, wherein the antibody is a chimeric, humanized, or human antibody.

[0591] Example 28A: The ABP of any of Examples 1A-27A, wherein the ABP is multispecific.

[0592] Example 29A: The ABP of any of Examples 1A-28A, wherein the ABP comprises an antibody fragment.

[0593] Example 30A: The ABP of any of Examples 1A-29A, wherein the ABP comprises an alternative scaffold.

[0594] Example 31A: The ABP of any of Examples 1A-30A, wherein the ABP comprises an immunoglobulin constant region.

[0595] Example 32A: The ABP of any of Examples 1A-31A, wherein the ABP comprises an antibody selected from an IgA, an IgD, an IgE, an IgG, or an IgM.

[0596] Example 33A: The ABP of Example 32A, wherein the ABP comprises an IgG selected from an IgG4, an IgG1, an IgG2, or an IgG3.

[0597] Example 34A: The ABP of any of Examples 1A-33A, wherein the ABP binds hTIGIT (SEQ ID NO: 1) with an affinity of less than about 20 nM.

[0598] Example 35A: The ABP of any of Examples 1A-34A, wherein the ABP binds cTIGIT (SEQ ID NO: 2) with an affinity of less than about 200 nM.

[0599] Example 36A: The ABP of any of Examples 1A-35A, wherein the ABP binds mTIGIT (SEQ ID NO: 3 or 138) with an affinity of less than about 200 nM.

[0600] Example 37A: An isolated polynucleotide encoding an ABP of any of Examples 1A-36A, a V_H or V_L thereof, or an antigen-binding portion thereof.

[0601] Example 38A: A vector comprising the polynucleotide of Example 37A.

[0602] Example 39A: A host cell comprising the vector of Example 38A.

[0603] Example 40A: A method of producing an ABP of any of Examples 1A-36A, comprising expressing the ABP in the host cell of Example 39A and isolating the expressed ABP.

[0604] Example 41A: A pharmaceutical composition comprising an ABP of any of Examples 1A-36A.

[0605] Example 42A: The pharmaceutical composition of Example 41A, wherein the amount of the ABP in the pharmaceutical composition is sufficient to (a) increase effector T cell activity; (b) increase cytolytic T cell activity; (c) increase NK cell activity; (d) inhibit TIGIT-mediated signaling; (e) inhibit or block the binding of CD155 and or CD112 to TIGIT; or (f) any combination of (a) - (e), in a subject.

[0606] Example 43A: The pharmaceutical composition of any of Examples 41A-42A, further comprising an antibody that antagonizes PD-1.

[0607] Example 44A: A method of treating or preventing a disease or condition in a subject in need thereof, comprising administering to the subject an effective amount of an ABP of any of Examples 1A-36A or a pharmaceutical composition of any of Examples 41A-43A.

[0608] Example 45A: The method of Example 44A, wherein the disease or condition is a cancer or viral infection.

[0609] Example 46A: A method of modulating an immune response in a subject in need thereof, comprising administering to the subject an effective amount of an ABP of any of Examples 1A-36A or a pharmaceutical composition of any of Examples 41A-43A.

[0610] Example 47A: The method of any of Examples 44A-46A, further comprising administering one or more additional therapeutic agents to the subject.

[0611] Example 48A: The method of Example 47A, wherein the additional therapeutic agent is selected from a PD-1 antagonist antibody, a chemotherapy, an immunostimulatory agent, and radiation.

[0612] Example 49A: The method of Examples 47A, wherein the additional therapeutic agent is an immunostimulatory agent that blocks signaling of an inhibitory receptor of an immune cell or a ligand thereof.

[0613] Example 50A: The method of Example 49A, wherein the inhibitory receptor or ligand thereof is selected from CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5, VISTA, LAIR1, CD160, 2B4, TGF-R, KIR, and combinations thereof.

[0614] Example 51A: The method of Example 48A, wherein the additional therapeutic agent is an immunostimulatory agent that is an agonist to a stimulatory receptor of an immune cell.

[0615] Example 52A: The method of Example 51A, wherein the stimulatory receptor of an immune cell is selected from OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD28, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, CD83 ligand, and combinations thereof.

[0616] Example 53A: The method of Example 48A, wherein the additional therapeutic agent is an immunostimulatory agent that is a cytokine.

[0617] Example 54A: The method of Example 53A, wherein the cytokine is selected from IL-2, IL-5, IL-7, IL-12, IL-15, IL-21, and combinations thereof.

[0618] Example 55A: The method of Example 48A, wherein the additional therapeutic agent is an immunostimulatory agent that is an oncolytic virus.

[0619] Example 56A: The method of Example 55A, wherein the oncolytic virus is selected from herpes simplex virus, vesicular stomatitis virus, adenovirus, Newcastle disease virus, vaccinia virus, a maraba virus, and combinations thereof.

[0620] Example 57A: The method of Example 48A, wherein the immunostimulatory agent

comprises a T cell expressing a chimeric antigen receptor.

[0621] Example 58A: The method of Example 48A, wherein the immunostimulatory agent comprises a bi- or multi-specific T cell directed antibody.

[0622] Example 59A: The method of Example 48A, wherein the immunostimulatory agent comprises an anti-TGF- β antibody, a TGF- β trap, or a combination thereof.

[0623] Example 60A: The method of Example 48A, wherein the immunostimulatory agent comprises a vaccine to a cancer-associated antigen.

[0624] Example 61A: A method of screening for ABPs capable of inhibiting the interaction of a ligand of TIGIT with TIGIT, comprising (a) contacting a sample comprising a ligand of TIGIT and TIGIT with an ABP of any of Examples 1A-36A, and (b) determining if the binding of the ligand of TIGIT to TIGIT is decreased in the presence of the ABP, in comparison to the binding of the ligand of TIGIT to TIGIT in the absence of the ABP.

EXAMPLES

[0625] The following are examples of methods and compositions of the invention. It is understood that various other embodiments may be practiced, given the general description provided herein.

Example 1: Selection of TIGIT Antigen-Binding Proteins

[0626] TIGIT ABPs were selected from a synthetic library of human antibodies expressed and displayed on the surface of yeast cells in IgG format, as generally described, e.g., in WO2009036379; WO2010105256; WO2012009568; and Xu et al., Protein Eng. Des. Sel., 2013, 26:663-670, and more specifically as provided below. The sequences and characteristics of the ABPs isolated from the recombinant library are provided in Table 5.

[0627] Eight naive human synthetic yeast libraries each of $\sim 10^9$ diversity were propagated as described in WO2009036379; WO2010105256; WO2012009568; and Xu et al., Protein Eng. Des. Sel., 2013, 26:663-670. For the first two rounds of selection, a magnetic bead sorting technique utilizing the Miltenyi MACS[®] system was performed, as described in Siegel et al., J. Immunol. Meth., 2004, 286:141-153. Briefly, yeast cells ($\sim 10^{10}$ cells/library) were incubated with biotinylated TIGIT-Fc antigen in FACS wash buffer (phosphate-buffered saline (PBS)/0.1% bovine serum albumin (BSA)). After washing once with 50 ml ice-cold wash buffer, the cell pellet was resuspended in 40 mL wash buffer, and 500 μ l streptavidin MicroBeads[™] (Miltenyi Biotec) were added to the yeast and incubated for 15 min at 4°C. Next, the yeast were

pelleted, resuspended in 5 mL wash buffer, and loaded onto a Miltenyi LS column. After the 5 mL was loaded, the column was washed 3 times with 3 mL FACS wash buffer. The column was then removed from the magnetic field, and the yeast were eluted with 5 mL of growth media and then grown overnight. The following rounds of sorting were performed using flow cytometry. Approximately 1×10^8 yeast were pelleted, washed three times with wash buffer, and incubated with decreasing concentrations of biotinylated TIGIT-Fc fusion antigen (100 to 1 nM) under equilibrium conditions at room temperature. Yeast were then washed twice and stained with LC-FITC (diluted 1:100) and either SA-633 (diluted 1:500) or EA-PE (diluted 1:50) secondary reagents for 15 min at 4°C. After washing twice with ice-cold wash buffer, the cell pellets were resuspended in 0.4 mL wash buffer and transferred to strainer-capped sort tubes. Sorting was performed using a FACS ARIA sorter (BD Biosciences) and sort gates were assigned to select for specific binders relative to a background control. Subsequent rounds of selection were employed in order to reduce the number of non-specific binders utilizing soluble membrane proteins from CHO cells (see WO2014179363 and Xu et al., Protein Eng. Des. Sel., 2013, 26:663-670), and identify binders with improved affinity to TIGIT using the TIGIT-Fc antigen. After the final round of sorting, yeast were plated and individual colonies were picked for characterization and for nomination of clones for affinity maturation.

Example 2: Affinity Maturation

[0628] Optimization of naive clones was carried out utilizing three maturation strategies: light chain diversification; diversification of CDR-H1 and CDR-H2; and performing VH mutagenesis.

[0629] *Light Chain Diversification:* Heavy chain plasmids were extracted from naive outputs (described above) and transformed into a light chain library with a diversity of 1×10^6 . Selections were performed as described above with one round of MACS sorting and two rounds of FACS sorting using 10 nM or 1 nM biotinylated TIGIT-Fc antigen for respective rounds.

[0630] *CDR-H1 and CDR-H2 Selection:* The CDR-H3s from clones selected from the light chain diversification procedure were recombined into a premade library with CDR-H1 and CDR-H2 variants of a diversity of 1×10^8 and selections were performed using monomeric HIS-TIGIT antigen. Affinity pressures were applied by using decreasing concentrations of biotinylated HIS-TIGIT antigen (100 to 1 nM) under equilibrium conditions at room temperature.

[0631] *V_Hmut Selection:* Clones obtained from the CDR-H1 and CDR-H2 selection procedure were subject to additional rounds of affinity maturation via error prone PCR-based mutagenesis of the heavy chain. Selections were performed using HIS-TIGIT as antigen generally as described above but with the addition of employing FACS sorting for all selection rounds.

Example 3: Antibody Production and Purification

[0632] In order to produce sufficient amounts of selected antibodies for further characterization, the yeast clones were grown to saturation and then induced for 48 h at 30°C with shaking. After induction, yeast cells were pelleted and the supernatants were harvested for purification. IgGs were purified using a Protein A column and eluted with acetic acid, pH 2.0. Fab fragments were generated by papain digestion and purified over KappaSelect® (GE Healthcare LifeSciences).

[0633] Antibodies were also produced by transient transfection of Expi293 cells according to the manufacturer's protocol (Thermo Fisher), transient transfection of CHO cells, or stable expression of CHO cells. Antibodies were purified by Protein A chromatography.

and germlines (GL) of TIGIT ABPs.

CDR-H1	CDR-H2	CDR-H3	VH Protein	VL GL	CDR-L1	CDR-L2	CDR-L3	VL Protein
GSITSS SYWWG (SEQ ID NO: 48)	SIYYSG ATFYN PSLKS (SEQ ID NO: 36)	ARDAN YYGSA WAFDP (SEQ ID NO: 29)	QLQLQESGPGLVKPSSETLSLT CTVSGGSITSSYYWGWIRQP PGKGLEWIGSIYYSGSTFYNPS SLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDANYYG SAWAFDPWGQGTLLVTVSS (SEQ ID NO: 4)	VK3-11	RASQS VSSYL A (SEQ ID NO: 70)	DASNR AT (SEQ ID NO: 67)	QQHFN LPT (SEQ ID NO: 63)	EIVLTQSPATLSLSP GERATLSRASQSV SSYLAWYQQKPGQ APRLIYDASNRAT GIPARFSGSGGTDF TLTISSLEPEDFAVY YCQQHFNLPFTGGG TKVEIK (SEQ ID NO: 25)
GSISST KYYWG (SEQ ID NO: 49)	SIYYSG STFYN PSLKS (SEQ ID NO: 37)	ARDAN YYGSA WAFDP (SEQ ID NO: 29)	QLQLQESGPGLVKPSSETLSLT CTVSGGSISSTSHYWGWIRQP PGKGLEWIGSIYYSGSTFYNPS LKSRVTISVDTSKNQFSLKLS VTAADTAVYYCARDANYYG AWAFDPWGQGTLLVTVSS (SEQ ID NO: 5)	VK3-11	RASQS VSSYL A (SEQ ID NO: 70)	DASNR AT (SEQ ID NO: 67)	QQHFN LPT (SEQ ID NO: 63)	EIVLTQSPATLSLSP GERATLSRASQSV SSYLAWYQQKPGQ APRLIYDASNRAT GIPARFSGSGGTDF TLTISSLEPEDFAVY YCQQHFNLPFTGGG TKVEIK (SEQ ID NO: 25)
GSISST SHYWG (SEQ ID NO: 50)	SIYYSG STFYN PSLKS (SEQ ID NO: 37)	ARDAN YYGSA WAFDP (SEQ ID NO: 29)	QLQLQESGPGLVKPSSETLSLT CTVSGGSISSTSHYWGWIRQP PGKGLEWIGSIYYSGSTFYNPS LKSRVTISVDTSKNQFSLKLS VTAADTAVYYCARDANYYG AWAFDPWGQGTLLVTVSS (SEQ ID NO: 6)	VK3-11	RASQS VSSYL A (SEQ ID NO: 70)	DASNR AT (SEQ ID NO: 67)	QQHFN LPT (SEQ ID NO: 63)	EIVLTQSPATLSLSP GERATLSRASQSV SSYLAWYQQKPGQ APRLIYDASNRAT GIPARFSGSGGTDF TLTISSLEPEDFAVY YCQQHFNLPFTGGG TKVEIK (SEQ ID NO: 25)

Table 5. Sequences 4

Ab	VH	GL
MAB1-IgG4	VH4-39	
MAB2-IgG4	VH4-39	
MAB3-IgG4	VH4-39	

MAB4-IgG4	VH4-39	QQLQESGPGGLVKPSETLSLT CTVSGGSISSISHYWGWRQP PGKGLEWIGSIYSGSTFYNPS LKSRVTISVDTSKNQFSLKLS VTAADTAVYYCARDANYYG GAWAFDPWGQGTTLVTSS (SEQ ID NO: 7)	ARDAN YYGGA WAFDP (SEQ ID NO: 30)	SIYYS STFYN PSLKS (SEQ ID NO: 37)	GSISST SHYWG (SEQ ID NO: 50)	QQHFN LPT (SEQ ID NO: 63) DASNR AT (SEQ ID NO: 67) RASQS VSSYL A (SEQ ID NO: 70)	EIVLTQSPATLSLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLLIYDASNRAT GIPARFSGSGGTDF TLTSLEPEDFAVY YCQQHFNLPTFGGG TKVEIK (SEQ ID NO: 25)
MAB5-IgG4	VH4-39	QQLQESGPGGLVKPSETLSLT CTVSGGSISSISHYWGWRQP PGKGLEWIGSIYSGSTFYNPS LKGRVTISVDTSKNQFSLKLS VTAADTAVYYCARDANYYG AWAADPWGQGTTLVTSS (SEQ ID NO: 8)	ARDAN YYGSA WAFDP (SEQ ID NO: 29)	SIYYS STFYN PSLKG (SEQ ID NO: 38)	GSISST SHYWG (SEQ ID NO: 50)	QQHFN LPT (SEQ ID NO: 63) DASNR AT (SEQ ID NO: 67) RASQS VSSYL A (SEQ ID NO: 70)	EIVLTQSPATLSLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLLIYDASNRAT GIPARFSGSGGTDF TLTSLEPEDFAVY YCQQHFNLPTFGGG TKVEIK (SEQ ID NO: 25)
MAB6-IgG4	VH4-39	QQLQESGPGGLVKPSETLSLT CTVSGGSISSISHYWGWRQP PGKGLEWIGSIYSGGTYYNP SLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDGVLTL NKRSFDIWGQGTMTVSS (SEQ ID NO: 9)	ARDGV LTLNK RSFDI (SEQ ID NO: 31)	SIYYS GTYYN PSLKS (SEQ ID NO: 39)	GSIESG SYWYG (SEQ ID NO: 51)	QHHTV RPPLT (SEQ ID NO: 64) GASSR AT (SEQ ID NO: 68) RASQS VSSSY LA (SEQ ID NO: 71)	EIVLTQSPGTLSLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLLIYGASSRATG IPDRFSGSGGTDF LTISRLEPEDFAVY CQHTVVRPPLTFGG GTKVEIK (SEQ ID NO: 26)
MAB7-IgG4	VH4-31	QVQLQESGPGGLVKPSQTLST CTVSGGSISSISHYWGWRQP PGKGLEWIGSIYSGSTYYNP SLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDGVLTL NKRSFDIWGQGTMTVSS (SEQ ID NO: 10)	ARDGV LTLNK RSFDI (SEQ ID NO: 31)	SIYYS STYYN PSLKS (SEQ ID NO: 40)	GSIESG VYYWG (SEQ ID NO: 52)	QHHTV RPPLT (SEQ ID NO: 64) GASSR AT (SEQ ID NO: 68) RASQS VSSSY LA (SEQ ID NO: 71)	EIVLTQSPGTLSLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLLIYGASSRATG IPDRFSGSGGTDF LTISRLEPEDFAVY CQHTVVRPPLTFGG GTKVEIK (SEQ ID NO: 26)

2HTV *PLT EQ ID): 64)	EIVLTQSPGTLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLIYGASSRATG IPDRFSGSGSDTFT LTISRLEPEDFAVYY CQQHTVRPPLTFGG GTKVEIK (SEQ ID NO: 26)
2HTV *PLT EQ ID): 64)	EIVLTQSPGTLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLIYGASSRATG IPDRFSGSGSDTFT LTISRLEPEDFAVYY CQQHTVRPPLTFGG GTKVEIK (SEQ ID NO: 26)
2YVV *PLT EQ ID): 65)	EIVMTQSPATLSVSP GERATLSCRASQSV SSNLAWYQQKPGQ APRLIYGASTRATG IPARFSGSGSGTEFT LTISSLQSEDFAVYY CQQYVWVWPPLTFGG GTKVEIK (SEQ ID NO: 27)
2YVV *PLT EQ ID): 65)	EIVMTQSPATLSVSP GERATLSCRASQSV SSNLAWYQQKPGQ APRLIYGASTRATG IPARFSGSGSGTEFT LTISSLQSEDFAVYY CQQYVWVWPPLTFGG GTKVEIK (SEQ ID NO: 27)

MAB8- IgG4	VH4- 39	GSIASG SYWVG (SEQ ID NO: 53)	SIYYSG QTYYN PSLKS (SEQ ID NO: 41)	ARDGV LTLNK RSFDI (SEQ ID NO: 31)	QLQLQESGPGLVKPSQTLST CTVSGGSIESGLYYWGWRQP PGKGLEWIGSIYYSQSTYYNP SLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDGVLTLL NKRSEDIWGQGTMTVTVSS (SEQ ID NO: 11)	VK3- 20	RASQS VSSSY LA (SEQ ID NO: 71)	GASSR AT (SEQ ID NO: 68)	QQHTV RPPLT (SEQ ID NO: 64)	EIVLTQSPGTLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLIYGASSRATG IPDRFSGSGSDTFT LTISRLEPEDFAVYY CQQHTVRPPLTFGG GTKVEIK (SEQ ID NO: 26)
MAB9- IgG4	VH4- 31	GSIESG LYWVG (SEQ ID NO: 54)	SIYYSG STYYN PSLKS (SEQ ID NO: 40)	ARDGV LTLNK RSFDI (SEQ ID NO: 31)	QVQLQESGPGLVKPSQTLST CTVSGGSIESGLYYWGWRQP PGKGLEWIGSIYYSQSTYYNP SLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDGVLTLL NKRSEDIWGQGTMTVTVSS (SEQ ID NO: 12)	VK3- 20	RASQS VSSSY LA (SEQ ID NO: 71)	GASSR AT (SEQ ID NO: 68)	QQHTV RPPLT (SEQ ID NO: 64)	EIVLTQSPGTLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLIYGASSRATG IPDRFSGSGSDTFT LTISSLQSEDFAVYY CQQHTVRPPLTFGG GTKVEIK (SEQ ID NO: 26)
MAB10- IgG4	VH4- 31	GSIESG LYWVG (SEQ ID NO: 54)	SIYYSG STYYN PSLKS (SEQ ID NO: 40)	ARDGV LALNK RSFDI (SEQ ID NO: 32)	QVQLQESGPGLVKPSQTLST CTVSGGSIESGLYYWGWRQP PGKGLEWIGSIYYSQSTYYNP SLKSRATISVDTSKNQFSLKLS SVTAADTAVYYCARDGVLTLL NKRSEDIWGQGTMTVTVSS (SEQ ID NO: 13)	VK3- 20	RASQS VSSSY 1/A (SEQ ID NO: 71)	GASSR AT (SEQ ID NO: 68)	QQHTV RPPLT (SEQ ID NO: 64)	EIVLTQSPGTLSP GERATLSCRASQSV SSSYLAWYQQKPGQ APRLIYGASSRATG IPDRFSGSGSDTFT LTISSLQSEDFAVYY CQQHTVRPPLTFGG GTKVEIK (SEQ ID NO: 26)

				(SEQ ID NO: 27)
VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QQYVV WPPLT (SEQ ID NO: 65)	EIVMTQSPATLSVSP GERATLSRASQSV SSNLAWYQQKPGQ APRLIYGASTRATG IPARFSGSGSGTEFT LTISLSQSEDFAVYY CQQYVVWPPLTFGG GTKVEIK (SEQ ID NO: 27)
VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QQYVV WPPLT (SEQ ID NO: 65)	EIVMTQSPATLSVSP GERATLSRASQSV SSNLAWYQQKPGQ APRLIYGASTRATG IPARFSGSGSGTEFT LTISLSQSEDFAVYY CQQYVVWPPLTFGG GTKVEIK (SEQ ID NO: 27)
VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QQYVV WPPLT (SEQ ID NO: 65)	EIVMTQSPATLSVSP GERATLSRASQSV SSNLAWYQQKPGQ APRLIYGASTRATG IPARFSGSGSGTEFT LTISLSQSEDFAVYY CQQYVVWPPLTFGG GTKVEIK (SEQ ID NO: 27)

MAB11-IgG4	VH4-31	GSIESG LYYW/G (SEQ ID NO: 54)	SIYYSG STYYN PSLKS (SEQ ID NO: 40)	ARDGV LALNK RSFDI (SEQ ID NO: 32)	QVQLQESGPGLVKPSQTLST CTVSGGSIESGLYYWGWRQP PGKGLW/GSIYYSGSTYYNP SLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDGV/LAL NKRSFDIWGGQGTMTVSS (SEQ ID NO: 14)	VK3-20	RASQS VSSSY LA (SEQ ID NO: 71)	GASSR AT (SEQ ID NO: 68)	QC RP (SI NC)
MAB12-IgG4	VH4-31	GSIESG LYYW/G (SEQ ID NO: 54)	SIYYSG STYYN PSLKS (SEQ ID NO: 40)	ARDGV LALNK RSFDI (SEQ ID NO: 32)	QVQLQESGPGLVKPSQTLST CTASGGSIESGLYYWGWRQP PGKGLW/GSIYYSGSTYYNP SLKSRVTISVDTSKNQFSLKLS SVTAADTAVYYCARDGV/LAL NKRSFDIWGGQGTMTVSS (SEQ ID NO: 15)	VK3-20	RASQS VSSSY LA (SEQ ID NO: 71)	GASSR AT (SEQ ID NO: 68)	QC RP (SI NC)
MAB13-IgG4	VH1-46	YTFGN YYMH (SEQ ID NO: 58)	IINPSL GLTSY AQKFG (SEQ ID NO: 42)	ARGGR TTWIG AFDI (SEQ ID NO: 33)	QVQLVQSGAEVKKPGASVKV SCKASGYTFGNYYMHWRQ APGQGLEWMGHNPSLGLTSY AQKFGQGRVTMTTRDTSTVY MELSSLRSEDTAVYYCARGG RTTWIGAFDIWGQGTMTVTS S (SEQ ID NO: 16)	VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QC WI (SI NC)
MAB14-IgG4	VH1-46	YTFPA YYMII (SEQ ID NO: 59)	IINPSL GLTSY AQKFG (SEQ ID NO: 42)	ARGGR TTWIG AFDI (SEQ ID NO: 33)	QVQLVQSGAEVKKPGASVKV SCKASGYTFPAAYYMIWVRQA PGQGLEWMGHNPSLGLTSYA QKFGQGRVTMTTRDTSTVYM ELSSLRSEDTAVYYCARGGRT TWIGAFDIWGQGTMTVTS (SEQ ID NO: 17)	VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QC WI (SI NC)

MAB15-IgG4	VH1-46	YTPRE YYMH (SEQ ID NO: 60)	INPSIG LTSYA RKFG (SEQ ID NO: 43)	ARGGR TTWIG AEDI (SEQ ID NO: 33)	QVQLVQSGAEVKKPGASVKV SCKASGYTFREYYMHWRQA PGGLEWMGINPSIGLTSYAR KFGQGRVTMTTRDTSSTVYME LSSLRSEDTAVYYCARGGRTT WIGAFDIWGQGTMTVTVSS (SEQ ID NO: 18)
MAB16-IgG4	VH1-46	YTPRE YYMH (SEQ ID NO: 60)	INPSIG LTSYA RKFG (SEQ ID NO: 43)	ARGGR TTWIG ALDI (SEQ ID NO: 34)	QVQLVQSGAEVKKPGASVKV SCKASGYTFREYYMHWRQA PGGLEWMGINPSIGLTSYAR KFGQGRVTMTTRDTSSTVYME LSSLRSEDTAVYYCARGGRTT WIGALDIWGQGTMTVTVSS (SEQ ID NO: 19)
MAB17-IgG4	VH1-46	YTHPA YYIH (SEQ ID NO: 61)	INPSL GLTSY ARKFG G (SEQ ID NO: 44)	ARGGR TTWIG ALDI (SEQ ID NO: 34)	QVQLVQSGAEVKKPGASVKV SCKASGYTFPAYYIHWVRQAP GGGLEWMGINPSLGLTSYAR KFGQGRVTMTTRDTSSTVYME LSSLRSEDTAVYYCARGGRTT WIGALDIWGQGTMTVTVSS (SEQ ID NO: 20)

QVLVQSGAEVKKPGASVKV KASGYTFPAYYMHWRQA QGLEWMGINPSLGLTSYA KFGQGRVTMTTRDTSSTVYM LSSLRSEDTAVYYCARGGRTT WIGAFDIWGQGTMTVTVSS (SEQ ID NO: 21)	VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QQYIVF WPPLT (SEQ ID NO: 65)	EIVMTQSPATLSVSP GERATLSRASQSV SSNLAWYQQKPGQ APRLLIYGASTRATG IPARESGSGGTEFT LTISLQSEDFAVY CQQYVVPWPPLTFFG GTKVEIK (SEQ ID NO: 27)
QVLVQSGAEVKKPGASVKV KASGYTFTSHYMGWVRQA QGLEWMGINPSMGATSY KFGQGRVTMTTRDTSSTVY LSSLRSEDTAVYYCARLH SS YYPAYLDYWGQGTMTV (SEQ ID NO: 22)	VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QQYIVF PWT (SEQ ID NO: 66)	EIVMTQSPATLSVSP GERATLSRASQSV SSNLAWYQQKPGQ APRHLIYGASTRAT GIPARFSGSGGTEF TLTISLQSEDFAVY YCQQYIVFPWTFGG GTKVEIK (SEQ ID NO: 28)
QVLVQSGAEVKKPGASVKV KASGYTFTSHYMGWVRQA QGLEWMGINPSMGATSYA KFGQGRVTMTTRDTSSTVYM LSSLRSEDTAVYYCARLHVS YYPAYLDYWGQGTMTV (SEQ ID NO: 23)	VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QQYIVF PWT (SEQ ID NO: 66)	EIVMTQSPATLSVSP GERATLSRASQSV SSNLAWYQQKPGQ APRHLIYGASTRAT GIPARESGSGGTEF TLTISLQSEDFAVY YCQQYIVFPWTFGG GTKVEIK (SEQ ID NO: 28)
QVLVQSGAEVKKPGASVKV KASGYTFTSHYMGWVRQA QGLEWMGINPSMGATSYT KFGQGRVTMTTRDTSSTVYM LSSLRSEDTAVYYCARLHVS YYPAYLDYWGQGTMTV (SEQ ID NO: 24)	VK3-15	RASQS VSSNL A (SEQ ID NO: 72)	GASTR AT (SEQ ID NO: 69)	QQYIVF PWT (SEQ ID NO: 66)	EIVMTQSPATLSVSP GERATLSRASQSV SSNLAWYQQKPGQ APRHLIYGASTRAT GIPARFSGSGGTEF TLTISLQSEDFAVY YCQQYIVFPWTFGG GTKVEIK

							(SEQ ID NO: 28)

defined by both the Chothia and Kabat numbering systems, inclusive of the boundaries of both numbering systems.
at numbering system.
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ut, Chothia, and IMGT numbering systems.

MAB18-IgG4	VH1-46	YTFPA YYMH (SEQ ID NO: 59)	IINPSL GLTSY ARKTQ G (SEQ ID NO: 44)	ARGGR TTWIG AFDI (SEQ ID NO: 33)	QV SC PG RK EL TW (SE
MAB19-IgG4	VH1-46	YTF ¹ TSH YMG (SEQ ID NO: 62)	VINPS MGATS YAQKF QG (SEQ ID NO: 45)	ARLHV SGSY PAYLD Y (SEQ ID NO: 35)	QV SC PG AQ ME VS TV (SE
MAB20-IgG4	VH1-46	YTF ¹ TSH YMG (SEQ ID NO: 62)	IINPSM GATSY AQKFQ G (SEQ ID NO: 46)	ARLHV SGSY PAYLD Y (SEQ ID NO: 35)	QV SC PG QK EL GS SS (SE
MAB21-IgG4	VH1-46	YTF ¹ TSH YMG (SEQ ID NO: 62)	IINPSM GATSY TQKFR G (SEQ ID NO: 47)	ARLHV SGSY PAYLD Y (SEQ ID NO: 35)	QV SC PG QK EL GS SS (SE

¹ Includes CDR-H1 as c
² According to the Kab
³ According to the IMG
⁴ According to the Kab
⁵ According to the Kab
⁶ According to the Kab

Example 4: Antibody Characterization

[0634] ForteBio K_D Measurements: Quantitative binding of antibodies to recombinant monomeric human, mouse (SEQ ID NO: 3), cynomolgus monkey TIGIT was measured using biolayer interferometry (BLI) with a FORTEBIO®. Affinity measurements of selected antibodies were performed generally as described in Estep et al., *Mabs*, 2013, 5:270-278. FORTEBIO affinity measurements were performed by loading IgGs on-line onto AHQ 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 a single concentration of antigen (100 nM) for 3 minutes. Afterwards they were transferred to assay buffer for 3 minutes for off-rate measurement. Kinetics were analyzed using the 1:1 binding model. A summary of K_D measurements for antibodies binding a single concentration of human, cynomolgus monkey, and mouse (SEQ ID NO: 3) TIGIT is shown in Table 6 below.

[0635] MSD-SET K_D Measurements: Solution equilibrium affinity measurements of selected antibodies binding to monomeric recombinant human and cynomolgus monkey TIGIT were performed generally as previously described. See Estep et al., *supra*. Briefly, solution equilibrium titrations (SET) were performed in PBS + 0.1% IgG-Free BSA (PBSF) with antigen (TIGIT monomer) held constant at 10-100 pM and incubated with 3-to 5-fold serial dilutions of Fab or mAbs starting at 10pM-10nM. Antibodies (20 nM in PBS) were coated onto standard bind MSD-ECL plates overnight at 4°C or at room temperature for 30 min. Plates were then blocked by BSA for 30 min with shaking at 700 rpm, followed by three washes with wash buffer (PBSF + 0.05% Tween 20). SET samples were applied and incubated on the plates for 150s with shaking at 700 rpm followed by one wash. Antigen captured on a plate was detected with 250ng/mL sulfotag-labeled streptavidin in PBSF by incubation on the plate for 3 min. The plates were washed three times with wash buffer and then read on the MSD Sector Imager 2400 instrument using 1x Read Buffer T with surfactant. The percent free antigen was plotted as a function of titrated antibody in Prism and fit to a quadratic equation to extract the K_D . To improve throughput, liquid handling robots were used throughout MSD-SET experiments, including SET sample preparation.

Table 6: K_D Measurements for Human, Cyno, and Mouse (SEQ ID NO: 3) TIGIT

Antibody	ForteBio K _D (M) Human TIGIT His	ForteBio K _D (M) Cyno TIGIT His	ForteBio K _D (M) Mouse TIGIT His	MSD-SET K _D (M) Human TIGIT His	MSD-SET K _D (M) Cyno TIGIT His
MAB1	5.24E-10	2.64E-09	N.B.	5.40E-11	3.20E-10
MAB2	4.57E-10	1.57E-09	N.B.	2.50E-11	2.30E-10
MAB3	3.32E-10	8.02E-10	N.B.	8.10E-12	3.50E-11
MAB4	2.46E-10	3.69E-10	N.B.	5.00E-12	1.50E-11
MAB5	1.96E-10	8.98E-10	N.B.	4.90E-12	4.60E-11
MAB6	3.11E-09	1.75E-08	N.B.	N.D	N.D
MAB7	2.54E-09	P.F.	N.B.	N.D	N.D
MAB8	3.13E-09	2.58E-08	N.B.	N.D	N.D
MAB9	2.83E-09	9.35E-09	N.B.	N.D	N.D
MAB10	1.71E-09	6.55E-09	P.F.	1.10E-10	N.D
MAB11	2.47E-09	8.14E-09	N.B.	1.50E-10	N.D
MAB12	2.35E-09	6.57E-09	P.F.	5.60E-11	N.D
MAB13	1.44E-09	N.B.	N.B.	4.00E-10	N.D
MAB14	1.23E-09	N.B.	N.B.	3.80E-10	N.D
MAB15	5.26E-10	7.94E-08	N.B.	2.10E-10	N.D
MAB16	3.78E-10	7.04E-08	N.B.	7.00E-11	N.D
MAB17	4.29E-10	1.10E-07	N.B.	4.10E-11	N.D
MAB18	4.48E-10	7.20E-08	N.B.	N.D	N.D
MAB19	P.F.	N.B.	N.B.	N.D	N.D
MAB20	P.F.	N.B.	N.B.	3.00E-11	N.D
MAB21	P.F.	N.B.	N.B.	8.00E-11	N.D
N.B.: Non-binder or weak binder P.F.: Poor Fit (good binding response with unreportable K _D based on a 1:1 fitting model) N.D.: MSD affinity measurement was not performed					

Example 5: Evaluation of Blockade of TIGIT Ligands

[0636] Quantitative ligand blocking studies were conducted by using a cell surface TIGIT binding assay. Binding of fluorescently labeled PVR-Fc or PVRL2-Fc to human TIGIT expressing Jurkat cells was measured by flow cytometry. A dilution series of each test antibody was incubated with the TIGIT Jurkat cells in order to measure each antibody's ability to block PVR-Fc or PVRL2-Fc binding and determine the IC₅₀ values shown in Table 7.

Table 7: Ligand blocking IC₅₀ Values for Antibody Panel

Antibody	PVR IC ₅₀ (nM)	PVRL2 IC ₅₀ (nM)
MAB1-IgG4	2.2	1.4
MAB2-IgG4	2.3	1.3
MAB3-IgG4	1.6	1.2
MAB4-IgG4	1.9	1.6
MAB5-IgG4	1.7	1.4
MAB6-IgG4	3.2	1.4
MAB7-IgG4	2.6	2
MAB8-IgG4	2.9	1.2
MAB9-IgG4	1.9	1.1
MAB 10-IgG4	3.3	1
MAB11-IgG4	2	1.2
MAB12-IgG4	1.7	1.2
MAB13-IgG4	2.1	1.8
MAB 14-IgG4	2.6	1.6
MAB15-IgG4	2.2	1.1
MAB16-IgG4	2.1	1.3
MAB17-IgG4	2.6	1.9
MAB18-IgG4	1.8	1.9
MAB 19-IgG4	6.4	2
MAB20-IgG4	2.3	1.9
MAB21-IgG4	1	0.8

Example 6: Additional TIGIT Binding Assays to Measure Affinity and Cross-Reactivity of Antibodies to TIGIT

[0637] The affinity of antibodies binding to human TIGIT was measured with multiple concentrations of antigen in order to more accurately measure binding kinetics. Additionally, quantitative binding of MAB10 to human, mouse (SEQ ID NO: 3), cynomolgus monkey TIGIT was measured using biolayer interferometry (BLI) and flow cytometry. Figure 1A shows an alignment of TIGIT from different species. The percent identities across the whole TIGIT protein are summarized in Table 8 below.

Table 8: Percent identities between TIGIT proteins of different species.

	Human	Cynomolgus Monkey	Mouse
Human	100	89.17	68.38
Cynomolgus Monkey	89.17	100	66.67
Mouse	68.38	66.67	100

Kinetic Measurements for Antibodies Binding to Human, Cynomolgus Monkey, and Mouse TIGIT

[0638] The binding affinities and kinetics for antibodies binding to human TIGIT-His were measured using an Octet® QKe instrument (ForteBio) in a method similar to that described above in Example 4 but with multiple concentrations of antigen used. Additionally, binding of MAB10 to cynomolgus monkey and mouse (SEQ ID NO: 3) TIGIT-His was measured. A strategy of capturing anti-TIGIT antibodies on sensors following association/dissociation of monomeric TIGIT proteins was used to avoid avidity effects in the assay. The BLI analysis was performed at 29°C using IX kinetics buffer (ForteBio) as assay buffer. Anti-human IgG Fc capture (AHC) biosensors (ForteBio) were first presoaked in assay buffer for over five minutes. Anti-TIGIT antibody (5 µg/mL) was captured on the sensor for 300 seconds. Sensors were then dipped in assay buffer for 120 seconds to establish a baseline before measuring binding to each TIGIT protein. Sensors were then dipped into varying concentrations of human TIGIT-His (12.4 to 0.8nM or 6.2 to 0.8nM, 2-fold dilutions in assay buffer), cynomolgus monkey TIGIT-His (24.6 to 1.5nM or 12.3 to 1.5nM, 2-fold dilutions in assay buffer, for MAB10 only), or mouse TIGIT-His (303 to 4.7nM, 2-fold dilutions in assay buffer, for MAB10 only) for 300 seconds or 600 seconds, depending on the experiment, to measure association. Dissociation of TIGIT was measured by dipping the sensors into assay buffer for 600, 1200, or 1800 seconds, depending on the experiment (600 seconds was only used for mouse TIGIT-His). Agitation at all steps was 1000 rpm.

[0639] Kinetic parameters were generated with Octet® Data Analysis Software Version 8.2.0.7 using reference subtraction, dissociation based inter-step correction, 1-to-1 binding model, and global fit (R_{max} unlinked by sensor). The association rate constant (k_a), dissociation rate constant (k_d) and equilibrium constant (K_D) values were individually averaged across experiments, and a summary of the data for antibodies binding to human TIGIT are shown in Table 9. A summary of MAB10 binding to monomeric human, cynomolgus monkey, and mouse TIGIT (SEQ ID NO: 3) is shown in Table 10.

Table 9: TIGIT Antibody Multi-Concentration Kinetics for Binding Human TIGIT

Antibody	Average of k_a (1/Ms)	Average of k_d (1/s)	Average of K_D (M)	n
MAB2	3.2E+05	2.3E-04	7.1E-10	2
MAB4	7.0E+05	6.3E-05	8.1E-11	3

Antibody	Average of k_a (1/Ms)	Average of k_d (1/s)	Average of K_D (M)	n
MAB5	7.7E+05	1.4E-04	1.9E-10	2
MAB9	1.6E+06	8.5E-04	5.6E-10	2
MAB10	2.0E+06	3.8E-04	2.4E-10	6
MAB11	1.3E+06	3.5E-04	2.8E-10	2
MAB12	1.5E+06	2.4E-04	1.6E-10	2
MAB15	1.1E+06	6.6E-04	5.8E-10	2
MAB16	4.5E+05	3.5E-04	1.1E-09	3
MAB18	7.5E+05	5.9E-04	8.1E-10	3
MAB20	8.9E+05	3.8E-04	4.6E-10	2
MAB21	1.4E+06	5.0E-04	3.6E-10	2

Table 10: MAB10 Kinetic Parameters for Binding Human, Cynomolgus Monkey, and Mouse

Species	Average k_a (1/Ms)	Average k_d (1/s)	Average K_D (M)	n
Human	2.0E+06	3.8E-04	2.4E-10	6
Cynomolgus Monkey	7.9E+05	4.6E-03	6.2E-09	5
Mouse	-	-	>7.0E-07*	3

* K_D could not be determined due to minimal binding (very low binding response), indicating that any binding is poorer than the limit of the instrument's sensitivity.
 K_D Measurements for Binding to Cells Engineered to Express TIGIT

[0640] The K_D for MAB10 binding to cell surface TIGIT in engineered cell lines was measured using flow cytometry. Jurkat cells (acute T cell leukemia, ATCC® TIB-152™) were engineered to stably express human or cynomolgus monkey TIGIT, and CHO-K1 cells were engineered to stably express mouse TIGIT (SEQ ID NO: 3). The K_D values are shown in Table 11. The K_D values for MAB10 binding to cell surface human and cynomolgus monkey TIGIT are very similar.

Table 11: Measurement of K_D for MAB10 Binding to Cell Surface TIGIT on Engineered Cells

Cell Line	Average K_D (M)	n
Human TIGIT Jurkat	5.1E-10	2
Cynomolgus Monkey TIGIT Jurkat	4.0E-10	1
Mouse TIGIT CHO-K1	9.8E-9	1

K_D Measurements for Binding to Primary Cells

[0641] The K_D for MAB10 binding to cell surface TIGIT on primary cells was measured using flow cytometry. For both human and cynomolgus monkey PBMCs, CD8+ T cells had the greatest detectable TIGIT expression, and therefore were used to calculate the binding of MAB10 to primary cells in these species. For analysis purposes, CD8+ T cells were defined as cells with a lymphocyte size and granularity that expressed the following combination of molecular markers: CD3+CD4-CD8+. Similarly, murine Tregs demonstrated the highest binding of MAB10, and were therefore used for these calculations. Murine Tregs were defined as CD4+CD8-CD25+FoxP3+ cells of lymphocyte size and granularity. The K_D values are shown in Table 12. The K_D values for MAB10 binding to cell surface human and cynomolgus monkey TIGIT on primary cells are very similar.

Table 12: Measurement of K_D for MAB10 Binding to Cell Surface TIGIT on Primary Cells

Cells	Average K_D (M)	n
Human CD8	1.3E-9	2
Cynomolgus Monkey CD8	2.8E-9	2
Mouse Tregs	2.5E-8	2

Antibody binding to human PVRL4

[0642] In order to confirm the specificity of anti-TIGIT antibodies, binding to human PVRL4, the Ig family member most closely related to TIGIT (29% identity in extracellular region of homology), was measured by BLI. Figure 1B shows an alignment of the human TIGIT and PVRL4 extracellular domains. The BLI analysis was performed at 30°C using IX kinetics buffer as assay buffer. AHC sensors were first presoaked in assay buffer for greater than 5 minutes. Antibody (5 µg/mL) was captured on the sensor for 300 seconds. Sensors were then dipped in assay buffer for 120 seconds to establish a baseline before measuring binding to human PVRL4-His protein. Sensors were then dipped into human PVRL4-His (200nM in assay buffer) for 200 seconds to measure association. Dissociation of PVRL4 was then measured by dipping sensors into assay buffer for 200 seconds. Results were analyzed using Octet® Data Analysis Software Version 8.2.0.7. MAB1 through MAB21 did not bind PVRL4, thus demonstrating that the MABs disclosed herein are highly specific for TIGIT.

Example 7: Production of IL-2 in Jurkat Cells Engineered to Respond to Human TIGIT Signaling Following Treatment with Anti-TIGIT Antibodies

[0643] An assay for testing the ability of antibodies to inhibit the function of TIGIT was developed using two engineered cell lines. This co-culture assay was developed to mimic the

interaction of a TIGIT expressing T cell with a second cell expressing TIGIT ligand (PVR and PVRL2), thus replicating TIGIT's ability to suppress T cell activation. This interaction causes an inhibition of T cell function (e.g. cytokine release) in the TIGIT expressing cell. Jurkat cells (acute T cell leukemia) normally express IL-2 upon stimulation of the T cell receptor (using anti-CD3 and anti-CD28 agonist antibodies). The expression of TIGIT in Jurkat cells would reduce IL-2 expression induced by anti-CD3/CD28 agonist antibodies if PVR and/or PVRL2 was present and bound to TIGIT, thus providing a suppressive signal to the Jurkat cell. Therefore, a Jurkat cell line was engineered to express human TIGIT.

[0644] A second cell line, HT-1080 (human fibrosarcoma cell line, ATCC® CCL121™), was engineered to express a membrane tethered anti-CD3 single chain Fv (scFv) antibody that can provide an activating signal to the TIGIT Jurkat cells. The activating signal was also enhanced by including soluble anti-CD28 agonist antibody. HT-1080 cells naturally express high levels of PVR and PVRL2, thus providing ligand for TIGIT in a TIGIT Jurkat/anti-CD3 HT-1080 co-culture assay. In this co-culture assay, TIGIT antagonist antibodies increase the production of IL-2 compared to negative control antibodies. An overview of this assay system is shown in Figure 3.

[0645] The co-culture assay was used to determine the EC₅₀ of anti-TIGIT antibodies by treatment with a dose range of antibody. EC₅₀ was measured for anti-TIGIT antibodies MAB1-MAB21, as well as the hamster anti-mouse antibody SEC1 (see Example 8) and the commercial anti-human anti-TIGIT antibody MBSA43 (available, e.g., from eBioscience, Cat. No. 16-9500). The supernatants were harvested as described above 24 hours post treatment and analyzed by an IL-2 ELISA. A summary of the experimentally determined EC₅₀ values in human TIGIT Jurkat cells is in Table 13. As can be seen in Table 13, all of the MABs except for MAB13, MAB 14, MAB 16, and SEC1, perform better in this assay than the commercial antibody MBSA43.

Table 13: Average EC₅₀ Values in Human TIGIT Jurkat Co-Culture Assay

Antibody	Average EC ₅₀ (nM)
MAB1	0.22
MAB2	0.31
MAB3	0.33
MAB4	0.34
MAB5	0.34
MAB6	data not available
MAB7	0.25
MAB8	0.24
MAB9	0.06
MAB10	0.14
MAB11	0.24

Antibody	Average EC ₅₀ (nM)
MAB12	0.16
MAB13	1.40
MAB14	0.71
MAB15	0.21
MAB16	1.11
MAB17	0.13
MAB18	0.25
MAB19	0.20
MAB20	0.68
MAB21	0.61
SEC1 (see below)	8.46
MBSA43	0.45

[0646] Additionally, the Jurkat co-culture assay was repeated with MAB10 using a subcloned isolate of the anti-CD3 scFv HT1080 cells. Figure 4A shows the EC₅₀ curves from an exemplary experiment comparing MAB10 and an IgG4 control. That experiment was conducted 3 times, and the average EC₅₀ was 0.11 nM.

[0647] As described above for human TIGIT expressing Jurkat cells, a co-culture stimulation assay was set up with HT-1080 anti-CD3 scFv cells in the presence of cynomolgus monkey TIGIT expressing Jurkat cells and soluble anti-human CD28. Figure 4B shows the EC₅₀ curves from an exemplary experiment comparing MAB10 and IgG4 control. As shown in Figure 4B, MAB10 induces IL-2 production in cynomolgus monkey TIGIT expressing Jurkat cells, whereas the IgG4 isotype control does not. The average EC₅₀ for MAB10 in the cynomolgus monkey TIGIT Jurkat/anti-CD3 HT-1080 co-culture assay was determined to be 2.87 nM.

Example 8: Characterization of the anti-TIGIT antibody "SEC1"

[0648] Additional studies were conducted to characterize the hamster anti-TIGIT antibody 10A7 (disclosed, e.g., in U.S. Pat. Pub. No. 20090258013). The antibody 10A7 was reformatted in two different ways for use in this study. The first was to make a chimeric antibody with hamster variable regions and human IgG4 S228P (human S228P heavy chain, SEQ ID NO:73) and kappa constant regions (constant regions used for MAB10, SEQ ID NO:75). The second was to make a chimeric antibody with hamster variable regions and mouse IgG2a N297A and kappa constant regions (heavy chain: SEQ ID NO:77; light chain: SEQ ID NO:79). The variable regions of the antibodies are provided in SEQ ID NOs:74, 76, 78 and 80. The reformatted 10A7 antibodies are referred to herein as "SEC1".

Kinetic Measurements for SEC1 Binding to Recombinant Human, Cynomolgus Monkey, and Mouse TIGIT

[0649] The binding affinities and kinetics of binding of SEC1 mouse IgG2a N297A to human TIGIT-His, cynomolgus monkey TIGIT-His, and mouse (SEQ ID NO: 3) TIGIT-His were measured using BLI with an Octet QKe instrument. A strategy of capturing SEC1 on sensors followed by association/dissociation of monomeric TIGIT proteins was used to avoid avidity effects in the assay. The BLI analysis was performed at 29°C using IX Kinetics Buffer (ForteBio) as assay buffer. Anti-Mouse IgG Fc Capture (AMC) biosensors (ForteBio) were first presoaked in assay buffer for greater than 5 minutes. SEC1 mouse IgG2a N297A (5 µg/mL) was captured on the sensor for 300 seconds. Sensors were then dipped in assay buffer for 120 seconds to establish a baseline before measuring binding to each TIGIT protein. Sensors were then dipped into varying concentrations of human TIGIT-His (33.8 to 1.25nM, 3 fold dilutions in assay buffer), cynomolgus monkey TIGIT-His (302.8 to 0.42nM, 3 fold dilutions in assay buffer), or mouse TIGIT-His (33 to 1.22nM, 3 fold dilutions in assay buffer) for 300 seconds to measure association. Dissociation of TIGIT was then measured by dipping sensors into assay buffer for 600 seconds. Agitation at all steps was 1000 rpm. Kinetic parameters and sensorgrams were generated with Octet® Data Analysis Software using reference subtraction, dissociation based inter-step correction, 1 to 1 binding model, and global fit (Rmax unlinked by sensor). The K_D values are shown in Table 14.

Table 14: SEC1 IgG2a N297A Kinetic Parameters for Binding TIGIT

Species	k_a (1/Ms)	k_d (1/s)	K_D (M)
Human	1.7E+06	7.9E-03	4.7E-09
Cynomolgus Monkey	No Binding		
Mouse	1.9E+06	6.0E-04	3.2E-10

K_D Measurements for Binding to Primary Cells

[0650] The K_D for SEC1 (IgG4 S228P) binding to cell surface TIGIT on primary cells was measured using flow cytometry as described in Example 6. For both human and cynomolgus monkey PBMCs, CD8+ T cells had the greatest detectable TIGIT expression, and therefore were used to calculate the binding of SEC1 to primary cells in these species. For analysis purposes, CD8+ T cells were defined as cells with a lymphocyte size and granularity that expressed the following combination of molecular markers: CD3+CD4-CD8+. Similarly, murine Tregs demonstrated the highest expression of TIGIT, and were therefore used for these calculations. Murine Tregs were defined as CD4+CD8-CD25+FoxP3+ cells of lymphocyte size and granularity. The K_D values are shown in Table 15.

Table 15: Measurement of K_D for SEC1 Binding to Cell Surface TIGIT on Primary Cells

Cells	Average K_D (M)	n
Human CD8	3.6E-9	1
Cynomolgus Monkey CD8	No binding	1
Mouse Tregs	4.1E-10	2

Engineered TIGIT Jurkat/anti-CD3 HT-1080 Assay

[0651] SEC1 antagonizes TIGIT function in the engineered human TIGIT Jurkat/anti-CD3 HT-1080 co-culture assay described in Example 7. The experiment was conducted 3 times, and the average EC_{50} was 8.5 nM. In comparison, the average EC_{50} for MAB10 in this assay is 0.14nM.

[0652] Like MAB10, SEC1 has been described as a ligand blocking antibody, and both antibodies inhibit the function of TIGIT in an engineered TIGIT Jurkat/anti-CD3 scFv HT-1080 co-culture assay.

Example 9: Increase in cytokine production in sub-optimally stimulated human T cells following treatment with MAB10

[0653] A study was developed in order to determine whether MAB10 is efficacious in a cellular *in vitro* system using human primary T cells obtained from healthy donors. Two different forms of the assay were used: stimulation of T cells within a mix of PBMCs and stimulation of CD4+ T cells after isolation from PBMCs. TIGIT is expressed in exhausted intra-tumoral CD8+ T cells, NK and regulatory T cells. This study was designed to identify and obtain more readily available TIGIT expressing human primary T cells to use as a surrogate system for the intra-tumoral target cells.

[0654] In CD4+ T cells, TIGIT expression is primarily restricted to memory cells (CD45RO+). Suboptimal stimulation of CD4+ T cells permits assaying the efficacy of MAB10 by measuring the increased production of IFN- γ following inhibition of TIGIT - ligand interactions.

[0655] Human primary T cells were obtained from healthy donors. Total peripheral blood mononuclear cells (PBMCs) were isolated from leukapheresis preparations and CD4+ T cells were in turn isolated from PBMCs.

[0656] PBMCs were purified using Ficoll® density gradients. PBMCs were then used to purify CD4+ cells using negative selection (CD4 T cell isolation kit, Miltenyi) following manufacturer's protocol.

FACS Analysis of Key Markers on Human CD4⁺ T Cells.

[0657] CD4⁺ T cells were sub-optimally stimulated with plate-bound anti-CD3 antibody (1µg/mL) and soluble anti-CD28 antibody (2µg/mL) for 60 hours. For staining and FACS analysis, cells from unstimulated and stimulated samples were used. The following antibodies were used for staining: anti-TIGIT-PE-Cy7, anti-PVR-PE, anti-CD4-APC-eFluor780 and anti-CD45RA-APC, anti-CD45RO PerCP-eFluor710, and CD226-FITC. Cells were analyzed by flow cytometry using a BD LSRFortessa™ instrument.

[0658] Sub-optimal stimulation of PBMCs was achieved by addition of low concentrations of anti-CD3 antibody (0.2µg/mL). Sub-optimal stimulation of CD4⁺ T cells was achieved by culturing the cells on 96-well flat-bottom plates that had been previously coated with 1µg/mL of anti-CD3 antibody and 2µg/mL soluble anti-CD28 antibody. After 60 hours of culture, supernatants were collected and frozen for cytokine quantification using ELISA, AlphaLISA® or multiplex/Luminex® technology. The effect of MAB10 addition was compared to the addition of a non-specific control IgG4 antibody.

[0659] Purified CD4⁺ T cells were left unstimulated or were stimulated for 60 hours using plate-bound anti-CD3 antibody (1µg/mL) and soluble anti-CD28 antibody (2µg/mL). FACS analysis was performed on both unstimulated (Figure 5A) and stimulated cells (Figure 5B). Population percentages and mean fluorescence intensity (MFI) were calculated. Expression analysis of cell markers TIGIT, PVR, and CD226 prior and post-activation showed that the percentage of both PVR and CD226 positive cells increases upon activation. For TIGIT, the percentage of TIGIT positive cells only increased moderately with these activation conditions, but the MFI values indicated a clear upregulation of TIGIT expression in the positive cell population. FACS analysis also confirmed that TIGIT expression was restricted primarily to memory cells (CD45RO⁺). CD4⁺ T cells from a representative donor were stained for CD45RA (naive T cell marker) and CD45RO (activated or memory T cell marker) markers to differentiate naive and memory T cells. Expression levels of TIGIT were analyzed within each of these populations (see Figure 5C).

[0660] Purified PBMCs obtained from healthy donors were stimulated for 60 hours using soluble anti-CD3 antibody (0.2µg/mL) in the presence of different concentrations of a MAB or a control IgG4 antibody. Cell culture supernatants were collected and used to measure production of pro-inflammatory cytokines. The analysis of samples from two human donors, illustrated in Figures 6A-6K, show that treatment with each of the MABs induces the upregulation IFN-γ. MAB10 was then used to induce the production of several pro-inflammatory cytokines in PBMCs from Donor 1, including tumor necrosis factor alpha (TNF, Figure 6L), lymphotoxin alpha (LT-α, Figure 6M), and interferon gamma (IFN-γ, Figure 6N). A graphical analysis of the EC₅₀ for IFN-γ is shown in Figure 6O. PBMCs from Donor 2 were similarly treated with MAB10 and cytokines induced as shown in Figure 7A (IFN-γ), Figure 7B

(TNF), Figure 7C (IL-6), Figure 7D (GM-CSF), and Figure 7E (LT- α). EC₅₀ value for MAB10 in this assay in the two donors tested was averaged as ~16nM, by determining the concentration of MAB10 required to induce 50% of the increase in IFN- γ , TNF and LT- α signal. A summary of the TNF data for the two donors (Figure 6) is shown in Table 16.

Table 16: Data Summary for Two Donors (TNF Analyzed)

Donor	EC ₁₀ (nM)	EC ₅₀ (nM)	EC ₉₀ (nM)
1	5.02	12.60	31.59
2	18.86	20.60	22.49
Average	11.94	16.60	27.04

[0661] Purified CD4⁺ T cells obtained from 3 different healthy donors were stimulated for 60 hours using plate-bound anti-CD3 antibody (1 μ g/mL) and soluble anti-CD28 antibody (2 μ g/mL) in the presence of different concentrations of a control IgG4 antibody or MAB10. Cell culture supernatants were collected and used to measure levels of IFN- γ production.

[0662] In these sub-optimally stimulated CD4⁺ T cells, MAB10 addition results in an upregulation of IFN- γ in a dose dependent manner in all three donors, demonstrating the anti-TIGIT antagonistic function of MAB10 (see Figure 8A (Donor 1), Figure 8B (Donor 2), and Figure 8C (Donor 3)). IFN- γ production in cells treated with either MAB10 (black bars) or the IgG4 isotype control (light gray bars) is shown in the left panel of each Figure. EC₅₀ average value for MAB10 in this assay was calculated as 1.02nM by determining the concentration of MAB10 required to induce 50% of the increase in IFN- γ signal (plotted in the right panel of each of Figures 8A-8C). The data are summarized in Table 17.

Table 17: Data Summary for Three Donors

Donor	EC ₁₀ (nM)	EC ₅₀ (nM)	EC ₉₀ (nM)
1	0.37	1.00	2.72
2	0.85	0.94	1.04
3	1.05	1.12	1.19
Average	0.75	1.02	1.65

[0663] As described above, addition of MAB10 to sub-optimally stimulated human T cells antagonizes TIGIT function and induces the upregulation of pro-inflammatory cytokines (e.g., IFN- γ and TNF) when compared to a non-specific control IgG4 antibody. This effect is dose-dependent with an estimated EC₅₀ of 1nM for the isolated CD4⁺ T cell assay. These data demonstrate *in vitro* efficacy of MAB10 in normal primary human T cells.

Example 10: Characterization of MAB10 in PD-1/TIGIT Combination Bioassay

[0664] PD-1 is an immune inhibitory receptor expressed on activated T cells and B cells and plays a critical role in regulating immune responses to tumor antigens and autoantigens. Engagement of PD-1 by either of its ligands, PD-L1 or PD-L2, on an adjacent cell inhibits T-cell receptor (TCR) signaling and TCR-mediated proliferation, transcriptional activation and cytokine production. Therapeutic antibodies and Fc fusion proteins designed to block the PD-1/PD-L1 interaction show promising results in clinical trials for the treatment of a variety of cancers.

[0665] The PD-1/TIGIT Combination Bioassay (Promega) is a biologically relevant mechanism of action-based assay that can be used to measure the potency and stability of antibodies and other biologics designed to block the PD-1/PD-L1 and TIGIT/CD155 interactions in combination. The assay consists of two genetically engineered cell lines: PD-1/TIGIT Effector Cells, which are Jurkat T-cells stably expressing human PD-1, TIGIT, and a luciferase reporter, and PD-L1/CD155 APC/CHO-K1 Cells, which are CHO-K1 cells stably expressing human PD-L1, human CD155, and a cell surface protein (in this case, TIGIT) designed to activate cognate TCRs in an antigen-independent manner.

[0666] When the two cell types are co-cultured, the PD-1/PD-L1 and TIGIT/CD155 interactions inhibit TCR signaling and luciferase activity. Addition of an antibody, e.g., an ABP disclosed herein or known in the art, that binds TIGIT and blocks ligand binding (e.g., CD155), in combination with a second antibody that blocks the interaction of PD-1 with its ligand (e.g., PD-L1), releases the inhibitory signal and results in TCR signaling and NFAT-mediated luciferase activity.

[0667] Figure 9A shows the results of the assay in which a 1:1 ratio of MAB10 and pembrolizumab (anti-PD-1 antibody) was used. Concentrations for each antibody were 25, 10, 4, 1.6, 0.64, 0.256, 0.1024, 0.04096, and 0.016384 $\mu\text{g/ml}$. An untargeted IgG4 was used as a control. As shown in the Figure, only the combination of MAB10 and pembrolizumab (EC_{50} of 5.06 nM) blocked binding sufficiently to induce luciferase activity in the Jurkat cells. Neither the IgG4 control alone or the IgG4 + MAB10 combination induced luciferase activity.

[0668] The assay was then repeated with a 1 $\mu\text{g/ml}$ fixed dose of pembrolizumab (and a 1 $\mu\text{g/ml}$ fixed dose of the IgG4 control) and a varying dose of MAB10 (50, 20, 8, 3.2, 1.28, 0.512, 0.2048, 0.08192, and 0.032768 $\mu\text{g/ml}$). As shown in Figure 9B, while the fixed dose of pembrolizumab resulted in a low level of activation of luciferase induction, the combination of pembrolizumab and MAB10 was much more effective at induction of luciferase, with an EC_{50} of 0.78 nM. As in Figure 9A, neither the IgG4 control alone or the IgG4 + MAB10 combination induced luciferase activity.

Example 11: Combination therapy of CMV+ T-cells with MAB10 and Pembrolizumab

[0669] A lymphoproliferation assay was used to test for T-cell responses in cytomegalovirus

positive (CMV+) T-cells. PBMCs from individual donors that have been screened for CMV antigen reactivity were purchased from Astarte Biologics (Bothell, WA). Cell lysates from CMV-infected cells were also purchased from Astarte Biologics. The PBMCs were plated and the antigen-specific stimulation is performed by the addition of cell lysate, which stimulates the CMV+ T-cells in the sample. MAB10, an IgG4 control, and/or the anti-PD-1 antibody pembrolizumab were added. Cells were cultured for five days, and the supernatants were collected and analyzed for the production of the effector cytokine TNF. Further data were collected performing intracellular cytokine staining for other effector molecules including IL-2, IFN- γ , perforin and granzyme-B.

[0670] Cells from a single donor (Donor 1) were stimulated and cultured as described above. As shown in Figure 10, by gating on CD4+ cells, incubation with MAB10 (black bars) increases the production of the effector cytokines in a dose-dependent matter, as measured by intracellular staining, including TNF (Figure 10A), IL-2 (Figure 10B), and IFN- γ (Figure 10C) to a greater extent than cells incubated with the IgG4 control (white bars). Incubation with MAB10 also increases the proportion of antigen-specific activated CD4+ T-cells, as shown in Figure 10D, in which cells that were treated with 20 μ g/ml of the IgG4 control or MAB10 were analyzed by FACS by expression of CD3 (a marker of mature T-cells) and expression of TNF and IL-2.

[0671] Similar results were obtained by gating on CD8+ cells. As shown in Figure 11, on gated CD8+ cells, incubation with MAB10 (black bars) increases the production of the effector cytokines in a dose-dependent matter, including TNF (Figure 11A), perforin (Figure 11B), and granzyme B (Figure 11C) compared to cells incubated with the IgG4 control (white bars). Perforin and granzyme B are markers of activated cytotoxic T-lymphocytes. Incubation with MAB10 also increases the proportion of antigen-specific activated CD8+ T-cells, as shown in Figure 11D. Cells that were treated with 20 μ g/ml of the IgG4 control or MAB10 were analyzed by FACS by expression of CD3 and expression of perforin and granzyme B.

[0672] Cells from the same donor were used in a similar set of experiments to show that blockade by MAB10 amplifies CMV-specific CD8+ T-cell responses. Cells were incubated with a range of concentrations of MAB10 (black bars) or the IgG4 control (white bars) and the percentage of double positive population perforin + granzyme B+ (Figure 12A) or IFN- γ + TNF+ (Figure 12C) was analyzed. Figures 12B (perforin + granzyme B+ analysis) and 12D (IFN- γ + TNF+ analysis) show the proportion of double positive cells comparing cells treated with 20 μ g/ml of the control antibody (left panels) or 20 μ g/ml of MAB10 (right panels). The cells treated with MAB10 showed a much greater production of effector cytokines compared with control-treated cells.

[0673] The combinatorial effect of MAB10 and the PD-1 antibody pembrolizumab was tested using the same donor as described above. Cells were stimulated with CMV lysates as described above and treated with 2 μ g/ml pembrolizumab or control IgG4, and 10, 20, or 40 μ g/ml control antibody or MAB10, and production of TNF in the supernatant was measured. As shown in Figure 13, four groups of cells were tested, treated with IgG4 control (white bars, left

most group), a constant amount of IgG4 control and a titration of MAB10 (dark gray bars, second group from left), a constant amount of pembrolizumab and a titration of IgG4 control (light gray bars, second group from right), or a constant amount of pembrolizumab and a titration of MAB10 (black bars, right hand group). The combination of pembrolizumab and MAB10 increased the production of TNF above the effect observed with the single agents.

[0674] The combination was again tested in three different donors, using the assay described above. Cells were stimulated with CMV lysate and treated with 20 µg/ml of MAB10 or 20 µg/ml of control IgG4 antibody and a titration of pembrolizumab, and production of TNF was measured. As shown in Figure 14A (Donor 1), Figure 14B (Donor 2), and Figure 14C (Donor 3), the addition of MAB10 (black bars), alone or in combination with increasing concentrations of pembrolizumab, results in greater production of TNF compared to the control antibody + pembrolizumab group (white bars). Additionally, MAB10 (black bars) in combination with pembrolizumab also resulted in increased activation compared to MAB10 alone. Statistical differences were calculated between MAB10 alone and MAB10+pembrolizumab groups using Student T test analysis (*=p<0.05, **=p<0.01, ***=p<0.005, ****=p<0.001)

[0675] Taken together, the data presented in the Example demonstrate a clear, dose-dependent effect of MAB10 as a single agent in antigen-specific recall assays. In addition, the data show increased efficacy when combining MAB10 and pembrolizumab in multiple donors, indicating the value of the ABPs disclosed herein and PD-1 inhibitors or PD-L1 inhibitors as combination therapies.

APPENDIX A: SEQUENCE REFERENCE TABLE

[0676]

SEQ ID NO	Molecule	Region	Sequence
1	hTIGIT		MRWCLLLIWAQGLRQAPLASGMMTGTIETTGNISAE KGGSIILQCHLSSTTAQVTQVNWEQQDQLLAICNAD LGWHISPSFKDRVAPGPGLGLTLQSLTVNDTGEYFCI YHTYPDGTYTGRIFLEVLESSVAEHGARFQIPLL AATLVVICTAVIVVVVALTRKKKALRIHSVEGDLRRK SAGQEEWSPSAPSPPGSCVQAEAAPAGLCGEQRGED CAELHDYFNVLSYRSLGNCSEFTTETG
2	cTIGIT		MRWCLFLIWAQGLRQAPLASGMMTGTIETTGNISAK KGGSVILQCHLSSTMAQVTQVNWEQHDHSLAIRN AELGWHIYPAFKDRVAPGPGLGLTLQSLTMNDTGEY FCTYHTYPDGTYRGRIFLEVLESSVAEHSARFQIPLL GAMAMMLVVICIAVIVVVVLARKKKSLRIHSVESGL QRKSTGQEEQIPSPSPPGSCVQAEAAPAGLCGEQQ GDDCAELHDYFNVLSYRSLGSCSEFTTETG

SEQ ID NO	Molecule	Region	Sequence
3	mTIGIT		MHGWL LLVWVQGLIQAAFLATGATAGTIDTKRNI AEEGGSVILQCHFSSDTAEVTQVDWKQQDQLLAIYS VDLGWHVASVFSDRVVPGPSLGLTFQSLTMNDTGE YFCTYHTYPGGIYKGRIFLKVQESSVAQFQTAPLGGT MAAVLGLICLMVTGVTVLARKKSIRMHSIESGLGRT EAEPQEWNLRLSSPGSPVQTQTAPAGPCGEQAEDD YADPQEYFNVLSYRSLESFIAVSKTG
4	MAB1-IgG4	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSITSSSYW WIRQPPGKGLEWIGSIYYSGATFYNPSLKSRVTISVD TSKNQFSLKLSSVTAADTAVYYCARDANYYGSAWA FDPWGQGT LVTVSS
5	MAB2-IgG4	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSKYYW WIRQPPGKGLEWIGSIYYSGSTFYNPSLKSRVTISVD SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF DPWGQGT LVTVSS
6	MAB3-IgG4	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSTSHYW WIRQPPGKGLEWIGSIYYSGSTFYNPSLKSRVTISVD SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF DPWGQGT LVTVSS
7	MAB4-IgG4	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSTSHYW WIRQPPGKGLEWIGSIYYSGSTFYNPSLKSRVTISVD SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF DPWGQGT LVTVSS
8	MAB5-IgG4	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSTSHYW WIRQPPGKGLEWIGSIYYSGSTFYNPSLKSRVTISVD TSKNQFSLKLSSVTAADTAVYYCARDANYYGSAWA FDPWGQGT LVTVSS
9	MAB6-IgG4	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIESGSYYW WIRQPPGKGLEWIGSIYYSGGTYYNPSLKSRVTISVD TSKNQFSLKLSSVTAADTAVYYCARDGVLT LNKRSF DIWGQGT MVTVSS
10	MAB7-IgG4	VH	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGVYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRVTISV DTSKNQFSLKLSSVTAADTAVYYCARDGVLT LNKRS FDIWGQGT MVTVSS

SEQ ID NO	Molecule	Region	Sequence
11	MAB8-IgG4	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIASGSYYWG WIRQPPGKGLEWIGSIYYSGQTYYNPSLKSRVTISVD TSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRSF DIWGQGTMTVTVSS
12	MAB9-IgG4	VH	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRVTISV DTSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRS FDIWGQGTMTVTVSS
13	MAB10-IgG4	VH	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRATISV DTSKNQFSLKLSSVTAADTAVYYCARDGV LALNKR SFDIWGQGTMTVTVSS
14	MAB11-IgG4	VH	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRVTISV DTSKNQFSLKLSSVTAADTAVYYCARDGV LALNKR SFDIWGQGTMTVTVSS
15	MAB12-IgG4	VH	QVQLQESGPGLVKPSQTLSTCTASGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRVTISV DTSKNQFSLKLSSVTAADTAVYYCARDGV LALNKR SFDIWGQGTMTVTVSS
16	MAB13-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFGNYYM HWVRQAPGQGLEWMGIINPSLGLT SYAQKFQGRVT MTRDTSTSTVYMESSLRSEDTAVYYCARGGRTTWI GAFDIWGQGTMTVTVSS
17	MAB14-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYMH WVRQAPGQGLEWMGIINPSLGLT SYAQKFQGRVTM TRDTSTSTVYMESSLRSEDTAVYYCARGGRTTWIG AFDIWGQGTMTVTVSS
18	MAB15-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFREYYMH WVRQAPGQGLEWMGIINPSIGLTSYARKFQGRVTMT RDTSTSTVYMESSLRSEDTAVYYCARGGRTTWIGA FDIWGQGTMTVTVSS
19	MAB16-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFREYYMH WVRQAPGQGLEWMGIINPSIGLTSYARKFQGRVTMT

SEQ ID NO	Molecule	Region	Sequence
			WVRQAPGQGLEWMGIINPSLGLTSYARKFQGRVTM RDTSTSTVYMELSSLRSEDNAVYYCARGGRTTWIGALDIWGQGTMTVTVSS
20	MAB17-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYYIH WVRQAPGQGLEWMGIINPSLGLTSYARKFQGRVTM TRDTSTSTVYMELSSLRSEDNAVYYCARGGRTTWIGALDIWGQGTMTVTVSS
21	MAB18-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYYMH WVRQAPGQGLEWMGIINPSLGLTSYARKFQGRVTM TRDTSTSTVYMELSSLRSEDNAVYYCARGGRTTWIGAFDIWGQGTMTVTVSS
22	MAB19-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWMGVINPSMGATSYAQKFQGRVT MTRDTSTSTVYMELSSLRSEDNAVYYCARLHVSGSYYPAYLDYWGGQGTMTVTVSS
23	MAB20-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWVGIINPSMGATSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDNAVYYCARLHVSGSYPAYLDYWGGQGTMTVTVSS
24	MAB21-IgG4	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWMGIINPSMGATSYTQKFRGRVTM TRDTSTSTVYMELSSLRSEDNAVYYCARLHVSGSYPAYLDYWGGQGTMTVTVSS
25	MAB1-IgG4	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTIS SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIK
25	MAB2-IgG4	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTIS SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIK
25	MAB3-IgG4	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTIS SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIK
25	MAB4-	VL	

SEQ ID NO	Molecule	Region	Sequence
	IgG4		EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLT SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIK
25	MAB5-IgG4	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLT SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIK
26	MAB6-IgG4	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIK
26	MAB7-IgG4	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIK
26	MAB8-IgG4	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIK
26	MAB9-IgG4	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIK
26	MAB10-IgG4	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIK
26	MAB11-IgG4	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIK
26	MAB12-IgG4	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIK
27	MAB13-IgG4	VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVWPPLTFGGGTKVEIK

SEQ ID NO	Molecule	Region	Sequence
27	MAB14-IgG4	VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVVPPLTFGGGTKVEIK
27	MAB15-IgG4	VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVVPPLTFGGGTKVEIK
27	MAB16-IgG4	VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVVPPLTFGGGTKVEIK
27	MAB17-IgG4	VL	
27	MAB18-IgG4	VL	
28	MAB19-IgG4	VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVVPPLTFGGGTKVEIK EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVVPPLTFGGGTKVEIK EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRHLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYIVFPWTFGGGTKVEIK EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRHLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYIVFPWTFGGGTKVEIK EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRHLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYIVFPWTFGGGTKVEIK
28	MAB20-IgG4	VL	
28	MAB21-IgG4	VL	
29	MAB1-IgG4	H3-IMGT	ARDANYYGSAWAFDP
29	MAB2-IgG4	H3-IMGT	ARDANYYGSAWAFDP
29	MAB3-IgG4	H3-IMGT	ARDANYYGSAWAFDP

SEQ ID NO	Molecule	Region	Sequence
30	MAB4-IgG4	H3-IMGT	ARDANYYYGGAWAFDP
29	MAB5-IgG4	H3-IMGT	ARDANYYYGSAWAFDP
31	MAB6-IgG4	H3-IMGT	ARDGVLTLNKRSFDI
31	MAB7-IgG4	H3-IMGT	ARDGVLTLNKRSFDI
31	MAB8-IgG4	H3-IMGT	ARDGVLTLNKRSFDI
31	MAB9-IgG4	H3-IMGT	ARDGVLTLNKRSFDI
32	MAB10-IgG4	H3-IMGT	ARDGVLALNKRSFDI
32	MAB11-IgG4	H3-IMGT	ARDGVLALNKRSFDI
32	MAB12-IgG4	H3-IMGT	ARDGVLALNKRSFDI
33	MAB13-IgG4	H3-IMGT	ARGGRTTWIGAFDI
33	MAB14-IgG4	H3-IMGT	ARGGRTTWIGAFDI
33	MAB15-IgG4	H3-IMGT	ARGGRTTWIGAFDI
34	MAB16-IgG4	H3-IMGT	ARGGRTTWIGALDI
34	MAB17-IgG4	H3-IMGT	ARGGRTTWIGALDI
33	MAB18-IgG4	H3-IMGT	ARGGRTTWIGAFDI
35	MAB19-IgG4	H3-IMGT	ARLHVSGSYYPAYLDY
35	MAB20-IgG4	H3-IMGT	ARLHVSGSYYPAYLDY
35	MAB21-IgG4	H3-IMGT	ARLHVSGSYYPAYLDY
36	MAB1-IgG4	H2-Kabat	SIYYSGATFYNPSLKS
37	MAB2-	H2-Kabat	SIYYSGSTFYNPSLKS

SEQ ID NO	Molecule	Region	Sequence
	IgG4		
37	MAB3-IgG4	H2-Kabat	SIYYSGSTFYNP SLKS
37	MAB4-IgG4	H2-Kabat	SIYYSGSTFYNP SLKS
38	MAB5-IgG4	H2-Kabat	SIYYSGSTFYNP SLKG
39	MAB6-IgG4	H2-Kabat	SIYYSGGTYYNP SLKS
40	MAB7-IgG4	H2-Kabat	SIYYSGSTYYNP SLKS
41	MAB8-IgG4	H2-Kabat	SIYYSGQTYYP SLKS
40	MAB9-IgG4	H2-Kabat	SIYYSGSTYYNP SLKS
40	MAB10-IgG4	H2-Kabat	SIYYSGSTYYNP SLKS
40	MAB11-IgG4	H2-Kabat	SIYYSGSTYYNP SLKS
40	MAB12-IgG4	H2-Kabat	SIYYSGSTYYNP SLKS
42	MAB13-IgG4	H2-Kabat	IINPSLGLTSYAQKFQG
42	MAB14-IgG4	H2-Kabat	IINPSLGLTSYAQKFQG
43	MAB15-IgG4	H2-Kabat	IINPSIGLTSYARKFQG
43	MAB16-IgG4	H2-Kabat	IINPSIGLTSYARKFQG
44	MAB17-IgG4	H2-Kabat	IINPSLGLTSYARKFQG
44	MAB18-IgG4	H2-Kabat	IINPSLGLTSYARKFQG
45	MAB19-IgG4	H2-Kabat	VINPSMGATSYAQKFQG
46	MAB20-IgG4	H2-Kabat	IINPSMGATSYAQKFQG
47	MAB21-IgG4	H2-Kabat	IINPSMGATSYTQKFRG

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48	MAB1-IgG4	H1-Chothia + Kabat	GSITSSSYWWG
49	MAB2-IgG4	H1-Chothia + Kabat	GSISSSKYYWG
50	MAB3-IgG4	H1-Chothia + Kabat	GSISSTSHYWG
50	MAB4-IgG4	H1-Chothia + Kabat	GSISSTSHYWG
50	MAB5-IgG4	H1-Chothia + Kabat	GSISSTSHYWG
51	MAB6-IgG4	H1-Chothia + Kabat	GSIESGSYYWG
52	MAB7-IgG4	H1-Chothia + Kabat	GSIESGVYYWG
53	MAB8-IgG4	H1-Chothia + Kabat	GSIASGSYYWG
54	MAB9-IgG4	H1-Chothia + Kabat	GSIESGL YYWG
54	MAB10-IgG4	H1-Chothia + Kabat	GSIESGL YYWG
54	MAB11-IgG4	H1-Chothia + Kabat	GSIESGL YYWG
54	MAB12-IgG4	H1-Chothia + Kabat	GSIESGL YYWG
55	IgG4	Constant, S228P hinge stabilizing	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSS SLGTKTYTCNVDHKPSNTKVDKRVESKYGPCCPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVS QEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISK AKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLT VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG K
56	IgG4	Constant S228P, N297A, C terminal Lys deleted	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSS SLGTKTYTCNVDHKPSNTKVDKRVESKYGPCCPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVS QEDPEVQFNWYVDGVEVHNAKTKPREEQFASTYRV VSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISK AKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLT VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG

SEQ ID NO	Molecule	Region	Sequence
57	IgG1	Constant (G1m(3) allotype)	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCP PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLY SKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLS LSPGK
58	MAB13-IgG4	H1-Chothia + Kabat	YTFGNYYMH
59	MAB14-IgG4	H1-Chothia + Kabat	YTFPAYMH
60	MAB15-IgG4	H1-Chothia + Kabat	YTFREYYMH
60	MAB16-IgG4	H1-Chothia + Kabat	YTFREYYMH
61	MAB17-IgG4	H1-Chothia+ Kabat	YTFPAYIH
59	MAB18-IgG4	H1-Chothia + Kabat	YTFPAYMH
62	MAB19-IgG4	H1-Chothia + Kabat	YTFTSHYMG
62	MAB20-IgG4	H1-Chothia + Kabat	YTFTSHYMG
62	MAB21-IgG4	H1-Chothia + Kabat	YTFTSHYMG
63	MAB1-IgG4	L3 - Chothia/Kabat/I MGT	QQHFNLPT
63	MAB2-IgG4	L3 - Chothia/Kabat/I MGT	QQHFNLPT
63	MAB3-IgG4	L3 - Chothia/Kabat/I MGT	QQHFNLPT
63	MAB4-IgG4	L3 - Chothia/Kabat/I MGT	QQHFNLPT

SEQ ID NO	Molecule	Region	Sequence
63	MAB5-IgG4	L3 - Chothia/Kabat/I MGT	QQHFNLP T
64	MAB6-IgG4	L3 - Chothia/Kabat/I MGT	QQHTVRPPL T
64	MAB7-IgG4	L3 - Chothia/Kabat/I MGT	QQHTVRPPL T
64	MAB8-IgG4	L3 - Chothia/Kabat/I MGT	QQHTVRPPL T
64	MAB9-IgG4	L3 - Chothia/Kabat/I MGT	QQHTVRPPL T
64	MAB10-IgG4	L3 - Chothia/Kabat/I MGT	QQHTVRPPL T
64	MAB11-IgG4	L3 - Chothia/Kabat/I MGT	QQHTVRPPL T
64	MAB12-IgG4	L3 - Chothia/Kabat/I MGT	QQHTVRPPL T
65	MAB13-IgG4	L3 - Chothia/Kabat/I MGT	QQYVWPPL T
65	MAB14-IgG4	L3 - Chothia/Kabat/I MGT	QQYVWPPL T
65	MAB15-IgG4	L3 - Chothia/Kabat/I MGT	QQYVWPPL T
65	MAB16-IgG4	L3 - Chothia/Kabat/I MGT	QQYVWPPL T
65	MAB17-IgG4	L3 - Chothia/Kabat/I MGT	QQYVWPPL T
65	MAB18-IgG4	L3 - Chothia/Kabat/I MGT	QQYVWPPL T

SEQ ID NO	Molecule	Region	Sequence
66	MAB19-IgG4	L3 - Chothia/Kabat/I MGT	QQYIVFPWT
66	MAB20-IgG4	L3 - Chothia/Kabat/I MGT	QQYIVFPWT
66	MAB21-IgG4	L3 - Chothia/Kabat/I MGT	QQYIVFPWT
67	MAB1-IgG4	L2 - Chothia/Kabat	DASNRAT
67	MAB2-IgG4	L2 - Chothia/Kabat	DASNRAT
67	MAB3-IgG4	L2 - Chothia/Kabat	DASNRAT
67	MAB4-IgG4	L2 - Chothia/Kabat	DASNRAT
67	MAB5-IgG4	L2 - Chothia/Kabat	DASNRAT
68	MAB6-IgG4	L2 - Chothia/Kabat	GASSRA T
68	MAB7-IgG4	L2 - Chothia/Kabat	GASSRA T
68	MAB8-IgG4	L2 - Chothia/Kabat	GASSRA T
68	MAB9-IgG4	L2 - Chothia/Kabat	GASSRA T
68	MAB10-IgG4	L2 - Chothia/Kabat	GASSRA T
68	MAB11-IgG4	L2 - Chothia/Kabat	GASSRA T
68	MAB12-IgG4	L2 - Chothia/Kabat	GASSRA T
69	MAB13-IgG4	L2 - Chothia/Kabat	GASTRA T
69	MAB14-IgG4	L2 - Chothia/Kabat	GASTRA T
69	MAB15-IgG4	L2 - Chothia/Kabat	GASTRA T
69	MAB16-	L2 -	GASTRA T

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	IgG4	Chothia/Kabat	
69	MAB17-IgG4	L2 - Chothia/Kabat	GASTRA T
69	MAB18-IgG4	L2 - Chothia/Kabat	GASTRA T
69	MAB19-IgG4	L2 - Chothia/Kabat	GASTRA T
69	MAB20-IgG4	L2 - Chothia/Kabat	GASTRA T
69	MAB21-IgG4	L2 - Chothia/Kabat	GASTRA T
70	MAB1-IgG4	L1 - Chothia/Kabat	RASQSVSSYLA
70	MAB2-IgG4	L1 - Chothia/Kabat	RASQSVSSYLA
70	MAB3-IgG4	L1 - Chothia/Kabat	RASQSVSSYLA
70	MAB4-IgG4	L1 - Chothia/Kabat	RASQSVSSYLA
70	MAB5-IgG4	L1 - Chothia/Kabat	RASQSVSSYLA
71	MAB6-IgG4	L1 - Chothia/Kabat	RASQSVSSSYLA
71	MAB7-IgG4	L1 - Chothia/Kabat	RASQSVSSSYLA
71	MAB8-IgG4	L1 - Chothia/Kabat	RASQSVSSSYLA
71	MAB9-IgG4	L1 - Chothia/Kabat	RASQSVSSSYLA
71	MAB10-IgG4	L1 - Chothia/Kabat	RASQSVSSSYLA
71	MAB11-IgG4	L1 - Chothia/Kabat	RASQSVSSSYLA
71	MAB12-IgG4	L1 - Chothia/Kabat	RASQSVSSSYLA
72	MAB13-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
72	MAB14-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA

SEQ ID NO	Molecule	Region	Sequence
72	MAB15-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
72	MAB16-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
72	MAB17-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
72	MAB18-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
72	MAB19-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
72	MAB20-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
72	MAB21-IgG4	L1 - Chothia/Kabat	RASQSVSSNLA
73	SEC1	Human IgG4 S228P Heavy Chain	EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHW VRQSPGKGLEWVAFIRSGSGIVFYADAVRGRFTISRD NAKNLLFLQMNDLKSEDTAMYVCARRPLGHNTFDS WGQGTLLVTVSSASTKGPSVFPLAPCSRSTSESTAALG CLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVTPSSSLGTKTYTCNVDPKPSNTKVDKRV ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRT
			PEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKP REEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK GLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHN HYTQKSLSLSLGK
74	SEC1	Heavy Chain Variable Region	EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHW VRQSPGKGLEWVAFIRSGSGIVFYADAVRGRFTISRD NAKNLLFLQMNDLKSEDTAMYVCARRPLGHNTFDS WGQGTLLVTVSS
75	SEC1	SEC1 Human Kappa Chain	DIVMTQSPSSLAIVSPGEKVTMTCKSSQSLYYSGVKE NLLAWYQQKPGQSPKLLIYYASIRFTGVPDRFTGSGS GTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDGTK LEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP REAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLS STLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRG EC
76	SEC1	Light Chain	

SEQ ID NO	Molecule	Region	Sequence
		Variable Region	DIVMTQSPSSSLAVSPGEKVTMTCKSSQSLYYSGVKE NLLAWYQQKPGQSPKLLIYYASIRFTGVPDRFTGSGS GTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDGTLK LEIK
77	SEC1	Mouse IgG2a N297A Heavy Chain	EVQLVESGGGLTQPGKSLKLSCEASGFTFSSTMHV VRQSPGKGLEWVAFIRSGSGIVFYADAVRGRFTISR NAKNLLFLQMNDLKSEDTAMYCARRPLGHNTFDS WGQGTLLTVSSAKTTAPSVYPLAPVCGDTTGSSVTL GCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVLQSDL YTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKIEP RGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMSL SPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQTQT HREDYASTLRVVSALPIQHQQDWMMSGKEFKCKVNNK DLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQV TLTCMVTDFMPEDIYVEWTNNGKTELNYKNTPEVL DSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLH NHHTTKSFSRTPGK
74	SEC1	Heavy Chain Variable region	EVQLVESGGGLTQPGKSLKLSCEASGFTFSSTMHV VRQSPGKGLEWVAFIRSGSGIVFYADAVRGRFTISR NAKNLLFLQMNDLKSEDTAMYCARRPLGHNTFDS WGQGTLLTVSS
78	SEC1	Mouse Kappa Chain	DIVMTQSPSSSLAVSPGEKVTMTCKSSQSLYYSGVKE NLLAWYQQKPGQSPKLLIYYASIRFTGVPDRFTGSGS GTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDGTLK LEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYP KDINVKWKIDGSRQNGVLNSWTDQDSKDSTYSMS STLTTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE C
76	SEC1	Light Chain Variable Region	DIVMTQSPSSSLAVSPGEKVTMTCKSSQSLYYSGVKE NLLAWYQQKPGQSPKLLIYYASIRFTGVPDRFTGSGS GTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDGTLK LEIK
79	MAB1	Full length IgG4 S228P	QLQLQESGPGLVKPSETLSLTCTVSGGSITSSSYW WIRQPPGKGLEWIGSIYYSGATFYNPSLKSRTISVD TSKNQFSLKLSVTAADTAVYYCARDANYGSAWA FDPWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS
			SGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVD KRVESKYGPPCPPCAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVHLHQQDWLNGKEYCKV SNKGI.PSSIEKTISKAKGPREPOVYTI.PPSOEFMTK

SEQ ID NO	Molecule	Region	Sequence
			NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSGDFLYSRLTVDKSRWQEGNVFSCSVMEAL HNHYTQKSLSLGK
80	MAB1	Full length IgG1	QLQLQESGPGLVKPSETLSLTCTVSGGSITSSSYW WIRQPPGKGLEWIGSIYYSGATFYNP SLKSRVTISVD TSKNQFSLKLSSVTAADTAVYYCARDANYYGSAWA FDPWGQGT LVT VSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQS SGLYSLSSV VTPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGDFLYSKLTVDKSRWQQGNVFSCSV MEALHNHYTQKSLSLSPGK
81	MAB1	Full length Kappa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGGTDFTLTI SSLEPEDFAVYYCQQHFNLPFGGGTKVEIKRTVAA PSVFIFPPSDEQLKSGTASVCLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDYSLSTLTLSKAD YEKHKVYACEVTHQGLSPVTKSFNRGEC
82	MAB2	Full length IgG4 S228P	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSKYYWG WIRQPPGKGLEWIGSIYYSGSTFYNP SLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF DPWGQGT LVT VSSASTKGPSVFPLAPCSRSTSESTA LGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSS GLYSLSSV VTPSSSLGTQTYTCNV DHKPSNTKVDK RVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMIS RTPEVTCVVDVSDQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSDGDFLYSRLTVDKSRWQEGNVFSCSVMEALH NHYTQKSLSLGK
83	MAB2	Full length IgG1	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSKYYWG WIRQPPGKGLEWIGSIYYSGSTFYNP SLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF DPWGQGT LVT VSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQS SGLYSLSSV VTPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGDFLYSKLTVDKSRWQQGNVFSCSV

SEQ ID NO	Molecule	Region	Sequence
			HEALHNHYTQKSLSLSPGK
81	MAB2	Full length Kappa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ
			QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTIS SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDYSLSTLTLSKAD YEKHKVYACEVTHQGLSPVTKSFNRGEC
84	MAB3	Full length IgG4 S228P	QLQLQESGPGGLVKPSETLSLTCTVSGGSISSTSHYWG WIRQPPGKGLEWIGSIYYSGSTFYNNPSLKSRTISVDT SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF DPWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVTVPSSSLGTQTYTCNVNHHKPSNTKVDK RVESKYGPPCPAPPEFLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV NKGLEPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSGDSFFLYSRLTVDKSRWQEGNVSFCSVMHEALH NHYTQKSLSLSLGK
85	MAB3	Full length IgG1	QLQLQESGPGGLVKPSETLSLTCTVSGGSISSTSHYWG WIRQPPGKGLEWIGSIYYSGSTFYNNPSLKSRTISVDT SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF DPWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS SGLYSLSSVTVPSSSLGTQTYICNVNHHKPSNTKVDK RVEPKSCDKHTHTCPAPPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TPPVLDSDGDSFFLYSKLTVDKSRWQQGNVSFCSVM HEALHNHYTQKSLSLSPGK
81	MAB3	Full length Kappa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTIS SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDYSLSTLTLSKAD YEKHKVYACEVTHQGLSPVTKSFNRGEC
86	MAB4	Full length IgG4 S228P	QLQLQESGPGGLVKPSETLSLTCTVSGGSISSTSHYWG WIRQPPGKGLEWIGSIYYSGSTFYNNPSLKSRTISVDT SKNQFSLKLSSVTAADTAVYYCARDANYYGSAWAF

SEQ ID NO	Molecule	Region	Sequence
			SKNQFSEKLESSVTAADTAVYYCARDANYYGAWAF DPWGQGTLLTVTVSSASTKGPSVFPLAPCSRSTSESTA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVTVPSSSLGKTYTCNVDHKPSNTKV RVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH EALHNHYTQKSLSLGLK
87	MAB4	Full length IgG1	QLQLQESGPGLVKPSSETLSLTCTVSGGSISSTSHYWG WIRQPPGKGLEWIGSIYYSGSTFYNP SLKSRVTISVDT SKNQFSLKLSSVTAADTAVYYCARDANYYGAWAF DPWGQGTLLTVTVSSASTKGPSVFPLAPSSKSTSGGTA
			ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS SGLYSLSSVTVPSSSLGKTYTCNVNHHKPSNTKV DKEVPEPKSCDKHTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
81	MAB4	Full length Kappa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLIYDASNRATGIPARFSGSGSGTDFTLT TISSLEPEDFAVYYCQQHFNLPFTFGGGTKVEIKRTVAA PSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKAD YEKHKVYACEVTHQGLSPVTKSFNRGEC
88	MAB5	Full length IgG4 S228P	QLQLQESGPGLVKPSSETLSLTCTVSGGSISSTSHYWG WIRQPPGKGLEWIGSIYYSGSTFYNP SLKGRVTISVD TSKNQFSLKLSSVTAADTAVYYCARDANYYGSAWA FDPWGQGTLLTVTVSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS SGLYSLSSVTVPSSSLGKTYTCNVDHKPSNTKV DKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEAL HNHYTQKSLSLGLK
89	MAB5	Full length IgG1	QLQLQESGPGLVKPSSETLSLTCTVSGGSISSTSHYWG WIRQPPGKGLEWIGSIYYSGSTFYNP SLKGRVTISVD

SEQ ID NO	Molecule	Region	Sequence
			TSKNQFSLKLSSVTAADTAVYYCARDANYYGSAWA FDPWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGK
81	MAB5	Full length Kappa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTI SSLEPEDFAVYYCQQHFNLPTFGGGTKVEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDSSTYSSTLTLSKAD YEKHKVYACEVTHQGLSPVTKSFNRGEC
90	MAB6	Full length IgG4 S228P	QLQLQESGPGLVKPSSETLSLTCTVSGGSIESGSYYWG WIRQPPGKGLEWIGSIYYSGGTYYNPSLKSRTISVD TSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRSF DIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSESTAA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNTKVDK RVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMIS
			RTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFCFSVMHEALHNHYTQKSLSLSPGK
91	MAB6	Full length IgG1	QLQLQESGPGLVKPSSETLSLTCTVSGGSIESGSYYWG WIRQPPGKGLEWIGSIYYSGGTYYNPSLKSRTISVD TSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRSF DIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGK
92	MAB6	Full length	

SEQ ID NO	Molecule	Region	Sequence
		Kappa	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIKRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDYSLSSLTLS KADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
93	MAB7	Full length IgG4 S228P	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGVYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRS FDIWGQGTMTVTSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVD KRVESKYGPPCPPCAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSGDGSFFLYSRLTVDKSRWQEGNVFSCSVMEAL HNHYTQKSLSLGLK
94	MAB7	Full length IgG1	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGVYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRS FDIWGQGTMTVTSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKHTHTCPPCAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEAL HNHYTQKSLSLSPGK
92	MAB7	Full length Kappa	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIKRT
			VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDYSLSSLTLS KADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
95	MAB8	Full length IgG4 S228P	QLQLQESGPGLVKPSQTLSTCTVSGGSIASGSYYWG WIRQPPGKGLEWIGSIYYSGQTYNPSLKSRTISVD TSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRSF DIWGQGTMTVTSSASTKGPSVFPLAPCSRSTSESTA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDK

SEQ ID NO	Molecule	Region	Sequence
			RVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALH NHYTQKSLSLSLGK
96	MAB8	Full length IgG1	QLQLQESGPGLVKPSSETLSLTCTVSGGSIASGSYYWG WIRQPPGKGLEWIGSIYYSGQTYYNPSLKSRTISVD TSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRSF DIWGQGTMTVTSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV HEALHNHYTQKSLSLSPGK
92	MAB8	Full length Kappa	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKEIKRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDSSTYLSSTLTLS KADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
97	MAB9	Full length IgG4 S228P	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRS FDIWGQGTMTVTSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYTCNVNHHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEAL HNHYTQKSLSLSLGK
98	MAB9	Full length IgG1	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGVLTNLKRS FDIWGQGTMTVTSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHHKPSNTKVDK

SEQ ID NO	Molecule	Region	Sequence
			RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK
92	MAB9	Full length Kappa	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFLTISRLEPEDFAVYYCQQHTVRPPLTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRGEC
99	MAB10	Full length IgG4 S228P	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYWGWIQQPPGKGLEWIGSIYYSGSTYYNPSLKSRAISVDTSKNQFSLKLSSVTAADTAVYYCARDGVLALNKR SFDIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTITTCNVDHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVSDQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSRLTVDKSRWQEGNVFCFSVMHEAL HNHYTQKSLSLSLGK
100	MAB10	Full length IgG1	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYWGWIQQPPGKGLEWIGSIYYSGSTYYNPSLKSRAISVDTSKNQFSLKLSSVTAADTAVYYCARDGVLALNKR SFDIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK
92	MAB10	Full length Kappa	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFLTISRLEPEDFAVYYCQQHTVRPPLTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRGEC

SEQ ID NO	Molecule	Region	Sequence
101	MAB11	Full length IgG4 S228P	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGV LALNKR SFDIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV
			SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDS DGSFFLYSRLTVDKSRWQEGNVFSCSV MHEAL HNHYTQKSLSLSLGK
102	MAB11	Full length IgG1	QVQLQESGPGLVKPSQTLSTCTVSGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGV LALNKR SFDIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SV MHEALHNHYTQKSLSLSPGK
92	MAB11	Full length Kappa	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSTDFTL TISRLEPEDFAVYYCQQHTVRPPLTFGGGTKVEIKRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLS KADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
103	MAB12	Full length IgG4 S228P	QVQLQESGPGLVKPSQTLSTCTASGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGV LALNKR SFDIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDS DGSFFLYSRLTVDKSRWQEGNVFSCSV MHEAL HNHYTQKSLSLSLGK

SEQ ID NO	Molecule	Region	Sequence
			HNHYTQKSESESGK
104	MAB12	Full length IgG1	QVQLQESGPGLVKPSQTLSTCTASGGSIESGLYYW GWIRQPPGKGLEWIGSIYYSGSTYYNPSLKSRTISV DTSKNQFSLKLSSVTAADTAVYYCARDGVLALNKR SFDIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSGSEFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
92	MAB12	Full length Kappa	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWY QQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQHTVRPPLTFGGGTKEIKRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLS
			KADYEKHKVYACEVTHQGLSPVTKSFNRGEC
105	MAB13	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFGNYYM HWVRQAPGQGLEWMGIINPSLGLTSAQKFQGRVT MTRDTSTSTVYMESSLRSEDFAVYYCARGGRITWI GAFDIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSE TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVTVPSSSLGTQTYTCNVNHDHPSNTKV DKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTL MISRTPEVTCVVDVSDQEDPEVQFNWYVDGVEVHN AKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC KVSNGKLPSSIEKTISKAKGQPREPQVYTLPPSQEEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSGSEFLYSRLTVDKSRWQEGNVFSCSV MHEALHNHYTQKSLSLSPGK
106	MAB13	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFGNYYM HWVRQAPGQGLEWMGIINPSLGLTSAQKFQGRVT MTRDTSTSTVYMESSLRSEDFAVYYCARGGRITWI GAFDIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK KDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSSEFLYSKLTVDKSRWQQGNVFSCSV

SEQ ID NO	Molecule	Region	Sequence
			VMHEALHNHYTQKSLSLSPGK
107	MAB13	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVWPPLTFGGGTKEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
108	MAB14	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYMH WVRQAPGQGLEWMGIINPSLGLTSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARGGRRTWIG AFDIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSVTVTPSSSLGKTCTYCNVDHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMHEAL HNHYTQKSLSLSLGK
109	MAB14	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYMH WVRQAPGQGLEWMGIINPSLGLTSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARGGRRTWIG AFDIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSVTVTPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
			HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV MHEALHNHYTQKSLSLSPGK
107	MAB14	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVWPPLTFGGGTKEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
110	MAB15	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFREYYMH WVRQAPGQGLEWMGIINPSIGLTSYARKFQGRVTMT

SEQ ID NO	Molecule	Region	Sequence
			RDTSTSTVYMELSSLRSEDTAVYYCARGGRTTWIGA FDIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMH EALHNHYTQKSLSLGLK
111	MAB15	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFREYYMH WVRQAPGQGLEWMGIINPSIGLTSYARKFQGRVTMT RDTSTSTVYMELSSLRSEDTAVYYCARGGRTTWIGA FDIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKHTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TPPVLDSGDSFFLYSKLTVDKSRWQQGNVFC SVMHEALHNHYTQKSLSLSPGK
107	MAB15	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVWPPLTFGGGTKVEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP PREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC
112	MAB16	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFREYYMH WVRQAPGQGLEWMGIINPSIGLTSYARKFQGRVTMT RDTSTSTVYMELSSLRSEDTAVYYCARGGRTTWIGA LDIWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP
			VLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMH EALHNHYTQKSLSLGLK
113	MAB16	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFREYYMH WVRQAPGQGLEWMGIINPSIGLTSYARKFQGRVTMT

SEQ ID NO	Molecule	Region	Sequence
			RDTSTSTVYMELSSLRSEDNAVYYCARGGRITWIGA LDIWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGK
107	MAB16	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVWPPLTFGGGTKEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
114	MAB17	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYYIH WVRQAPGQGLEWMGIINPSLGLTSYARKFQGRVTM TRDTSTSTVYMELSSLRSEDNAVYYCARGGRITWIG ALDIWGQGTMTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKV NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSRLTVDKSRWQEGNVFCFSVMHEAL HNHYTQKSLSLSLGK
115	MAB17	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYYIH WVRQAPGQGLEWMGIINPSLGLTSYARKFQGRVTM TRDTSTSTVYMELSSLRSEDNAVYYCARGGRITWIG ALDIWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSV MHEALHNHYTQKSLSLSPGK
107	MAB17	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYVWPPLTFGGGTKEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK

SEQ ID NO	Molecule	Region	Sequence
			VQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTL SKADYEHKVKYACEVTHQGLSSPVTKSFNRGEC
116	MAB18	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYMH
			WVRQAPGQGLEWMGIINPSLGLTSYARKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARGGRRTTWIG AFDIWGQGTMTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSVTVPSSSLGKTYTCNVDPHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEAL HNHYTQKSLSLGLK
117	MAB18	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFPAYMH WVRQAPGQGLEWMGIINPSLGLTSYARKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARGGRRTTWIG AFDIWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSVTVPSSSLGKTYICNVNHPKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFV MHEALHNHYTQKSLSLSPGK
107	MAB18	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTL TISSLSQSEDFAVYYCQQYVWPPLTFGGGTKVEIKR TVAAPSDFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTL SKADYEHKVKYACEVTHQGLSSPVTKSFNRGEC
118	MAB19	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFSTHYMG WVRQAPGQGLEWMGVINPSMGATSYAQKFQGRVT MTRDTSTSTVYMELSSLRSEDTAVYYCARLHVSGSY YPAYLDYWGQGTMTVSSASTKGPSVFPLAPCSRST SESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSVTVPSSSLGKTYTCNVDPHKPSN TKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPK DTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVE VHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFV MHEALHNHYTQKSLSLSPGK

SEQ ID NO	Molecule	Region	Sequence
			EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSGDSFFLYSRLTVDKSRWQEGNVFSCSV MHEALHNHYTQKSLSLGLK
119	MAB19	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWMGVINPSMGATSYAQKFQGRVT MTRDTSTSTVYMELSSLRSEDTAVYYCARLHVSGSY YPAYLDYWGGQTMVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSN TKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
			PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
120	MAB19	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRHLIYGASTRATGIPARFSGSGTEFTL TISSLQSEDFAVYYCQQYIVFPWTFGGGTKVEIKRTV AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ WKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSK ADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
121	MAB20	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWVGINPSMGATSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARLHVSGSYY PAYLDYWGGQTMVTVSSASTKGPSVFPLAPCSRSTS ESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVTVPSSSLGTQTYTCNVDPHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEV HNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSGDSFFLYSRLTVDKSRWQEGNVFSCSV MHEALHNHYTQKSLSLGLK
122	MAB20	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWVGINPSMGATSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARLHVSGSYY PAYLDYWGGQTMVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL

SEQ ID NO	Molecule	Region	Sequence
			KETKCKVSNKAEFAFTERTEKAKKQQTKEFYVYTFET SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SVMHEALHNHYTQKSLSLSPGK
120	MAB20	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRHLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYIVFPWTFGGGTKVEIKRTV AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ WKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSK ADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
123	MAB21	Full length IgG4 S228P	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWMGIINPSMGATSYTQKFRGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARLHVSGSYY PAYLDYWGQGMVTVSSASTKGPSVFPLAPCSRSTS ESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEV HNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSV MHEALHNHYTQKSLSLSLGK
124	MAB21	Full length IgG1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHYMG WVRQAPGQGLEWMGIINPSMGATSYTQKFRGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCARLHVSGSYY PAYLDYWGQGMVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SVMHEALHNHYTQKSLSLSPGK
120	MAB21	Full length Kappa	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWY QQKPGQAPRHLIYGASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQYIVFPWTFGGGTKVEIKRTV AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ WKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSK ADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
125	IgG1	Constant (G1m(17,1) allotype,	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCP

SEQ ID NO	Molecule	Region	Sequence
		N297A	SEGTQTTTCFVTVVTKTSNTKRVDRKVEFKSCDRTTTCF PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYAST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK
126	Kappa	Constant	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
127	Linker		GGGGS
128 ... 137 - See other portions of this disclosure and the electronic version of the Sequence Listing submitted herewith.			
138	mTIGIT2		MHGWLLLWVWQGLIQAAFLATAIGATAGTIDTKRNI SAEEGGSVILQCHFSSDTAEVTQVDWKQQDQLLAIY SVDLGWHVASVFSDRVVPGPSLGLTFQSLTMNDTGE YFCTYHTYPGGIYKGRIFLKVQESSDDRNGLAQFQT APLGGTMAAVLGLICLMVTGVTVLARKDKSIRMHSI ESGLGRTEAEPQEWNLRLSLSSPGSPVQTQTAPAGPC GEQAEDDYADPQEYFNVLSYRSLESFIAVSKTG

SEQUENCE LISTING

[0677]

<110> HICKLIN, Daniel et al.

<120> ANTI-TIGIT ANTIGEN-BINDING PROTEINS AND METHODS OF USE THEREOF

<130> 037856.0002

<150> US 62/235,990

<151> 2015-10-01

<160> 138

<170> PatentIn version 3.5

<210> 1

<211> 244

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(244)

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<400> 1

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Met Arg Trp Cys Leu Leu Ile Trp Ala Gln Gly Leu Arg Gln Ala
 1          5          10          15

Pro Leu Ala Ser Gly Met Met Thr Gly Thr Ile Glu Thr Thr Gly Asn
      20          25          30

Ile Ser Ala Glu Lys Gly Gly Ser Ile Ile Leu Gln Cys His Leu Ser
      35          40          45

Ser Thr Thr Ala Gln Val Thr Gln Val Asn Trp Glu Gln Gln Asp Gln
      50          55          60

Leu Leu Ala Ile Cys Asn Ala Asp Leu Gly Trp His Ile Ser Pro Ser
65          70          75          80

Phe Lys Asp Arg Val Ala Pro Gly Pro Gly Leu Gly Leu Thr Leu Gln
      85          90          95

Ser Leu Thr Val Asn Asp Thr Gly Glu Tyr Phe Cys Ile Tyr His Thr
      100          105          110

Tyr Pro Asp Gly Thr Tyr Thr Gly Arg Ile Phe Leu Glu Val Leu Glu
      115          120          125

Ser Ser Val Ala Glu His Gly Ala Arg Phe Gln Ile Pro Leu Leu Gly
      130          135          140

Ala Met Ala Ala Thr Leu Val Val Ile Cys Thr Ala Val Ile Val Val
145          150          155          160

Val Ala Leu Thr Arg Lys Lys Lys Ala Leu Arg Ile His Ser Val Glu
      165          170          175

Gly Asp Leu Arg Arg Lys Ser Ala Gly Gln Glu Glu Trp Ser Pro Ser
      180          185          190

Ala Pro Ser Pro Pro Gly Ser Cys Val Gln Ala Glu Ala Ala Pro Ala
      195          200          205

Gly Leu Cys Gly Glu Gln Arg Gly Glu Asp Cys Ala Glu Leu His Asp
      210          215          220

Tyr Phe Asn Val Leu Ser Tyr Arg Ser Leu Gly Asn Cys Ser Phe Phe
225          230          235          240

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Thr Glu Thr Gly

<210> 2

<211> 245

<212> PRT

<213> Macaca fascicularis

<220>

<221> misc_feature

<222> (1)..(245)

<223> cTIGIT

<400> 2

Met Arg Trp Cys Leu Phe Leu Ile Trp Ala Gln Gly Leu Arg Gln Ala
1 5 10 15

Pro Leu Ala Ser Gly Met Met Thr Gly Thr Ile Glu Thr Thr Gly Asn
20 25 30

Ile Ser Ala Lys Lys Gly Gly Ser Val Ile Leu Gln Cys His Leu Ser
35 40 45

Ser Thr Met Ala Gln Val Thr Gln Val Asn Trp Glu Gln His Asp His
50 55 60

Ser Leu Leu Ala Ile Arg Asn Ala Glu Leu Gly Trp His Ile Tyr Pro
65 70 75 80

Ala Phe Lys Asp Arg Val Ala Pro Gly Pro Gly Leu Gly Leu Thr Leu
85 90 95

Gln Ser Leu Thr Met Asn Asp Thr Gly Glu Tyr Phe Cys Thr Tyr His
100 105 110

Thr Tyr Pro Asp Gly Thr Tyr Arg Gly Arg Ile Phe Leu Glu Val Leu
115 120 125

Glu Ser Ser Val Ala Glu His Ser Ala Arg Phe Gln Ile Pro Leu Leu
130 135 140

Gly Ala Met Ala Met Met Leu Val Val Ile Cys Ile Ala Val Ile Val
145 150 155 160

Val Val Val Leu Ala Arg Lys Lys Lys Ser Leu Arg Ile His Ser Val
165 170 175

Glu Ser Gly Leu Gln Arg Lys Ser Thr Gly Gln Glu Glu Gln Ile Pro
180 185 190

Ser Ala Pro Ser Pro Pro Gly Ser Cys Val Gln Ala Glu Ala Ala Pro
195 200 205

Ala Gly Leu Cys Gly Gly Gln Gln Gly Asp Asp Cys Ala Gly Leu His

Ala Gly Leu Cys Gly Glu Gln Gln Gly Asp Asp Cys Ala Glu Leu His
210 215 220

Asp Tyr Phe Asn Val Leu Ser Tyr Arg Ser Leu Gly Ser Cys Ser Phe
225 230 235 240

Phe Thr Glu Thr Gly
245

<210> 3

<211> 241

<212> PRT

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(241)

<223> mTIGIT

<400> 3

Met His Gly Trp Leu Leu Val Trp Val Gln Gly Leu Ile Gln Ala
1 5 10 15

Ala Phe Leu Ala Thr Gly Ala Thr Ala Gly Thr Ile Asp Thr Lys Arg
20 25 30

Asn Ile Ser Ala Glu Glu Gly Gly Ser Val Ile Leu Gln Cys His Phe
35 40 45

Ser Ser Asp Thr Ala Glu Val Thr Gln Val Asp Trp Lys Gln Gln Asp
50 55 60

Gln Leu Leu Ala Ile Tyr Ser Val Asp Leu Gly Trp His Val Ala Ser
65 70 75 80

Val Phe Ser Asp Arg Val Val Pro Gly Pro Ser Leu Gly Leu Thr Phe
85 90 95

Gln Ser Leu Thr Met Asn Asp Thr Gly Glu Tyr Phe Cys Thr Tyr His
100 105 110

Thr Tyr Pro Gly Gly Ile Tyr Lys Gly Arg Ile Phe Leu Lys Val Gln
115 120 125

Glu Ser Ser Val Ala Gln Phe Gln Thr Ala Pro Leu Gly Gly Thr Met
130 135 140

Ala Ala Val Leu Gly Leu Ile Cys Leu Met Val Thr Gly Val Thr Val
145 150 155 160

Leu Ala Arg Lys Lys Ser Ile Arg Met His Ser Ile Glu Ser Gly Leu
165 170 175

Gly Arg Thr Glu Ala Glu Pro Gln Glu Trp Asn Leu Arg Ser Leu Ser
180 185 190

Ser Pro Gly Ser Pro Val Gln Thr Gln Thr Ala Pro Ala Gly Pro Cys
 195 200 205

Gly Glu Gln Ala Glu Asp Asp Tyr Ala Asp Pro Gln Glu Tyr Phe Asn
 210 215 220

Val Leu Ser Tyr Arg Ser Leu Glu Ser Phe Ile Ala Val Ser Lys Thr
 225 230 235 240

Gly

<210> 4

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4; VH

<400> 4

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 Thr 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 Ala Thr Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 5

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB2-IgG4; VH

<400> 5

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

Lys 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 Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 6

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB3-IgG4; VH

<400> 6

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

Ser His 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 Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 7

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB4-IgG4; VH

<400> 7

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

Ser His 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 Phe 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 Ala Asn Tyr Tyr Gly Gly Ala Trp Ala Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 8

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB5-IgG4; VH

<400> 8

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

Ser His 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 Phe Tyr Asn Pro Ser
50 55 60

Leu Lys Gly 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 9

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4; VH

<400> 9

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 Glu Ser Gly
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 Gly 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 Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 10

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB7-IgG4; VH

<400> 10

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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 Glu Ser Gly
          20           25           30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50           55           60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65           70           75           80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
          85           90           95

Cys Ala Arg Asp Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
          100          105          110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
          115          120

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<210> 11

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB8-IgG4; VH

<400> 11

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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 Ala Ser Gly
          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 Gln 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

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Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 12

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB9-IgG4; VH

<400> 12

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 Glu Ser Gly
20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 13

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB10-IgG4; VH

<400> 13

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 Glu Ser Gly
20 25 30

Leu 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 Ala 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 Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 14

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB11-IgG4; VH

<400> 14

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 Glu Ser Gly
20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

115 120

<210> 15
 <211> 123
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic - MAB12-IgG4; VH

<400> 15
 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 Ala Ser Gly Gly Ser Ile Glu Ser Gly
 20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Asp Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 16
 <211> 121
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic - MAB13-IgG4; VH

<400> 16
 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 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 Ile Ile Asn Pro Ser Leu Gly Leu Thr Ser Tyr Ala Gln Lys Phe
 50 55 60

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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
 100 105 110
 Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 17

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB14-IgG4; VH

<400> 17

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 Pro Ala 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 Leu Gly Leu 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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
 100 105 110
 Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 18

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB15-IgG4; VH

<400> 18

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 Arg Glu 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 Ile Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 19

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB16-IgG4; VH

<400> 19

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 Arg Glu 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 Ile Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Leu Asn Ile Trp Gly

Ala Arg Gly Gly Arg Thr Thr Asp Arg Gly Ala Leu Asp Arg Thr Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 20

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB17-IgG4; VH

<400> 20

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 Pro Ala Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Leu Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Leu Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 21

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB18-IgG4; VH

<400> 21

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

Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 22

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19-IgG4; VH

<400> 22

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 His
 20 25 30

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

Gly Val Ile Asn Pro Ser Met Gly Ala 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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 23

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB20-IgG4; VH

<400> 23

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 His
 20 25 30

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

Gly Ile Ile Asn Pro Ser Met Gly Ala 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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 24

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB21-IgG4; VH

<400> 24

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 His
 20 25 30

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

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

Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr

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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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
      100      105      110
Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
      115      120

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<210> 25

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4, MAB2-IgG4, MAB3-IgG4, MAB4-IgG4, MAB5-IgG4; VL

<400> 25

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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 His Phe Asn Leu Pro Thr
      85      90      95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
      100      105

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<210> 26

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4, MAB7-IgG4, MAB8-IgG4, MAB9-IgG4, MAB10-IgG4, MAB11-IgG4, MAB12-IgG4; VL

<400> 26

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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 His Thr Val Arg Pro
 85 90 95

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

<210> 27

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13-IgG4, MAB14-IgG4, MAB15-IgG4, MAB16-IgG4, MAB17-IgG4,
 MAB18-IgG4; VL

<400> 27

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 Val Val Trp Pro Pro
 85 90 95

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

<210> 28

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19-IgG4, MAB20-IgG4, MAB21-IgG4; VL

<400> 28

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	His	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	Ile	Val	Phe	Pro	Trp
				85					90					95	

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

<210> 29

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4, MAB2-IgG4, MAB3-IgG4, MAB5-IgG4; H3-IMGT

<400> 29

Ala	Arg	Asp	Ala	Asn	Tyr	Tyr	Gly	Ser	Ala	Trp	Ala	Phe	Asp	Pro
1				5				10					15	

<210> 30

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB4-IgG4; H3-IMGT

<400> 30

Ala	Arg	Asp	Ala	Asn	Tyr	Tyr	Gly	Gly	Ala	Trp	Ala	Phe	Asp	Pro
1				5				10					15	

<210> 31

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4, MAB7-IgG4, MAB8-IgG4, MAB9-IgG4; H3-IMGT

<400> 31

Ala	Arg	Asp	Gly	Val	Leu	Thr	Leu	Asn	Lys	Arg	Ser	Phe	Asp	Ile
1				5					10					15

<210> 32

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB10-IgG4, MAB11-IgG4, MAB12-IgG4; H3-IMGT

<400> 32

Ala	Arg	Asp	Gly	Val	Leu	Ala	Leu	Asn	Lys	Arg	Ser	Phe	Asp	Ile
1				5					10					15

<210> 33

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13-IgG4, MAB14-IgG4, MAB15-IgG4, MAB18-IgG4; H3-IMGT

<400> 33

Ala	Arg	Gly	Gly	Arg	Thr	Thr	Trp	Ile	Gly	Ala	Phe	Asp	Ile
1				5					10				

<210> 34

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB16-IgG4, MAB17-IgG4; H3-IMGT

<400> 34

Ala	Arg	Gly	Gly	Arg	Thr	Thr	Trp	Ile	Gly	Ala	Leu	Asp	Ile
1				5					10				

<210> 35

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19-IgG4, MAB20-IgG4, MAB21-IgG4; H3-IMGT

<400> 35

Ala	Arg	Leu	His	Val	Ser	Gly	Ser	Tyr	Tyr	Pro	Ala	Tyr	Leu	Asp	Tyr
1				5					10					15	

<210> 36

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4; H2-Kabat

<400> 36

Ser	Ile	Tyr	Tyr	Ser	Gly	Ala	Thr	Phe	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5					10					15	

<210> 37

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB2-IgG4, MAB3-IgG4, MAB4-IgG4; H2-Kabat

<400> 37

Ser	Ile	Tyr	Tyr	Ser	Gly	Ser	Thr	Phe	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5					10					15	

<210> 38

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB5-IgG4; H2-Kabat

<400> 38

Ser	Ile	Tyr	Tyr	Ser	Gly	Ser	Thr	Phe	Tyr	Asn	Pro	Ser	Leu	Lys	Gly
1				5					10					15	

<210> 39

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4; H2-Kabat

<400> 39

Ser	Ile	Tyr	Tyr	Ser	Gly	Gly	Thr	Tyr	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5					10					15	

<210> 40

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB7-IgG4, MAB9-IgG4, MAB10-IgG4, MAB11-IgG4, MAB12-IgG4; H2-Kabat

<400> 40

Ser	Ile	Tyr	Tyr	Ser	Gly	Ser	Thr	Tyr	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5					10					15	

<210> 41

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB8-IgG4; H2-Kabat

<400> 41

Ser	Ile	Tyr	Tyr	Ser	Gly	Gln	Thr	Tyr	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5					10					15	

<210> 42

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13-IgG4, MAB14-IgG4; H2-Kabat

<400> 42

Ile	Ile	Asn	Pro	Ser	Leu	Gly	Leu	Thr	Ser	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 43

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB15-IgG4, MAB16-IgG4; H2-Kabat

<400> 43

Ile	Ile	Asn	Pro	Ser	Ile	Gly	Leu	Thr	Ser	Tyr	Ala	Arg	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 44

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB17-IgG4, MAB18-IgG4; H2-Kabat

<400> 44

Ile	Ile	Asn	Pro	Ser	Leu	Gly	Leu	Thr	Ser	Tyr	Ala	Arg	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 45

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19-IgG4; H2-Kabat

<400> 45

Val	Ile	Asn	Pro	Ser	Met	Gly	Ala	Thr	Ser	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 46

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB20-IgG4; H2-Kabat

<400> 46

Ile	Ile	Asn	Pro	Ser	Met	Gly	Ala	Thr	Ser	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 47

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB21-IgG4; H2-Kabat

<400> 47

Ile	Ile	Asn	Pro	Ser	Met	Gly	Ala	Thr	Ser	Tyr	Thr	Gln	Lys	Phe	Arg
1				5					10					15	

Gly

<210> 48

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4; H1-Chothia + Kabat

<400> 48

Gly	Ser	Ile	Thr	Ser	Ser	Ser	Tyr	Tyr	Trp	Gly
1				5					10	

<210> 49

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB2-IgG4; H1-Chothia + Kabat

<400> 49

Gly	Ser	Ile	Ser	Ser	Ser	Lys	Tyr	Tyr	Trp	Gly
1				5					10	

<210> 50

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB3-IgG4, MAB4-IgG4, MAB5-IgG4; H1-Chothia + Kabat

<400> 50

Gly	Ser	Ile	Ser	Ser	Thr	Ser	His	Tyr	Trp	Gly
1				5					10	

<210> 51

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4; H1-Chothia + Kabat

<400> 51

Gly	Ser	Ile	Glu	Ser	Gly	Ser	Tyr	Tyr	Trp	Gly
1				5					10	

<210> 52

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB7-IgG4; H1-Chothia + Kabat

<400> 52

Gly	Ser	Ile	Glu	Ser	Gly	Val	Tyr	Tyr	Trp	Gly
1				5					10	

<210> 53

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB8-IgG4; H1-Chothia + Kabat

<400> 53

Gly	Ser	Ile	Ala	Ser	Gly	Ser	Tyr	Tyr	Trp	Gly
1				5					10	

<210> 54

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB9-IgG4, MAB10-IgG4, MAB11-IgG4, MAB12-IgG4; H1-Chothia + Kabat

<400> 54

Gly	Ser	Ile	Glu	Ser	Gly	Leu	Tyr	Tyr	Trp	Gly
1				5					10	

<210> 55

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - IgG4; Constant, S228P hinge stabilizing

<400> 55

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> 56

<211> 326

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - IgG4; Constant S228P, N297A, C terminal Lys deleted

<400> 56

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

- - - - - - - - - - - - - - - -

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu

195

200

205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly
325

<210> 57

<211> 330

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - IgG1; Constant (G1m(3) allotype)

<400> 57

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

```

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
      100                      105                      110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
      115                      120                      125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
      130                      135                      140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
      145                      150                      155                      160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
      165                      170                      175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
      180                      185                      190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
      195                      200                      205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
      210                      215                      220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
      225                      230                      235                      240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
      245                      250                      255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
      260                      265                      270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
      275                      280                      285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
      290                      295                      300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
      305                      310                      315                      320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

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325

330

<210> 58

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13-IgG4; H1-Chothia + Kabat

<400> 58

Tyr	Thr	Phe	Gly	Asn	Tyr	Tyr	Met	His
1				5				

<210> 59

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB14-IgG4, MAB18-IgG4; H1-Chothia + Kabat

<400> 59

Tyr	Thr	Phe	Pro	Ala	Tyr	Tyr	Met	His
1				5				

<210> 60

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB15-IgG4, MAB16-IgG4; H1-Chothia + Kabat

<400> 60

Tyr	Thr	Phe	Arg	Glu	Tyr	Tyr	Met	His
1				5				

<210> 61

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB17-IgG4; H1-Chothia + Kabat

<400> 61

Tyr	Thr	Phe	Pro	Ala	Tyr	Tyr	Ile	His
1				5				

<210> 62

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19-IgG4, MAB20-IgG4, MAB21-IgG4; H1-Chothia + Kabat

<400> 62

Tyr	Thr	Phe	Thr	Ser	His	Tyr	Met	Gly
1				5				

<210> 63

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4, MAB2-IgG4, MAB3-IgG4, MAB4-IgG4, MAB5-IgG4; L3 - Chothia/Kabat/IMGT

<400> 63

Gln	Gln	His	Phe	Asn	Leu	Pro	Thr
1				5			

<210> 64

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4, MAB7-IgG4, MAB8-IgG4, MAB9-IgG4, MAB10-IgG4, MAB11-IgG4, MAB12-IgG4; L3 - Chothia/Kabat/IMGT

<400> 64

Gln	Gln	His	Thr	Val	Arg	Pro	Pro	Leu	Thr
1				5				10	

<210> 65

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13-IgG4, MAB14-IgG4, MAB15-IgG4, MAB16-IgG4, MAB17-IgG4, MAB18-IgG4; L3 - Chothia/Kabat/IMGT

<400> 65

Gln	Gln	Tyr	Val	Val	Trp	Pro	Pro	Leu	Thr
1				5				10	

<210> 66

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19-IgG4, MAB20-IgG4, MAB21-IgG4; L3 - Chothia/Kabat/IMGT

<400> 66

Gln	Gln	Tyr	Ile	Val	Phe	Pro	Trp	Thr
1				5				

<210> 67

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4, MAB2-IgG4, MAB3-IgG4, MAB4-IgG4, MAB5-IgG4; L2 - Chothia/Kabat

<400> 67

Asp	Ala	Ser	Asn	Arg	Ala	Thr
1				5		

<210> 68

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4, MAB7-IgG4, MAB8-IgG4, MAB9-IgG4, MAB10-IgG4, MAB11-IgG4, MAB12-IgG4; L2 - Chothia/Kabat

<400> 68

Gly	Ala	Ser	Ser	Arg	Ala	Thr
1				5		

<210> 69

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13-IgG4, MAB14-IgG4, MAB15-IgG4, MAB16-IgG4, MAB17-IgG4, MAB18-IgG4, MAB19-IgG4, MAB20-IgG4, MAB21-IgG4; L2 - Chothia/Kabat

<400> 69

Gly	Ala	Ser	Thr	Arg	Ala	Thr
1				5		

<210> 70

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1-IgG4, MAB2-IgG4, MAB3-IgG4, MAB4-IgG4; L1 - Chothia/Kabat

<400> 70

Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Tyr	Leu	Ala
1				5					10	

<210> 71

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6-IgG4, MAB7-IgG4, MAB8-IgG4, MAB9-IgG4, MAB10-IgG4, MAB11-IgG4, MAB12-IgG4; L1 - Chothia/Kabat

<400> 71

Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Ser	Tyr	Leu	Ala
1				5					10		

<210> 72

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13-IgG4, MAB14-IgG4, MAB15-IgG4, MAB16-IgG4, MAB17-IgG4, MAB18-IgG4, MAB19-IgG4, MAB20-IgG4, MAB21-IgG4; L1 - Chothia/Kabat

<400> 72

Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Asn	Leu	Ala
1				5					10	

<210> 73

<211> 446

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - SEC1; Human IgG4 S228P Heavy Chain

<400> 73

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Thr	Gln	Pro	Gly	Lys
1				5					10					15	

Ser	Leu	Lys	Leu	Ser	Cys	Glu	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Phe
			20						25					30	

Thr	Met	His	Trp	Val	Arg	Gln	Ser	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
		35						40				45			

Ala	Phe	Ile	Arg	Ser	Gly	Ser	Gly	Ile	Val	Phe	Tyr	Ala	Asp	Ala	Val
	50						55				60				

Arg	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Leu	Leu	Phe
65					70					75					80

Leu	Gln	Met	Asn	Asp	Leu	Lys	Ser	Glu	Asp	Thr	Ala	Met	Tyr	Tyr	Cys
			85							90					95

Ala Arg Arg Pro Leu Gly His Asn Thr Phe Asp Ser Trp Gly Gln Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125
 Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
 130 135 140
 Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
 145 150 155 160
 Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
 165 170 175
 Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
 180 185 190
 Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
 195 200 205
 Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro
 210 215 220
 Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe
 225 230 235 240
 Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
 245 250 255
 Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val
 260 265 270
 Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
 275 280 285
 Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val
 290 295 300
 Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
 305 310 315 320
 Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser
 325 330 335
 Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
 340 345 350
 Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
 355 360 365
 Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
 370 375 380
 Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
 385 390 395 400

Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp
 405 410 415

Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
 420 425 430

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

<210> 74

<211> 119

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(119)

<223> SEC1; Heavy Chain Variable Region

<400> 74

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Thr Gln Pro Gly Lys
 1 5 10 15

Ser Leu Lys Leu Ser Cys Glu Ala Ser Gly Phe Thr Phe Ser Ser Phe
 20 25 30

Thr Met His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Phe Ile Arg Ser Gly Ser Gly Ile Val Phe Tyr Ala Asp Ala Val
 50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Leu Leu Phe

65 70 75 80

Leu Gln Met Asn Asp Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
 85 90 95

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

Thr Leu Val Thr Val Ser Ser
 115

<210> 75

<211> 220

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(220)

<223> SEC1 Human Kappa Chain

<400> 75

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ala	Val	Ser	Pro	Gly
1				5					10					15	

Glu	Lys	Val	Thr	Met	Thr	Cys	Lys	Ser	Ser	Gln	Ser	Leu	Tyr	Tyr	Ser
		20						25					30		

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

Ser	Pro	Lys	Leu	Leu	Ile	Tyr	Tyr	Ala	Ser	Ile	Arg	Phe	Thr	Gly	Val
	50					55					60				

Pro	Asp	Arg	Phe	Thr	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Thr	Leu	Thr
65					70					75					80

Ile	Thr	Ser	Val	Gln	Ala	Glu	Asp	Met	Gly	Gln	Tyr	Phe	Cys	Gln	Gln
				85					90					95	

Gly	Ile	Asn	Asn	Pro	Leu	Thr	Phe	Gly	Asp	Gly	Thr	Lys	Leu	Glu	Ile
			100					105					110		

Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp
		115					120					125			

Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn
	130					135					140				

Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu
145					150					155					160

Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp
			165						170					175	

Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr
			180					185					190		

Glu	Lys	His	Lys	Val	Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser
		195					200					205			

Ser	Pro	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly	Glu	Cys
	210					215					220

<210> 76

<211> 113

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(113)

<223> SEC1; Light Chain Variable Region

<400> 76

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Lys Ser Ser Gln Ser Leu Tyr Tyr Ser
 20 25 30

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

Ser Pro Lys Leu Leu Ile Tyr Tyr Ala Ser Ile Arg Phe Thr Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
 65 70 75 80

Ile Thr Ser Val Gln Ala Glu Asp Met Gly Gln Tyr Phe Cys Gln Gln
 85 90 95

Gly Ile Asn Asn Pro Leu Thr Phe Gly Asp Gly Thr Lys Leu Glu Ile
 100 105 110

Lys

<210> 77

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - SEC1; Mouse IgG2a N297A Heavy Chain

<400> 77

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Thr Gln Pro Gly Lys
 1 5 10 15

Ser Leu Lys Leu Ser Cys Glu Ala Ser Gly Phe Thr Phe Ser Ser Phe
 20 25 30

Thr Met His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Phe Ile Arg Ser Gly Ser Gly Ile Val Phe Tyr Ala Asp Ala Val
 50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Leu Leu Phe
 65 70 75 80

Leu Gln Met Asn Asp Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
 85 90 95

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

100	105	110
Thr Leu Val Thr Val Ser Ser Ala Lys Thr Thr Ala Pro Ser Val Tyr		
115	120	125
Pro Leu Ala Pro Val Cys Gly Asp Thr Thr Gly Ser Ser Val Thr Leu		
130	135	140
Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Leu Thr Trp		
145	150	155
Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val Leu		
	165	170
Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Thr Ser Ser		
	180	185
Thr Trp Pro Ser Gln Ser Ile Thr Cys Asn Val Ala His Pro Ala Ser		
	195	200
Ser Thr Lys Val Asp Lys Lys Ile Glu Pro Arg Gly Pro Thr Ile Lys		
	210	215
Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Gly Pro		
	225	230
Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser		
	245	250
Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp		
	260	265
Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr		
	275	280
Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Ala Ser Thr Leu Arg Val		
	290	295
Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu		
	305	310
Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg		
	325	330
Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val		
	340	345
Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr		
	355	360
Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr		
	370	375
Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu		
	385	390
		395
		400

Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys
 405 410 415

Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu
 420 425 430

Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly
 435 440 445

Lys

<210> 78

<211> 220

<212> PRT

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(220)

<223> SEC1; Mouse Kappa Chain

<400> 78

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Lys Ser Ser Gln Ser Leu Tyr Tyr Ser
 20 25 30

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

Ser Pro Lys Leu Leu Ile Tyr Tyr Ala Ser Ile Arg Phe Thr Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
 65 70 75 80

Ile Thr Ser Val Gln Ala Glu Asp Met Gly Gln Tyr Phe Cys Gln Gln
 85 90 95

Gly Ile Asn Asn Pro Leu Thr Phe Gly Asp Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser
 115 120 125

Glu Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn
 130 135 140

Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu
 145 150 155 160

Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp
 165 170 175

Ser Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr
 180 185 190

Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr
 195 200 205

Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
 210 215 220

<210> 79

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1; Full length IgG4 S228P

<400> 79

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 Thr 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 Ala Thr Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asp Val

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195      200      205
Ala Val Phe Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
210      215      220
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
225      230      235      240
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
245      250      255
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
260      265      270
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
275      280      285
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
290      295      300
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
305      310      315      320
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
325      330      335
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
340      345      350
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
355      360      365
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
370      375      380
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
385      390      395      400
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
405      410      415
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
420      425      430
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
435      440      445
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
450
Gly Lys
450
<210> 80
<211> 453
<212> PRT
<213> Artificial Sequence
<220>

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<223> Synthetic - MAB1; Full length IgG1

<400> 80

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 Thr 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 Ala Thr Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 81

<211> 213

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB1, MAB2, MAB3, MAB4, MAB5; Full length Kappa

<400> 81

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 Asn Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro

Ser Gly Ser Gly Thr Asp Phe Thr Ser Thr Thr Ser Thr Ser Thr Thr
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Phe Asn Leu Pro Thr
 85 90 95
 Phe Gly Gly Gly Thr Lys Val 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> 82
 <211> 450
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Synthetic - MAB2; Full length IgG4 S228P
 <400> 82
 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
 Lys 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 Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
 195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
 210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
 225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
 260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly Lys
450

<210> 83

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB2; Full length IgG1

<400> 83

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

Lys 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 Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe

165

170

175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Glu Lys

Leu Ser Pro Gly Lys
450

<210> 84

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB3; Full length IgG4 S228P

<400> 84

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

Ser His 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 Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly Lys
450

<210> 85

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB3; Full length IgG1

<400> 85

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

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1           5           10           15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Thr
    20                25                30

Ser His 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 Phe 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
    100               105               110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
    115               120               125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
    130               135               140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
    145               150               155               160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
    165               170               175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
    180               185               190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
    195               200               205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
    210               215               220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
    225               230               235               240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
    245               250               255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    260               265               270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
    275               280               285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
    290               295               300

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Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 86

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB4; Full length IgG4 S228P

<400> 86

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

Ser His 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 Phe 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 Ala Asn Tyr Tyr Gly Gly Ala Trp Ala Phe Asp Pro
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
 195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
 210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
 225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
 260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
 435 440 445

Gly Lys
 450

<210> 87

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB4; Full length IgG1

<400> 87

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

Ser His 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 Phe 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 Ala Asn Tyr Tyr Gly Gly Ala Trp Ala Phe Asp Pro
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val

145 - 150 - - 155 160
 Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175
 Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190
 Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205
 Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 210 215 220
 Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240
 Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255
 Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270
 Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285
 Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 290 295 300
 Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 305 310 315 320
 Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 325 330 335
 Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 340 345 350
 Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 355 360 365
 Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 370 375 380
 Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 385 390 395 400
 Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 405 410 415
 Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 420 425 430
 Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
450

<210> 88

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB5; Full length IgG4 S228P

<400> 88

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

Ser His 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 Phe Tyr Asn Pro Ser
50 55 60

Leu Lys Gly 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

210	215	220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly 225 230 235 240		
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile 245 250 255		
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu 260 265 270		
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His 275 280 285		
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg 290 295 300		
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys 305 310 315 320		
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu 325 330 335		
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr 340 345 350		
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu 355 360 365		
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp 370 375 380		
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val 385 390 395 400		
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp 405 410 415		
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His 420 425 430		
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu 435 440 445		
Gly Lys 450		

<210> 89

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB5; Full length IgG1

<400> 89

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

Ser His 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 Phe Tyr Asn Pro Ser
 50 55 60

Leu Lys Gly 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 Ala Asn Tyr Tyr Gly Ser Ala Trp Ala Phe Asp Pro
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 90

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6; Full length IgG4 S228P

<400> 90

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 Glu Ser Gly
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 Gly Thr Tyr Tyr Asn Pro Ser
50 55 60

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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 Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu

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355              360              365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370              375              380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385              390              395              400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405              410              415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420              425              430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435              440              445

Gly Lys
450

<210> 91
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic - MAB6; Full length IgG1

<400> 91
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 Glu Ser Gly
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 Gly 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 Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100             105             110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115             120             125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130             135             140

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Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
 450

<210> 92

<211> 216

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12; Full length Kappa

<400> 92

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 His Thr Val Arg Pro
 85 90 95

Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val
 100 105 110

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
 115 120 125

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
 130 135 140

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
 145 150 155 160

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
 165 170 175

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
 180 185 190

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
 195 200 205

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr

Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 93

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB7; Full length IgG4 S228P

<400> 93

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 Glu Ser Gly
20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val

145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly Lys
450

<210> 94

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB7; Full length IgG1

<400> 94

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

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-          ~          ~          ~          ~

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Glu Ser Gly
      20                      25                      30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
      50                      55                      60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
      65                      70                      75                      80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
      85                      90                      95

Cys Ala Arg Asp Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
      100                     105                     110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
      115                     120                     125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
      130                     135                     140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
      145                     150                     155                     160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
      165                     170                     175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
      180                     185                     190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
      195                     200                     205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
      210                     215                     220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
      225                     230                     235                     240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
      245                     250                     255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
      260                     265                     270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
      275                     280                     285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
      290                     295                     300

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Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 95

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB8; Full length IgG4 S228P

<400> 95

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 Ala Ser Gly
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 Gln 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 Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Ser Val Val Thr Gln Phe Thr Pro Ser Ser Thr Ala Val Glu Thr

Tnr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
 435 440 445

Gly Lys
 450

<210> 96

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB8; Full length IgG1

<400> 96

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 Ala Ser Gly
 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 Gln 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 Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val

145		150		155		160
Thr Val Ser Trp	Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe					
	165			170		175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val						
	180		185		190	
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val						
	195	200		205		
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys						
	210	215		220		
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu						
225	230		235			240
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr						
	245		250		255	
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val						
	260	265		270		
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val						
	275	280		285		
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser						
	290	295		300		
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu						
305	310		315			320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala						
	325		330			335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro						
	340	345		350		
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln						
	355	360		365		
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala						
	370	375		380		
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr						
385	390		395			400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu						
	405		410		415	
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser						
	420		425		430	
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser						
	435	440		445		

Leu Ser Pro Gly Lys
450

<210> 97

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB9; Full length IgG4 S228P

<400> 97

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 Glu Ser Gly
20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
 225 230 235 240
 Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 245 250 255
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
 260 265 270
 Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
 290 295 300
 Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
 325 330 335
 Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350
 Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 355 360 365
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400
 Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
 405 410 415
 Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430
 Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
 435 440 445
 Gly Lys
 450

<210> 98

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB9; Full length IgG1

<400> 98

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 Glu Ser Gly
 20 25 30
 Leu Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Asp Gly Val Leu Thr Leu Asn Lys Arg Ser Phe Asp Ile
 100 105 110
 Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125
 Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140
 Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160
 Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175
 Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190
 Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205
 Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 210 215 220
 Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240
 Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255
 Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270
 Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285
 Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

Asn	Val	Asn	Asn	Leu	Lys	Val	Leu	Val	Leu	Val	Leu	His	Gln	Asp	Trp	Leu
290						295					300					
Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	
305					310					315					320	
Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	
				325					330					335		
Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	
			340					345					350			
Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	
		355					360					365				
Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	
	370					375					380					
Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	
385					390					395					400	
Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	
				405					410						415	
Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	
			420					425					430			
Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	
		435					440					445				
Leu	Ser	Pro	Gly	Lys												
	450															
<210> 99																
<211> 450																
<212> PRT																
<213> Artificial Sequence																
<220>																
<223> Synthetic - MAB10; Full length IgG4 S228P																
<400> 99																
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	Glu	Ser	Gly	
			20					25					30			
Leu	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	Ala	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 Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
 435 440 445

Gly Lys
 450

<210> 100

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB10; Full length IgG1

<400> 100

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 Glu Ser Gly
 20 25 30

Leu 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 Ala 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 Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

- - - - -

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160
 Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175
 Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190
 Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205
 Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 210 215 220
 Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240
 Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255
 Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270
 Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285
 Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 290 295 300
 Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 305 310 315 320
 Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 325 330 335
 Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 340 345 350
 Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 355 360 365
 Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 370 375 380
 Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 385 390 395 400
 Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 405 410 415
 Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 420 425 430
 Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
450

<210> 101

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB11; Full length IgG4 S228P

<400> 101

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 Glu Ser Gly
20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val

145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys


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- 210 -                215 - - - 220 -
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225                230                235                240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                250                255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
                260                265                270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
                275                280                285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
                290                295                300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                310                315                320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
                325                330                335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
                340                345                350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
                355                360                365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
                370                375                380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                390                395                400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
                405                410                415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
                420                425                430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
                435                440                445
Gly Lys
450

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<210> 102

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB11; Full length IgG1

<400> 102

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 Glu Ser Gly
 20 25 30

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

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Asp Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 103

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB12; Full length IgG4 S228P

<400> 103

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 Ala Ser Gly Gly Ser Ile Glu Ser Gly
20 25 30

Leu 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 Asn Thr Ser Lys Asn Gln Phe

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	Gly	Val	Leu	Ala	Leu	Asn	Lys	Arg	Ser	Phe	Asp	Ile
			100					105					110		
Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly
		115					120					125			
Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser
	130					135					140				
Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val
145					150					155					160
Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
				165					170					175	
Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val
			180					185					190		
Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn	Val
		195					200					205			
Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys
	210					215					220				
Tyr	Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly
225					230					235					240
Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile
				245					250					255	
Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Gln	Glu
			260					265					270		
Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His
		275					280					285			
Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg
	290					295					300				
Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys
305					310					315					320
Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu
				325					330					335	
Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr
			340					345					350		
Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu

355 360 365
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400
 Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
 405 410 415
 Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430
 Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
 435 440 445
 Gly Lys
 450
 <210> 104
 <211> 453
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Synthetic - MAB12; Full length IgG1
 <400> 104
 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 Ala Ser Gly Gly Ser Ile Glu Ser Gly
 20 25 30
 Leu Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Asp Gly Val Leu Ala Leu Asn Lys Arg Ser Phe Asp Ile
 100 105 110
 Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125
 Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val

145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
 450

<210> 105

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13; Full length IgG4 S228P

<400> 105

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

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val

145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 210 215 220
 Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 225 230 235 240
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 260 265 270
 Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285
 Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 290 295 300
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320
 Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 325 330 335
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350
 Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
 405 410 415
 Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

<210> 106

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB13; Full length IgG1

<400> 106

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 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 Ile Ile Asn Pro Ser Leu Gly Leu 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
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys	85	90	95
Ala Arg Gly Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly	100	105	110
Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser	115	120	125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala	130	135	140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val	145	150	155
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala	165	170	175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val	180	185	190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His	195	200	205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys	210	215	220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly	225	230	235
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met	245	250	255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His	260	265	270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val	275	280	285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr	290	295	300

290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445
 Pro Gly Lys
 450
 <210> 107
 <211> 215
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Synthetic - MAB13, MAB14, MAB15, MAB16, MAB17, MAB18; Full length Kappa
 <400> 107
 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 Val Val Trp Pro Pro
85 90 95

Leu 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> 108

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB14; Full length IgG4 S228P

<400> 108

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

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 210 215 220

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 260 265 270

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp

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385      -          390      -      -          395          400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
          405          410          415

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
          420          425          430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
          435          440          445

<210> 109
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic - MAB14; Full length IgG1

<400> 109
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 Pro Ala 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 Leu Gly Leu 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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
          100          105          110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
          115          120          125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
          130          135          140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145          150          155          160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
          165          170          175

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Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445
 Pro Gly Lys
 450

<210> 110

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB15; Full length IgG4 S228P

<400> 110

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 Arg Glu 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 Ile Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 210 215 220

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
260 265 270

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
405 410 415

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<210> 111

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB15; Full length IgG1

<400> 111

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 Arg Glu 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 Ile Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445

Pro Gly Lys
 450

<210> 112

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB16; Full length IgG4 S228P

<400> 112

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 Arg Glu 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 Ile Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Leu Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

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110          120          130
Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
130          135          140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145          150          155          160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165          170          175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180          185          190

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
195          200          205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
210          215          220

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
225          230          235          240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245          250          255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
260          265          270

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275          280          285

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
290          295          300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305          310          315          320

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
325          330          335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340          345          350

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355          360          365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370          375          380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385          390          395          400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
405          410          415

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Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

<210> 113

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB16; Full length IgG1

<400> 113

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 Arg Glu 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 Ile Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Leu Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His

195

200

205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445

Pro Gly Lys
 450

<210> 114

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB17; Full length IgG4 S228P

<400> 114

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 Pro Ala Tyr
 20 25 30

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

Gly Ile Ile Asn Pro Ser Leu Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Leu Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 210 215 220

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 260 265 270

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
 405 410 415

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

<210> 115

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB17; Full length IgG1

<400> 115

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 Pro Ala Tyr
 20 25 30

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

Gly Ile Ile Asn Pro Ser Leu Gly Leu Thr Ser Tyr Ala Arg Lys Phe
 50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
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65	70	75	80
Met Glu Leu Ser	Ser Leu Arg Ser	Glu Asp Thr Ala Val	Tyr Tyr Cys
	85	90	95
Ala Arg Gly Gly	Arg Thr Thr Trp	Ile Gly Ala Leu Asp	Ile Trp Gly
	100	105	110
Gln Gly Thr Met	Val Thr Val Ser	Ser Ala Ser Thr	Lys Gly Pro Ser
	115	120	125
Val Phe Pro Leu	Ala Pro Ser Ser	Lys Ser Thr Ser	Gly Gly Thr Ala
	130	135	140
Ala Leu Gly Cys	Leu Val Lys Asp	Tyr Phe Pro Glu	Pro Val Thr Val
	145	150	155
Ser Trp Asn Ser	Gly Ala Leu Thr	Ser Gly Val His	Thr Phe Pro Ala
	165	170	175
Val Leu Gln Ser	Ser Gly Leu Tyr	Ser Leu Ser Ser	Val Val Thr Val
	180	185	190
Pro Ser Ser Ser	Leu Gly Thr Gln	Thr Tyr Ile Cys	Asn Val Asn His
	195	200	205
Lys Pro Ser Asn	Thr Lys Val Asp	Lys Arg Val Glu	Pro Lys Ser Cys
	210	215	220
Asp Lys Thr His	Thr Cys Pro Pro	Cys Pro Ala Pro	Glu Leu Leu Gly
	225	230	235
Gly Pro Ser Val	Phe Leu Phe Pro	Pro Lys Pro Lys	Asp Thr Leu Met
	245	250	255
Ile Ser Arg Thr	Pro Glu Val Thr	Cys Val Val Val	Asp Val Ser His
	260	265	270
Glu Asp Pro Glu	Val Lys Phe Asn	Trp Tyr Val Asp	Gly Val Glu Val
	275	280	285
His Asn Ala Lys	Thr Lys Pro Arg	Glu Glu Gln Tyr	Asn Ser Thr Tyr
	290	295	300
Arg Val Val Ser	Val Leu Thr Val	Leu His Gln Asp	Trp Leu Asn Gly
	305	310	315
Lys Glu Tyr Lys	Cys Lys Val Ser	Asn Lys Ala Leu	Pro Ala Pro Ile
	325	330	335
Glu Lys Thr Ile	Ser Lys Ala Lys	Gly Gln Pro Arg	Glu Pro Gln Val
	340	345	350
Tyr Thr Leu Pro	Pro Ser Arg Glu	Glu Met Thr Lys	Asn Gln Val Ser
	355	360	365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 116

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB18; Full length IgG4 S228P

<400> 116

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Pro Ala 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 Leu Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 210 215 220

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 260 265 270

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
 405 410 415

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

<210> 117

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB18; Full length IgG1

<400> 117

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Pro Ala 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 Leu Gly Leu Thr Ser Tyr Ala Arg 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 Gly Arg Thr Thr Trp Ile Gly Ala Phe Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly

225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 118

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19; Full length IgG4 S228P

<400> 118

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 His
 20 25 30

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

Gly Val Ile Asn Pro Ser Met Gly Ala 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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
 195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
 210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
 225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
 260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
 435 440 445

Gly Lys
 450

<210> 119

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19; Full length IgG1

<400> 119

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 His
 20 25 30

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

Gly Val Ile Asn Pro Ser Met Gly Ala 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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
 450

<210> 120

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB19, MAB20, MAB21; Full length Kappa

<400> 120

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 His 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 Ile Val Phe Pro Trp
 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> 121

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB20; Full length IgG4 S228P

<400> 121

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 His
20 25 30

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

Gly Ile Ile Asn Pro Ser Met Gly Ala 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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140

Thr Ala Ala Leu Glv Cvs Leu Val Lvs Asp Tyr Phe Pro Glu Pro Val

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145          150          155          160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
          165          170          175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
          180          185          190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
          195          200          205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
          210          215          220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
          225          230          235          240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
          245          250          255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
          260          265          270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
          275          280          285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
          290          295          300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
          305          310          315          320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
          325          330          335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
          340          345          350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
          355          360          365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
          370          375          380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
          385          390          395          400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
          405          410          415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
          420          425          430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
          435          440          445

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Gly Lys
450

<210> 122

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB20; Full length IgG1

<400> 122

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 His
20 25 30

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

Gly Ile Ile Asn Pro Ser Met Gly Ala 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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

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Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
 450

<210> 123

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB21; Full length IgG4 S228P

<400> 123

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 His	20	25	30
Tyr Met Gly Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	35	40	45
Gly Ile Ile Asn Pro Ser Met Gly Ala Thr Ser Tyr Thr Gln Lys Phe	50	55	60
Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr	65	70	75
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys	85	90	95
Ala Arg Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr	100	105	110
Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly	115	120	125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser	130	135	140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val	145	150	155
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe	165	170	175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val	180	185	190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val	195	200	205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys	210	215	220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly	225	230	235
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile	245	250	255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu	260	265	270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His	275	280	285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg	290	295	300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly Lys
450

<210> 124

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic - MAB21; Full length IgG1

<400> 124

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 His
20 25 30

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

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

Arg 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 Leu His Val Ser Gly Ser Tyr Tyr Pro Ala Tyr Leu Asp Tyr
 100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
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Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
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Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
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Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
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Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
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Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
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Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
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Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
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Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
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85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
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Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
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Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
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Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
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Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
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Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
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His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
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Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
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Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
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Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
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Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
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Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
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Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
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Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
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Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
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Ala Ser Val Phe Ser Asp Arg Val Val Pro Gly Pro Ser Leu Gly Leu
 85 90 95

Thr Phe Gln Ser Leu Thr Met Asn Asp Thr Gly Glu Tyr Phe Cys Thr
 100 105 110

Tyr His Thr Tyr Pro Gly Gly Ile Tyr Lys Gly Arg Ile Phe Leu Lys
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Val Gln Glu Ser Ser Asp Asp Arg Asn Gly Leu Ala Gln Phe Gln Thr
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 145 150 155 160

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Met His Ser Ile Glu Ser Gly Leu Gly Arg Thr Glu Ala Glu Pro Gln
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Glu Trp Asn Leu Arg Ser Leu Ser Ser Pro Gly Ser Pro Val Gln Thr
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Ala Asp Pro Gln Glu Tyr Phe Asn Val Leu Ser Tyr Arg Ser Leu Glu
 225 230 235 240

Ser Phe Ile Ala Val Ser Lys Thr Gly
 245

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PATENTKRAV

1. Isoleret antistof, eller antigenbindingsfragment deraf, der specifikt binder humant TIGIT (hTIGIT; SEQ ID NO: 1), omfattende:

(a) et CDR-H3 fra SEQ ID NO: 32, et CDR-H2 fra SEQ ID NO: 40, et CDR-H1 fra SEQ ID NO: 54, et CDR-L3 fra SEQ ID NO: 64, et CDR-L2 fra SEQ ID NO: 68 og et CDR-L1 fra SEQ ID NO: 71;

(b) et CDR-H3 fra SEQ ID NO: 31, et CDR-H2 fra SEQ ID NO: 40, et CDR-H1 fra SEQ ID NO: 54, et CDR-L3 fra SEQ ID NO: 64, et CDR-L2 fra SEQ ID NO: 68 og et CDR-L1 fra SEQ ID NO: 71;

(c) et CDR-H3 fra SEQ ID NO: 31, et CDR-H2 fra SEQ ID NO: 39, et CDR-H1 fra SEQ ID NO: 51, et CDR-L3 fra SEQ ID NO: 64, et CDR-L2 fra SEQ ID NO: 68 og et CDR-L1 fra SEQ ID NO: 71;

(d) et CDR-H3 fra SEQ ID NO: 31, et CDR-H2 fra SEQ ID NO: 40, et CDR-H1 fra SEQ ID NO: 52, et CDR-L3 fra SEQ ID NO: 64, et CDR-L2 fra SEQ ID NO: 68 og et CDR-L1 fra SEQ ID NO: 71; eller

(e) et CDR-H3 fra SEQ ID NO: 31, et CDR-H2 fra SEQ ID NO: 41, et CDR-H1 fra SEQ ID NO: 53, et CDR-L3 fra SEQ ID NO: 64, et CDR-L2 fra SEQ ID NO: 68 og et CDR-L1 fra SEQ ID NO: 71.

2. Antistof eller antigenbindingsfragment deraf ifølge krav 1, hvor:

(i) antistoffet eller antigenbindingsfragmentet deraf ifølge krav 1(a) omfatter en VH-sekvens af SEQ ID NO: 13 og en VL-sekvens fra SEQ ID NO: 26;

(ii) antistoffet eller antigenbindingsfragmentet deraf ifølge krav 1(b) omfatter en VH-sekvens af SEQ ID NO: 12 og en VL-sekvens fra SEQ ID NO: 26;

(iii) antistoffet eller antigenbindingsfragmentet deraf ifølge krav 1(a) omfatter en VH-sekvens af SEQ ID NO: 14 og en VL-sekvens fra SEQ ID NO: 26;

(iv) antistoffet eller antigenbindingsfragmentet deraf ifølge krav 1(a) omfatter en VH-sekvens af SEQ ID NO: 15 og en VL-sekvens fra SEQ ID NO: 26;

(v) antistoffet eller antigenbindingsfragmentet deraf ifølge krav 1(c) omfatter en VH-sekvens af SEQ ID NO: 9 og en VL-sekvens fra SEQ ID NO: 26;

(vi) antistoffet eller antigenbindingsfragmentet deraf ifølge krav 1(d) omfatter en VH-sekvens af SEQ ID NO: 10 og en VL-sekvens fra SEQ ID NO: 26; eller

(vii) antistoffet eller antigenbindingsfragmentet deraf ifølge krav 1(e) omfatter en VH-sekvens af SEQ ID NO: 11 og en VL-sekvens fra SEQ ID NO: 26.

3. Antistof eller antigenbindingsfragment deraf ifølge krav 2, hvor:

(aa) antistoffet eller antigenbindingsfragmentet deraf fra (i) omfatter (i) en tungkæde fra SEQ ID NO: 99 og en letkæde fra SEQ ID NO: 92; eller (ii) en tungkæde fra SEQ ID NO: 100 og en letkæde fra SEQ ID NO: 92;

(bb) antistoffet eller antigenbindingsfragmentet deraf fra (ii) omfatter (i) en tungkæde fra SEQ ID NO: 97 og en letkæde fra SEQ ID NO: 92; eller (ii) en tungkæde fra SEQ ID NO: 98 og en letkæde fra SEQ ID NO: 92;

(cc) antistoffet eller antigenbindingsfragmentet deraf fra (iii) omfatter (i) en tungkæde fra SEQ ID NO: 101 og en letkæde fra SEQ ID NO: 92; eller (ii) en tungkæde fra SEQ ID NO: 102 og en letkæde fra SEQ ID NO: 92;

(dd) antistoffet eller antigenbindingsfragmentet deraf fra (iv) omfatter (i) en tungkæde fra SEQ ID NO: 103 og en letkæde fra SEQ ID NO: 92; eller (ii) en tungkæde fra SEQ ID NO: 104 og en letkæde fra SEQ ID NO: 92;

(ee) antistoffet eller antigenbindingsfragmentet deraf fra (v) omfatter (i) en tungkæde fra SEQ ID NO: 90 og en letkæde fra SEQ ID NO: 92; eller (ii) en tungkæde fra SEQ ID NO: 91 og en letkæde fra SEQ ID NO: 92;

(ff) antistoffet eller antigenbindingsfragmentet deraf fra (vi) omfatter (i) en tungkæde fra SEQ ID NO: 93 og en letkæde fra SEQ ID NO: 92; eller (ii) en tungkæde fra SEQ ID NO: 94 og en letkæde fra SEQ ID NO: 92; eller

(gg) antistoffet eller antigenbindingsfragmentet deraf fra (vii) omfatter (i) en tungkæde fra SEQ ID NO: 95 og en letkæde fra SEQ ID NO: 92; eller (ii) en tungkæde fra SEQ ID NO: 96 og en letkæde fra SEQ ID NO: 92.

4. Antistof eller antigenbindingsfragment deraf ifølge krav 1, hvor antistoffet er et monoklonalt antistof, og eventuelt hvor antistoffet er valgt blandt et humant antistof, et humaniseret antistof eller et kimærisk antistof, og/eller hvor antistoffet eller antigenbindingsfragmentet deraf omfatter et konstant immunoglobulinområde, og/eller hvor antistoffet eller antigenbindingsfragmentet deraf omfatter et konstant tungkædeområde fra en klasse valgt blandt IgA, IgD, IgE, IgG eller IgM, eventuelt hvor antistoffet eller antigenbindingsfragmentet deraf omfatter et konstant tungkædeområde fra klasse IgG og en underklasse valgt blandt IgG4, IgG1, IgG2 eller IgG3.

5. Farmaceutisk sammensætning, der omfatter et antistof eller antigenbindingsfragment

deraf ifølge et hvilket som helst af kravene 1-4 og en farmaceutisk acceptabel excipiens.

6. Antistof eller antigenbindingsfragment deraf ifølge et hvilket som helst af kravene 1-4 eller farmaceutisk sammensætning ifølge krav 5 til anvendelse som et lægemiddel.

5

7. Antistof eller antigenbindingsfragment deraf ifølge et hvilket som helst af kravene 1-4 eller farmaceutisk sammensætning ifølge krav 5, til anvendelse i behandling af en cancer eller virusinfektion, eventuelt hvor canceren enten er en solid tumor eller et hæmatologisk tumor.

10 **8.** Antistof eller antigenbindingsfragment deraf ifølge et hvilket som helst af kravene 1-4 eller farmaceutisk sammensætning ifølge krav 5 til anvendelse som et lægemiddel i behandling af en sygdom eller tilstand, der ikke har reageret på tidligere terapi, eventuelt hvor den tidligere terapi er en terapi omfattende et middel, der hæmmer interaktionen mellem PD-1 og PD-L1.

15 **9.** Isoleret polynukleotid, der koder for et antistof eller antigenbindingsfragment deraf ifølge et hvilket som helst af kravene 1-4.

10. Vektor, der omfatter polynukleotidet ifølge krav 9.

20 **11.** Værtscelle, der omfatter polynukleotidet ifølge krav 9 eller vektoren ifølge krav 10.

12. Fremgangsmåde til fremstilling af et antistof eller antigenbindingsfragment deraf ifølge et hvilket som helst af kravene 1-4, hvilken fremgangsmåde omfatter ekspresion af antistoffet eller antigenbindingsfragmentet deraf i værtscellen ifølge krav 11 og isolering af det udtrykte
25 antistof eller antigenbindingsfragmentet deraf.

13. Antistof eller antigenbindingsfragment deraf ifølge et hvilket som helst af kravene 1-4, farmaceutisk sammensætning ifølge krav 5 eller antistof eller antigenbindingsfragment deraf eller farmaceutisk sammensætning til anvendelse ifølge et hvilket som helst af kravene 6 til 8,
30 der endvidere omfatter ét eller flere supplerende terapeutiske midler, eventuelt hvor det supplerende terapeutiske middel er formuleret i den samme farmaceutiske sammensætning som antistoffet, eller antigenbindingsfragmentet deraf, eller hvor det supplerende terapeutiske middel er formuleret i en anden farmaceutisk sammensætning end antistoffet eller antigenbindingsfragmentet deraf.

14. Antistof eller antigenbindingsfragment deraf eller farmaceutisk sammensætning ifølge krav 13 eller antistof eller antigenbindingsfragment deraf eller farmaceutisk sammensætning til anvendelse ifølge krav 13, hvor det supplerende terapeutiske middel er et antistof, der hæmmer interaktionen mellem PD-1 og PD-L1.
15. Antistof eller antigenbindingsfragment deraf eller farmaceutisk sammensætning ifølge krav 13 eller antistoffet eller antigenbindingsfragmentet deraf eller farmaceutisk sammensætning til anvendelse ifølge krav 13, hvor det supplerende terapeutiske middel er valgt blandt:
- 10 (a) et middel, der hæmmer interaktionen mellem PD-1 og PD-L1, hvor midlet er et antistof, der hæmmer interaktionen mellem PD-1 og PD-L1 og er valgt blandt pembrolizumab, nivolumab, atezolizumab, avelumab og durvalumab; eller
- 15 (b) et antistof, der blokerer signalering af en hæmmende receptor af en immuncelle eller en ligand deraf eller en nukleinsyre, der koder for et sådant antistof, og den hæmmende receptor eller ligand deraf er valgt blandt CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5, VISTA, LAIR1, CD160, 2B4, TGF-R, KIR og kombinationer deraf.
16. Kit, der omfatter den farmaceutiske sammensætning ifølge krav 5, og anvisninger til anvendelse af en sådan farmaceutisk sammensætning.

DRAWINGS

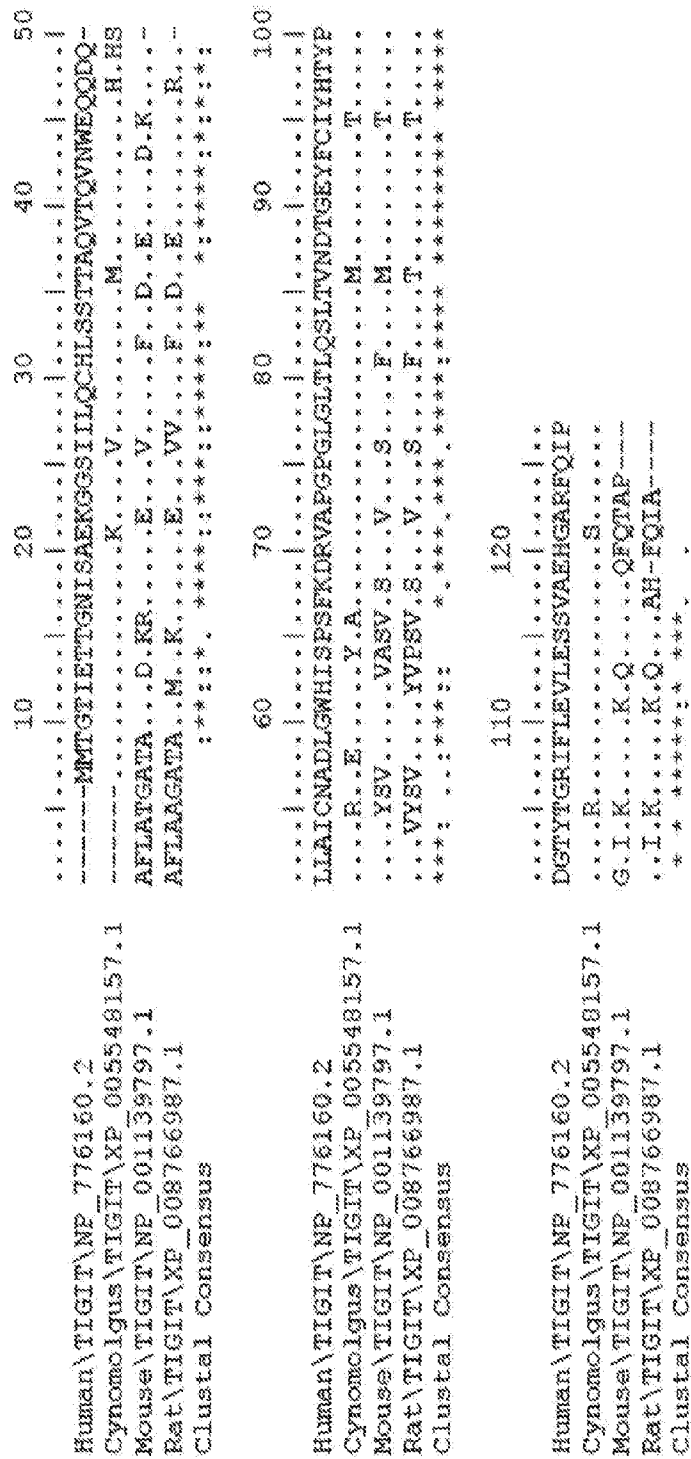


FIG. 1A

Human\PVRL4\ECD\Q96NY8	---GELETSDVVTVLGQDANKLPCFYREDSEQVQVAVARVDACEGAQELALLHSKYGL
Human\TIGIT\ECD\NP_776160.2	MMTGITETTCNISAEKGGSIILQCHLSS--TTAQVTQVNWEEQQ-----DQLLAICNAILGW
Clustal Consensus	* :*: : : * . * * . : * * * * * : * * * : : * *
Human\PVRL4\ECD\Q96NY8	HVSPAYEGRVEQPPPPRNPLDGSVLLRNVAQADEGEYECRVSTFPAGSFQARILRLRVLP
Human\TIGIT\ECD\NP_776160.2	HISPSFKDRVAPGPGILG-----LTLOSLTVNDTGEYFCIYHTYPDITTYTCGRIFLEVLSS
Clustal Consensus	*:***: : * * * * * : * : . * * * * * * : * * : : * : *
Human\PVRL4\ECD\Q96NY8	PLPSLNPCFALEGGQCLTLAASCTAEGSPAPSVTWDTVEVKGTTSSRSFKHSRSAVTSEF
Human\TIGIT\ECD\NP_776160.2	SVAEHGAREQIP-----
Clustal Consensus	: . ;
Human\PVRL4\ECD\Q96NY8	HIVPSRSMNGOPLTCVSHPGLLQDQRITHILHVSFLAESVRGLEQDQNIWHICEGAML
Human\TIGIT\ECD\NP_776160.2	-----
Clustal Consensus	-----
Human\PVRL4\ECD\Q96NY8	KCLSEGQPPFSYNWTRLDGELPSGVRVDGDTLGFPLTTEHSGIYVCHVSNFSSRPSQV
Human\TIGIT\ECD\NP_776160.2	-----
Clustal Consensus	-----
Human\PVRL4\ECD\Q96NY8	TVQVLDPEQEDSGKQVDLVSAS
Human\TIGIT\ECD\NP_776160.2	-----

FIG. 1B

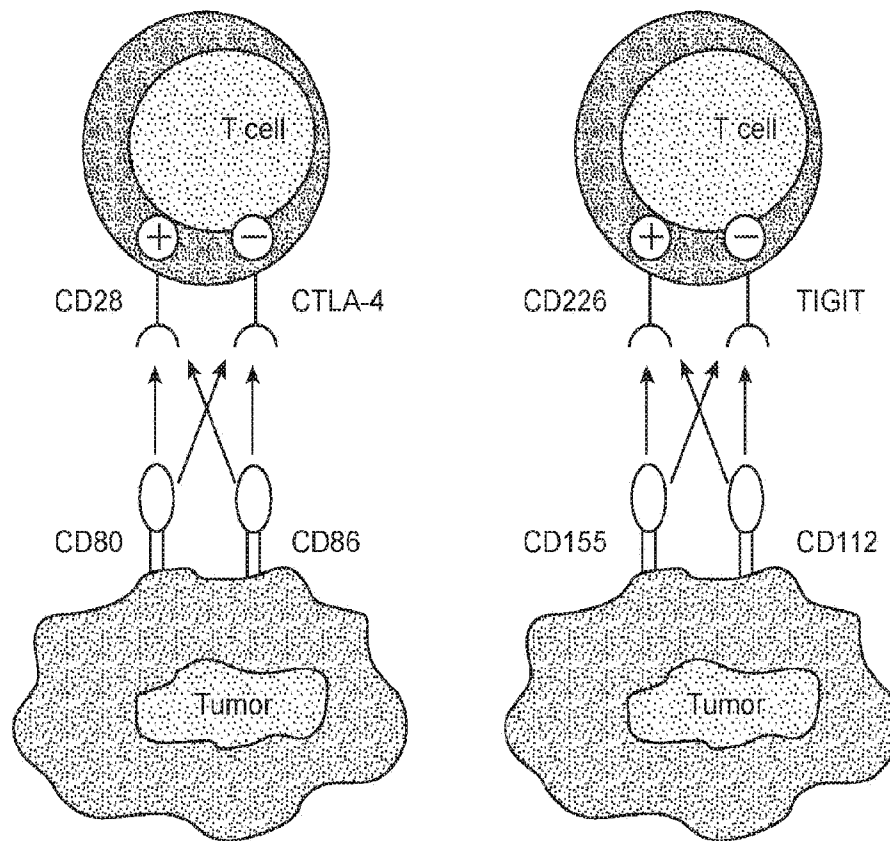


FIG. 2

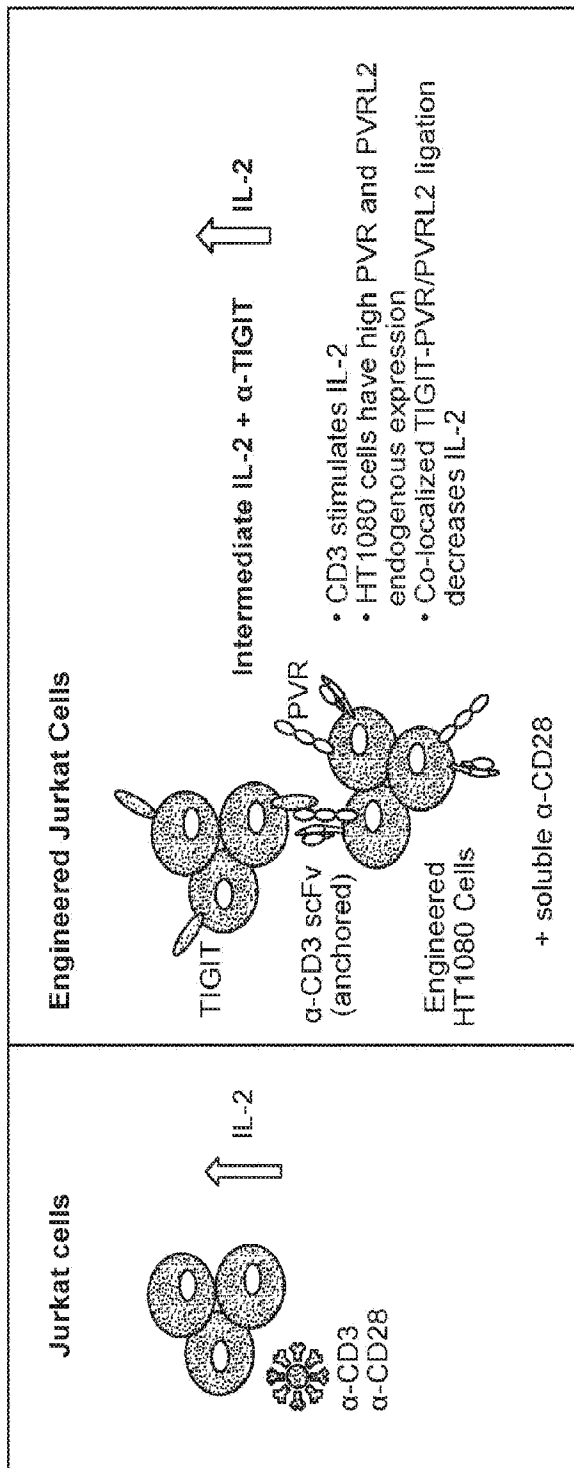


FIG. 3

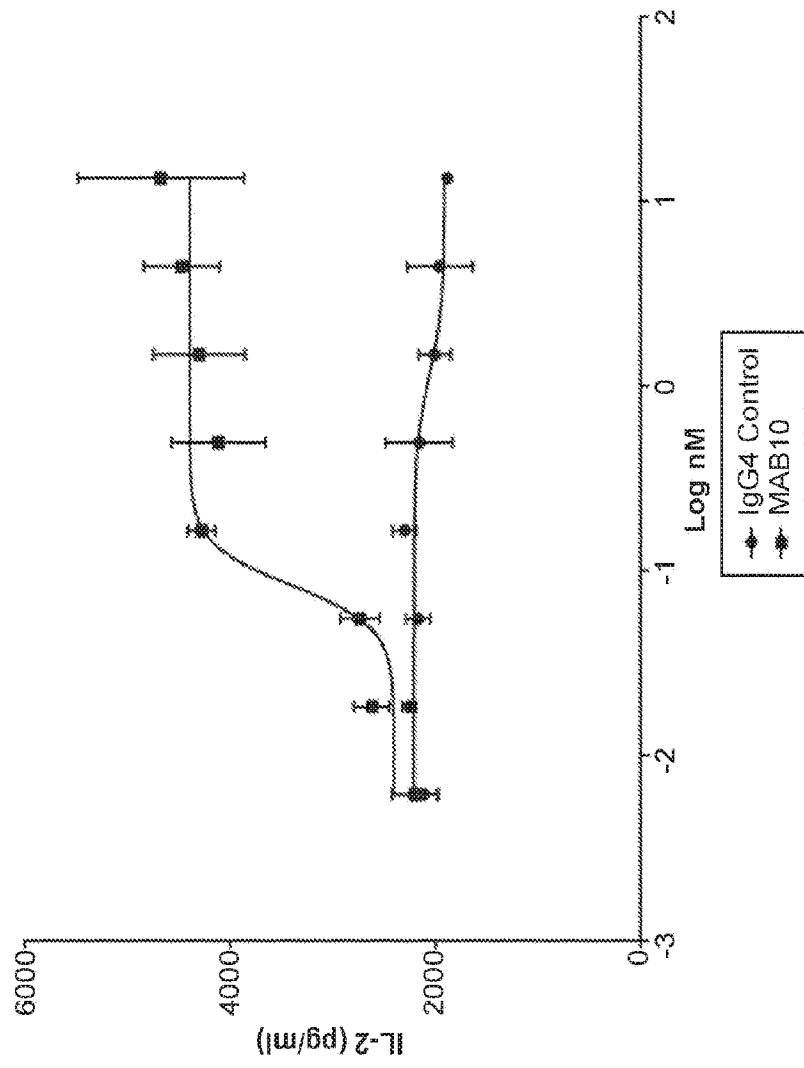


FIG. 4A

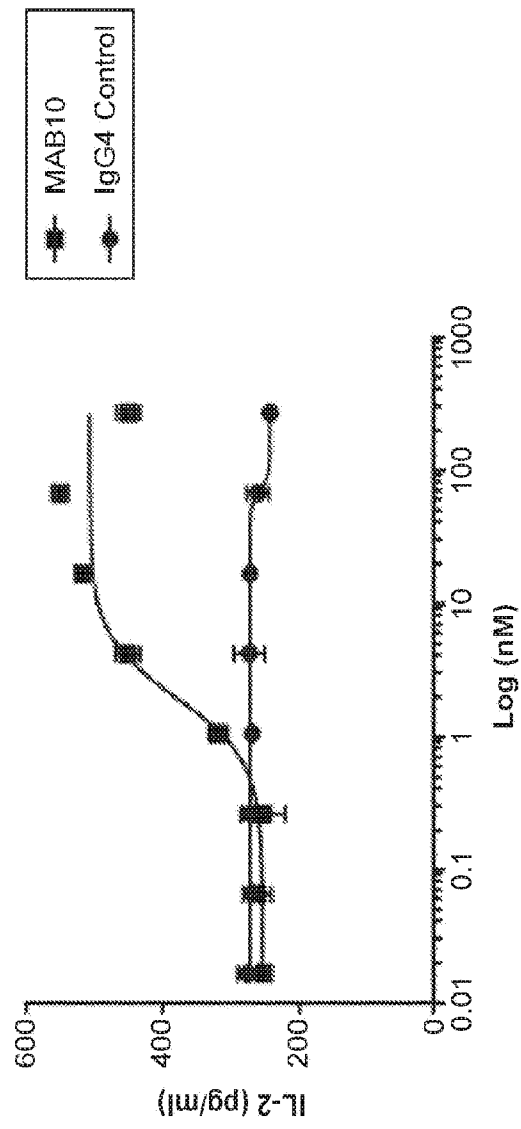


FIG. 4B

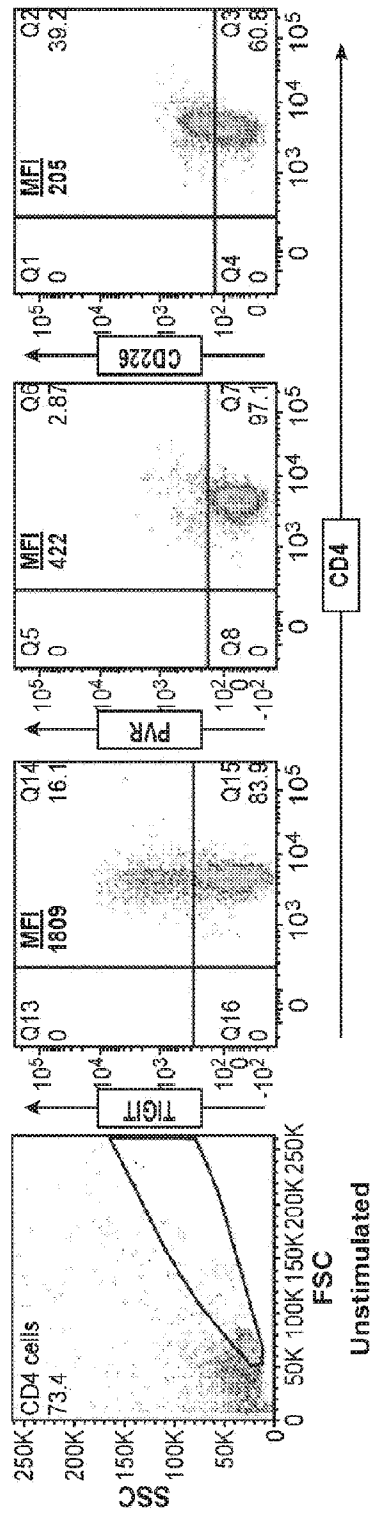


FIG. 5A

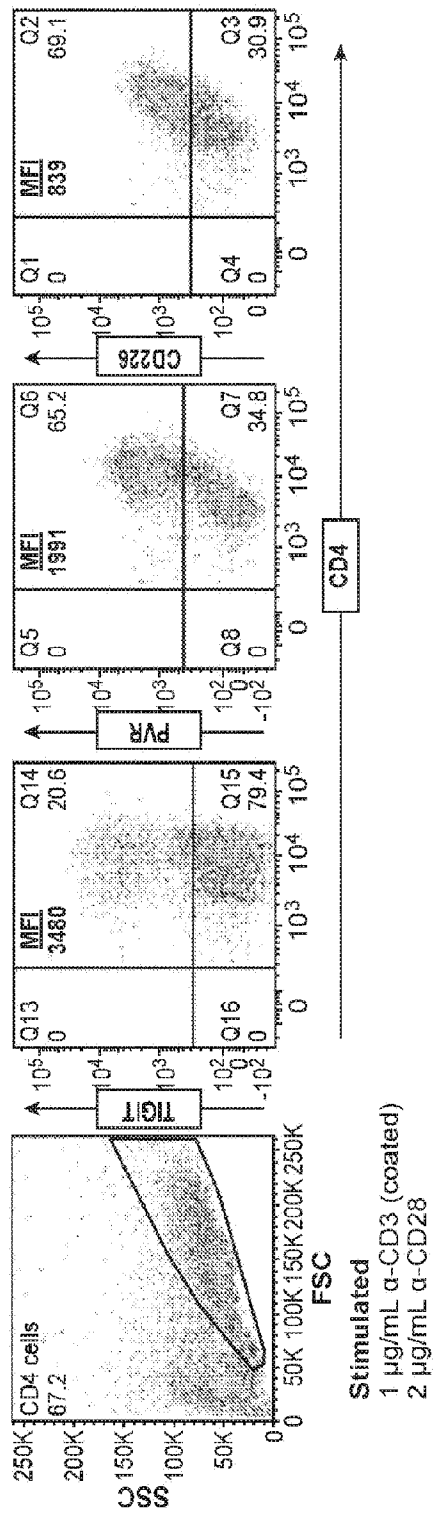


FIG. 5B

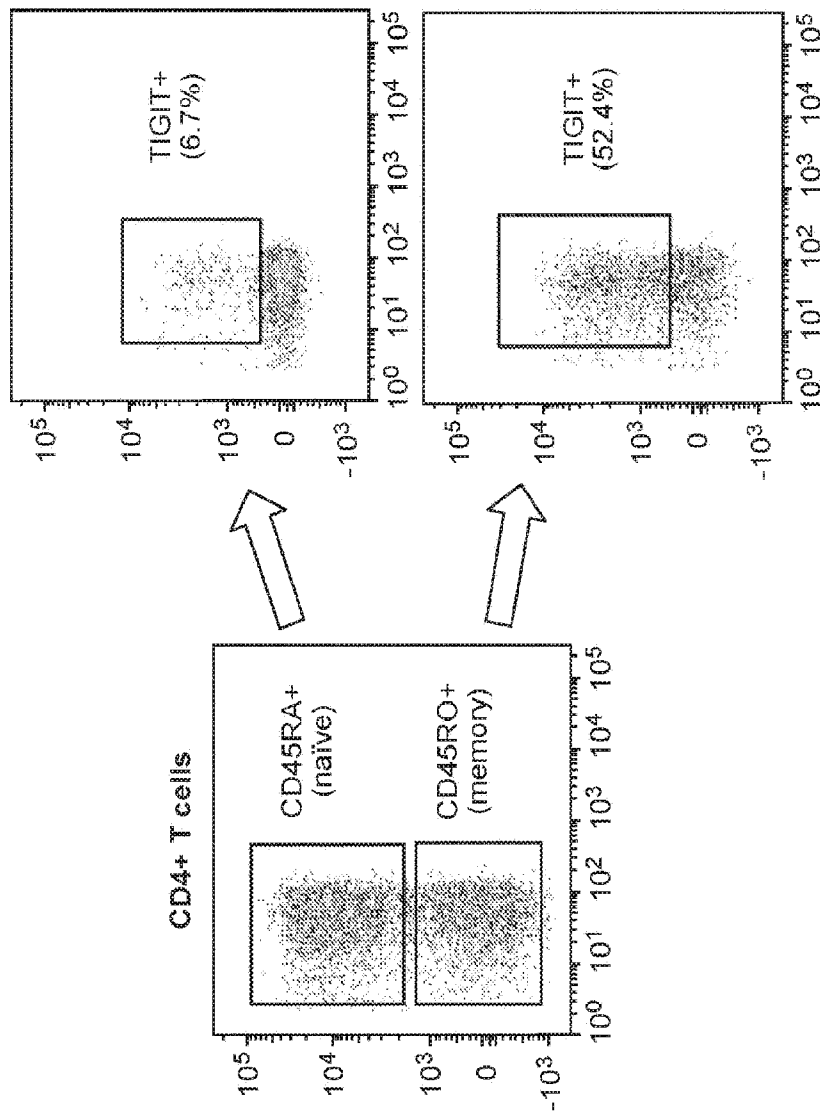


FIG. 5C

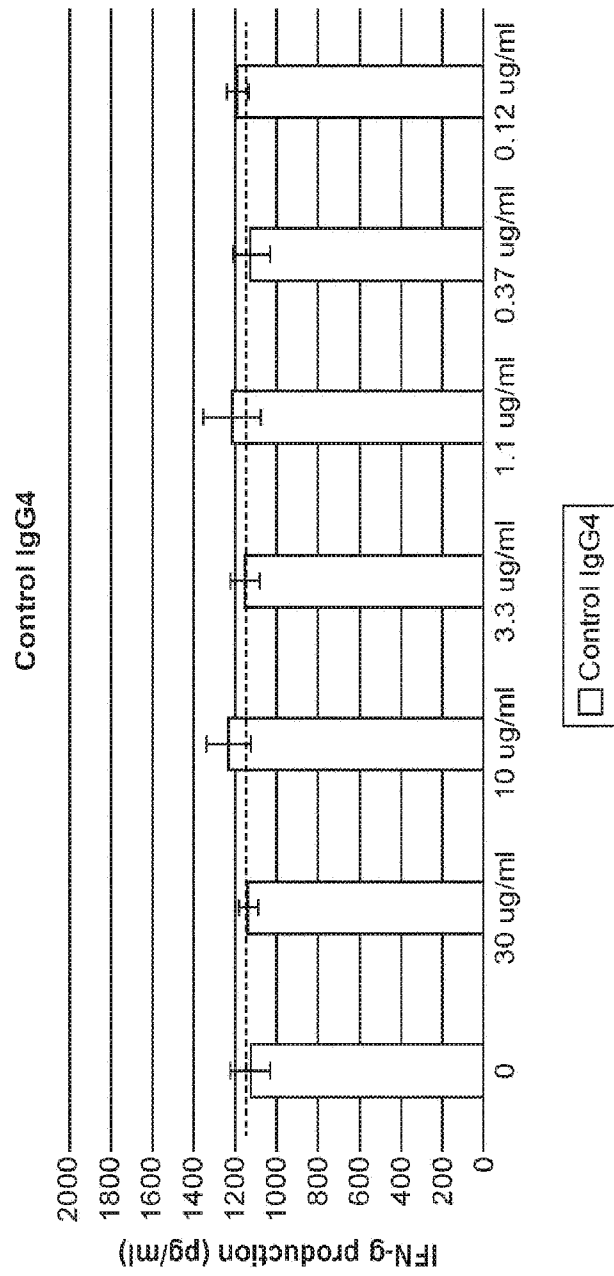


FIG. 6A

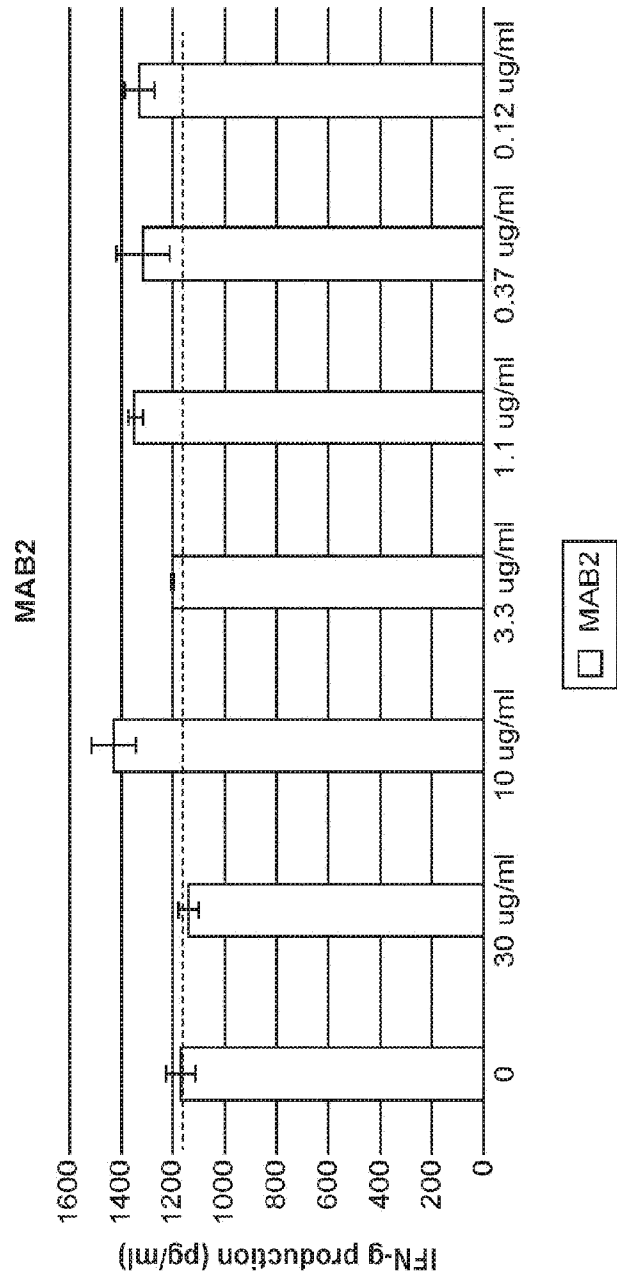
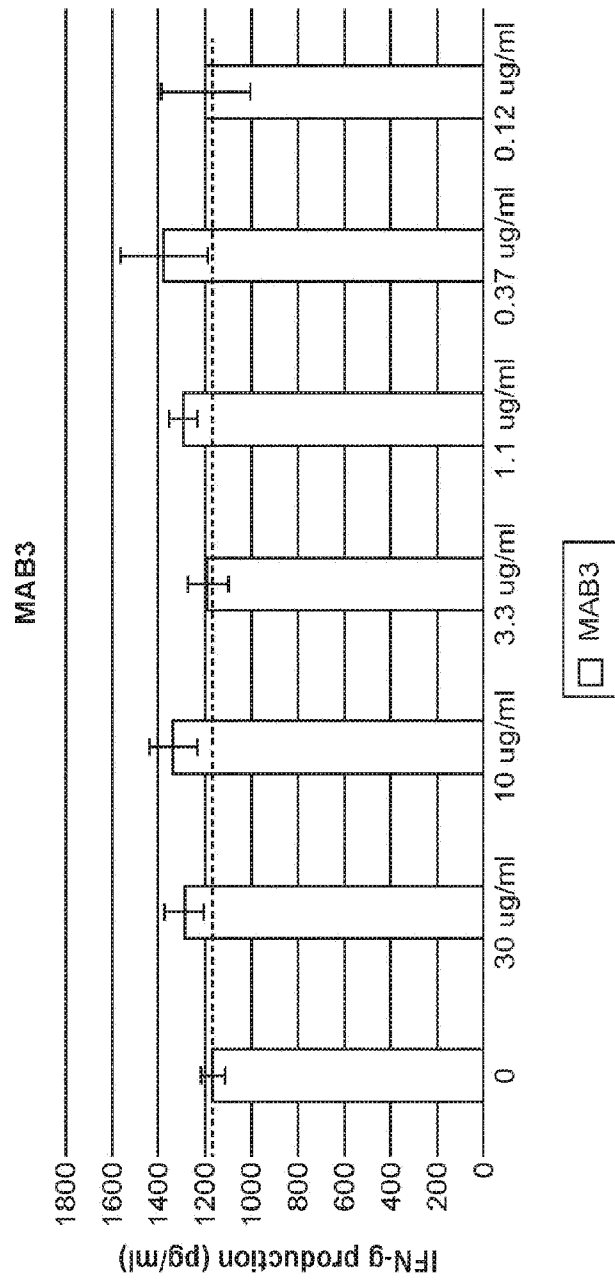


FIG. 6B

**FIG. 6C**

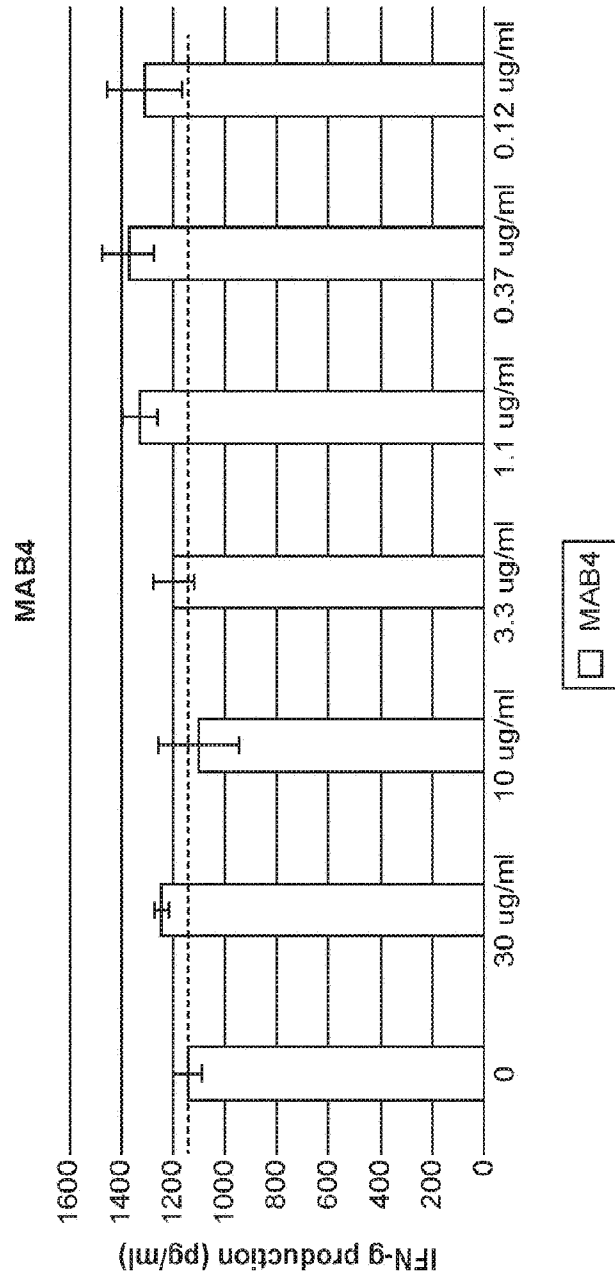
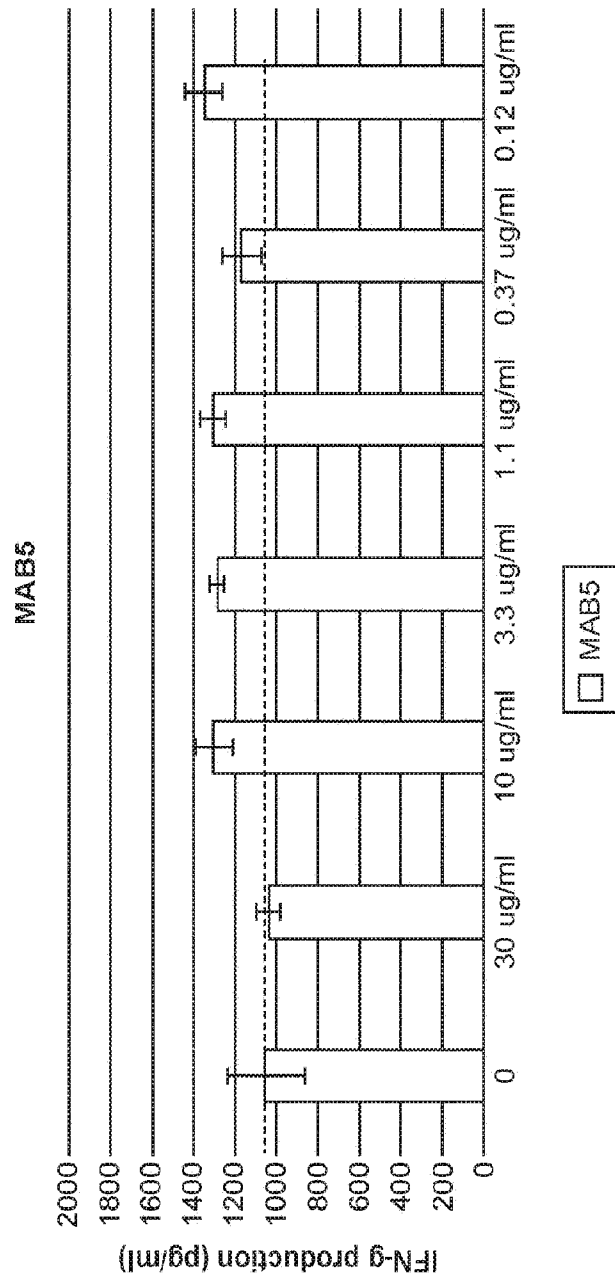
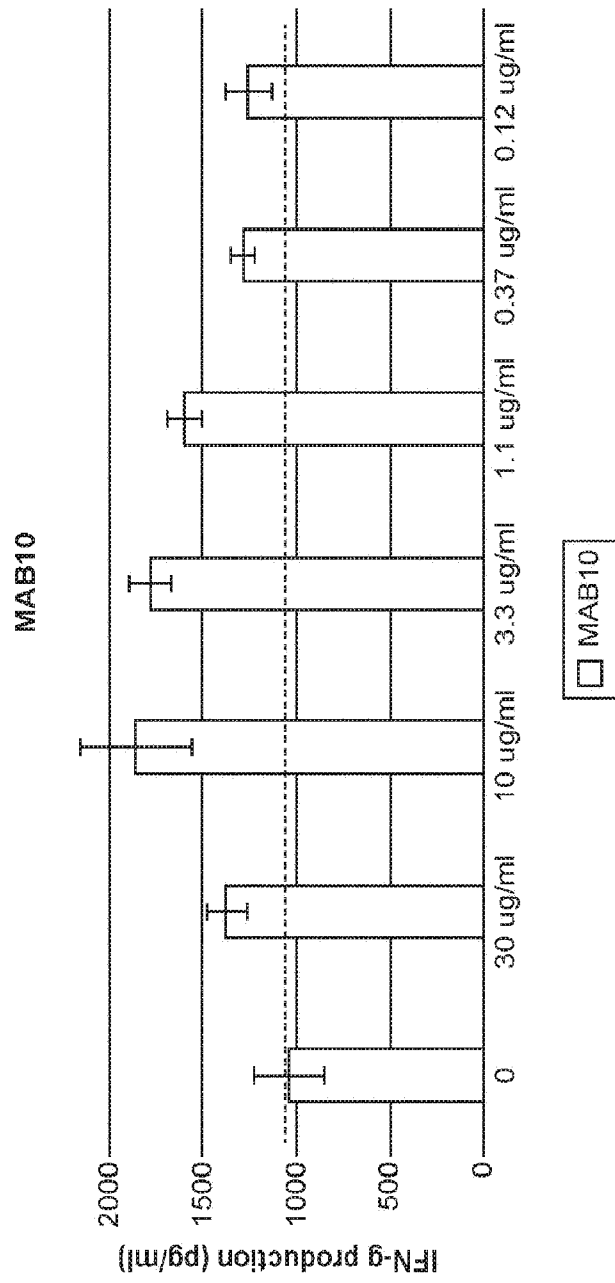
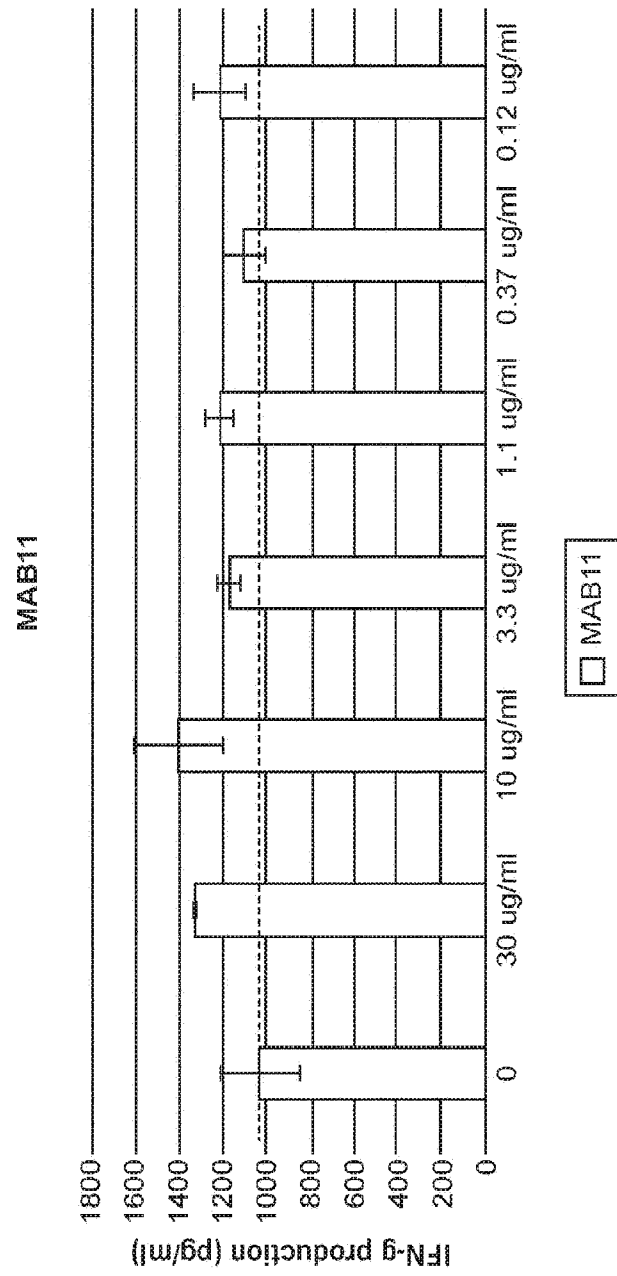


FIG. 6D

**FIG. 6E**

**FIG. 6F**

**FIG. 6G**

MAB12

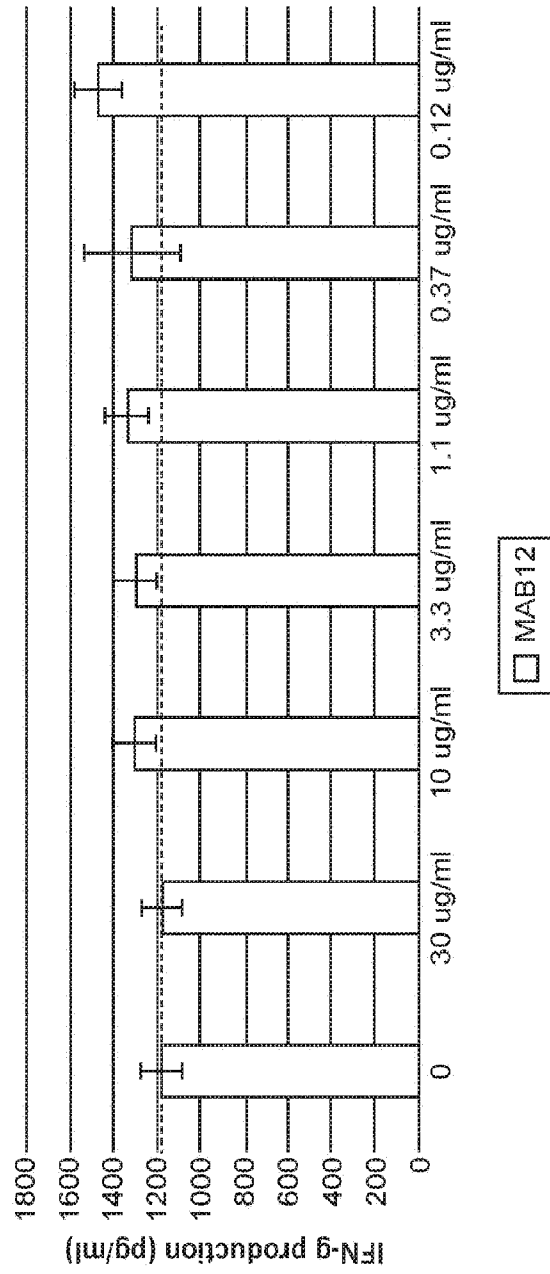


FIG. 6H

MAB15

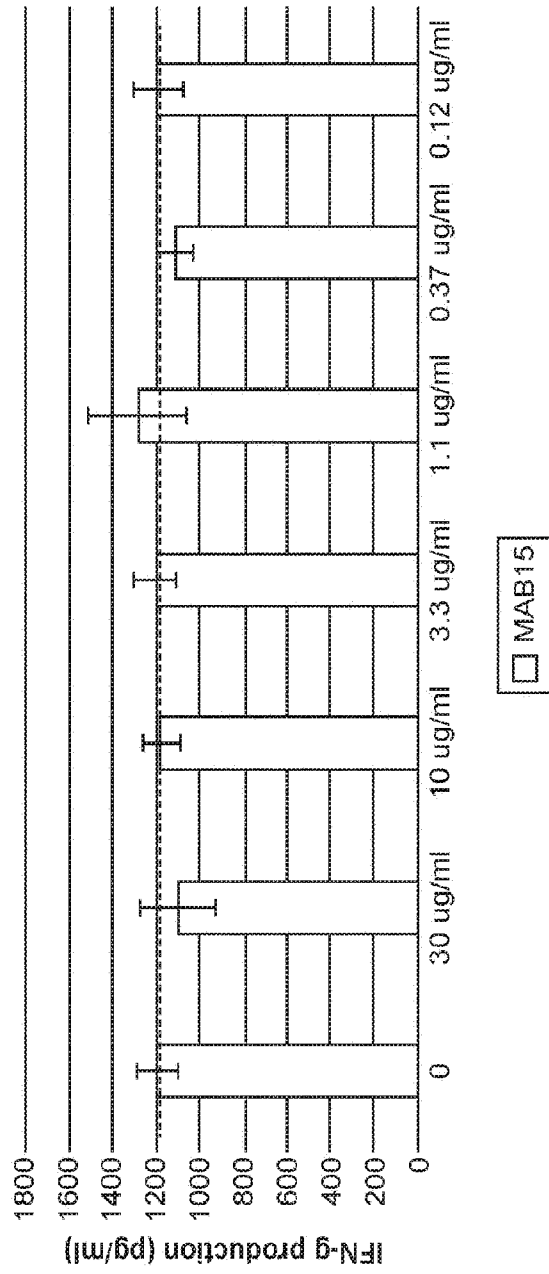
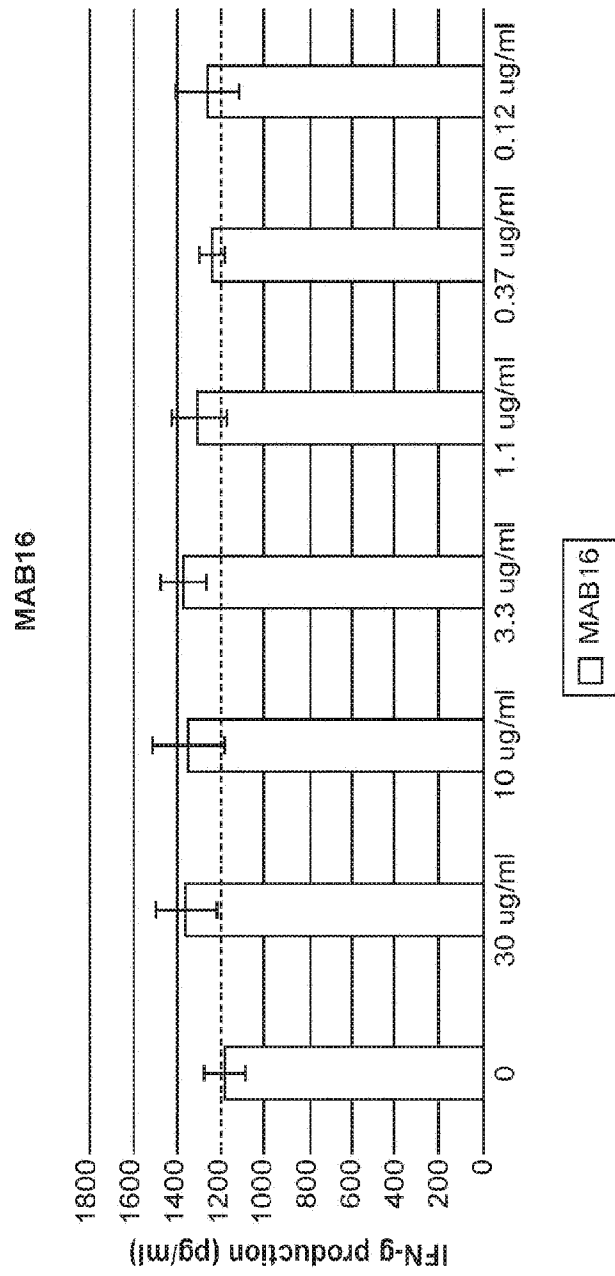


FIG. 6I

**FIG. 6J**

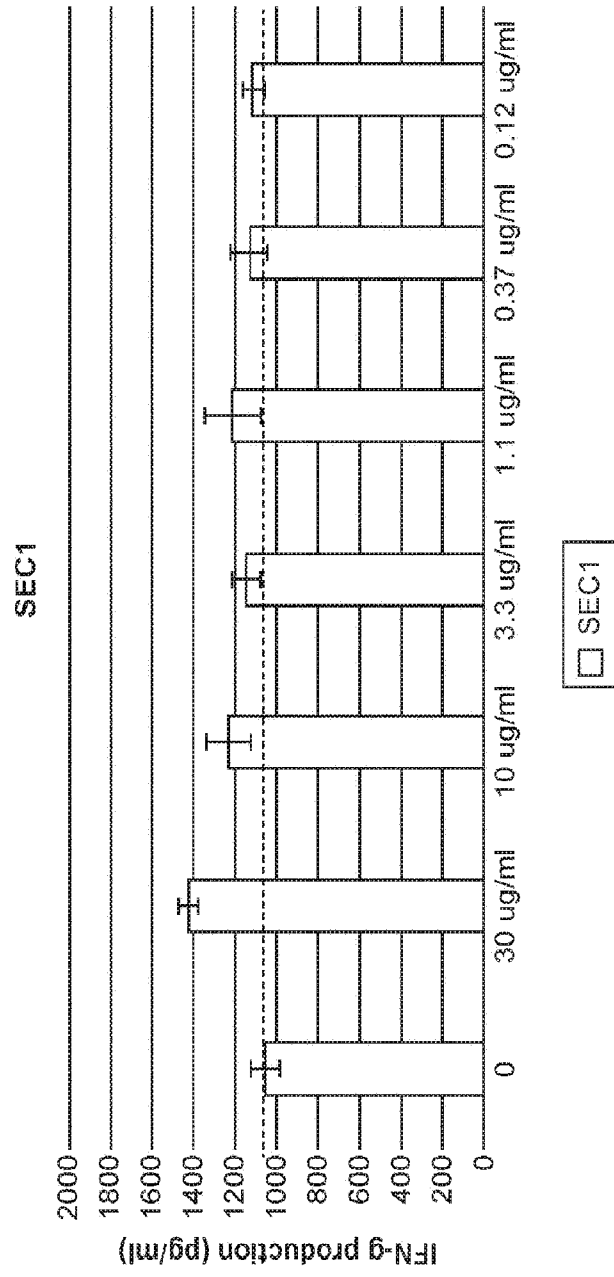


FIG. 6K

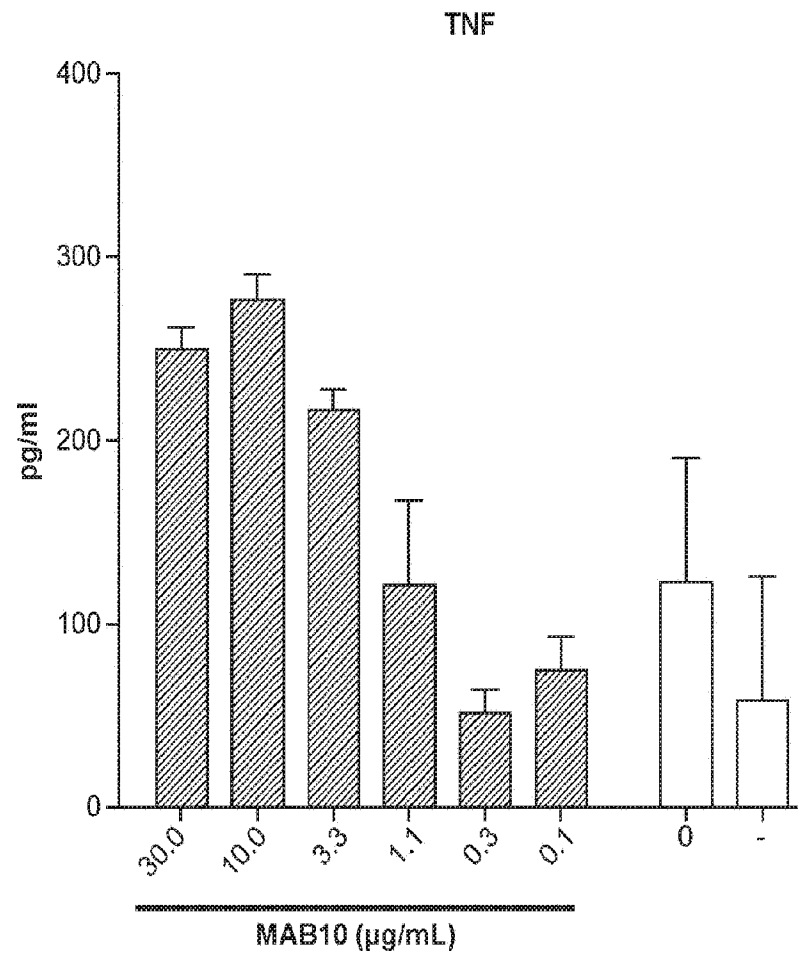


FIG. 6L

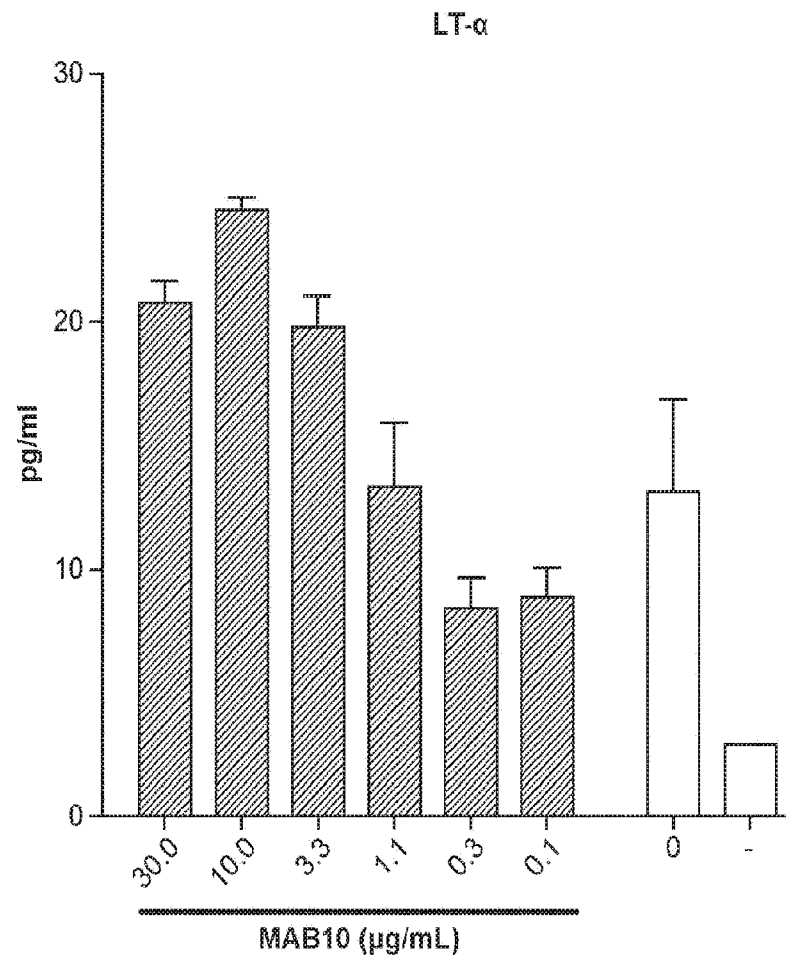


FIG. 6M

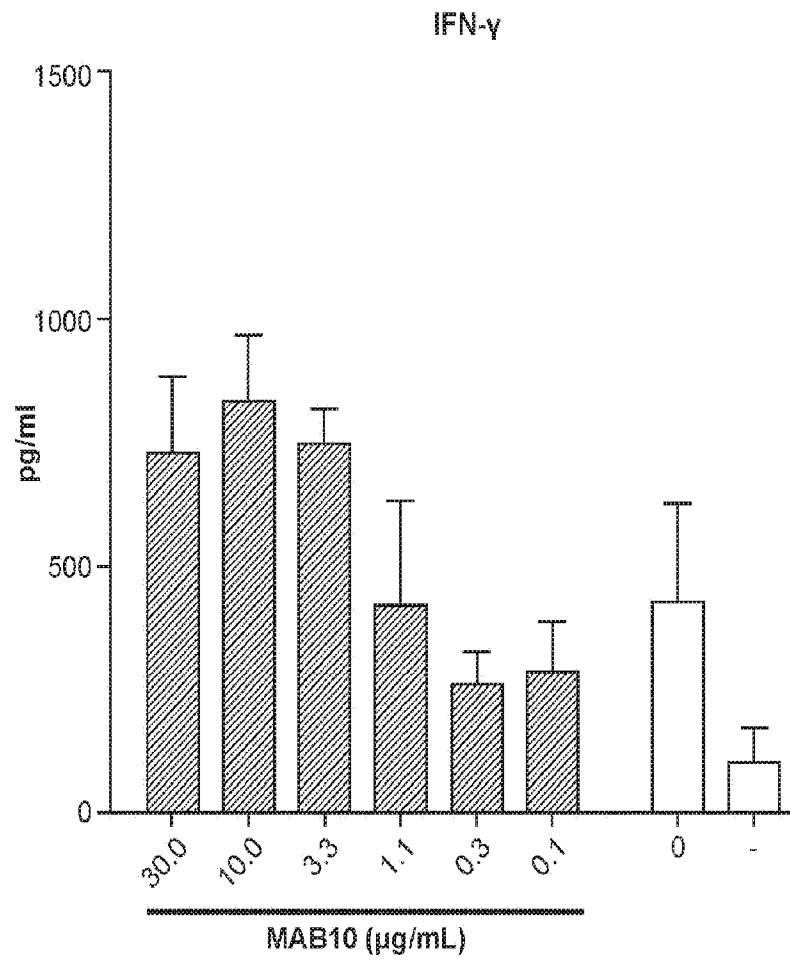


FIG. 6N

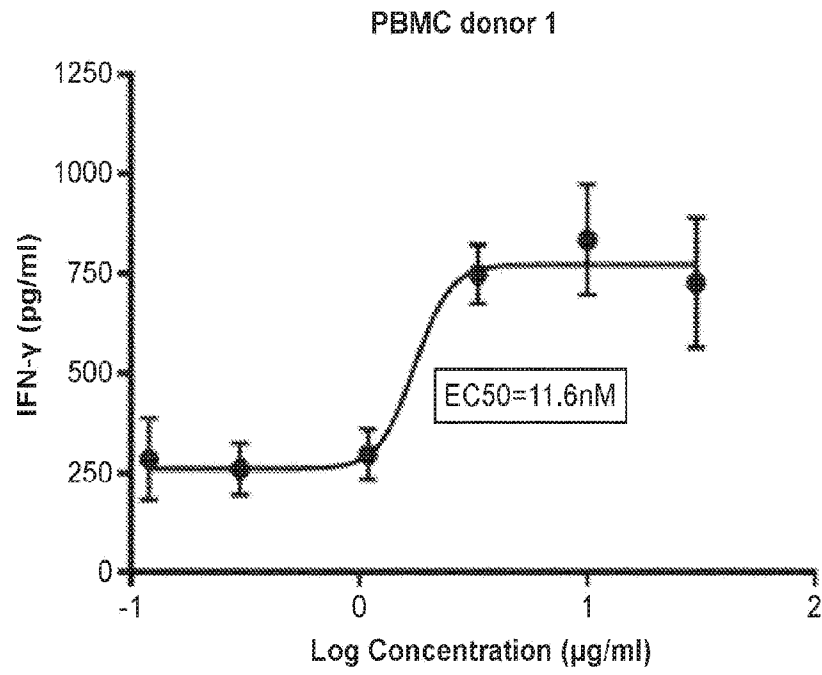


FIG. 60

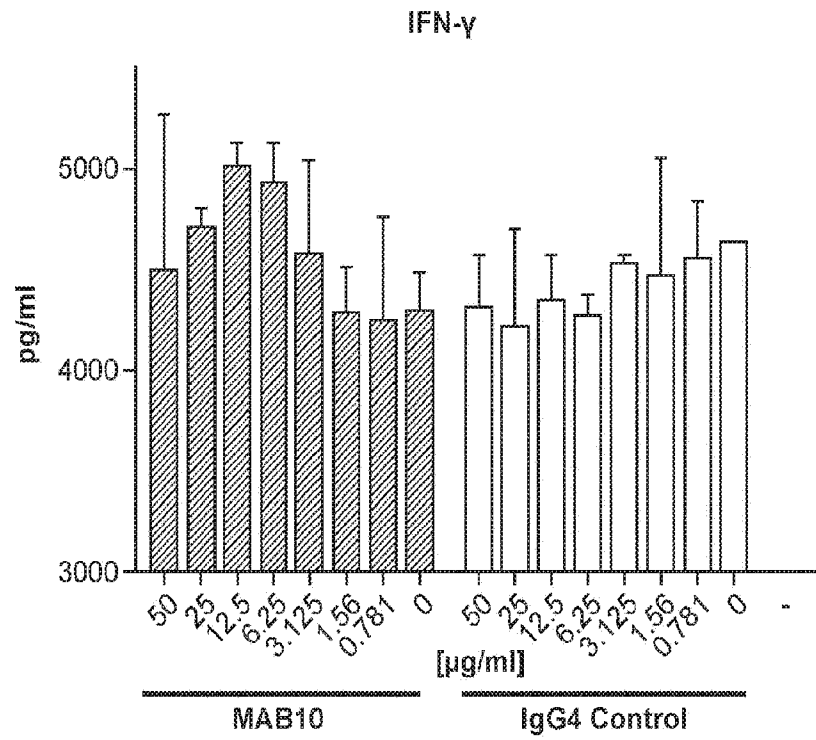


FIG. 7A

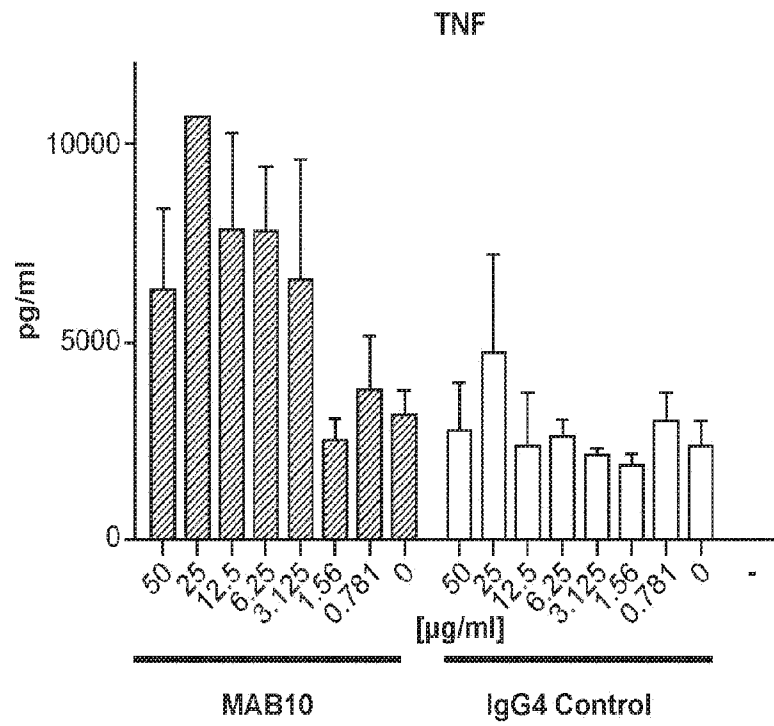


FIG. 7B

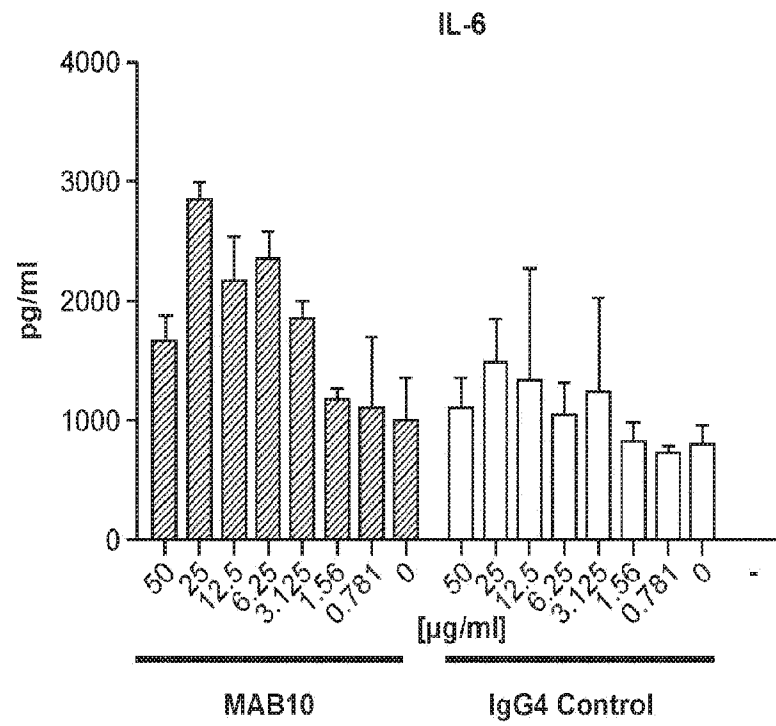


FIG. 7C

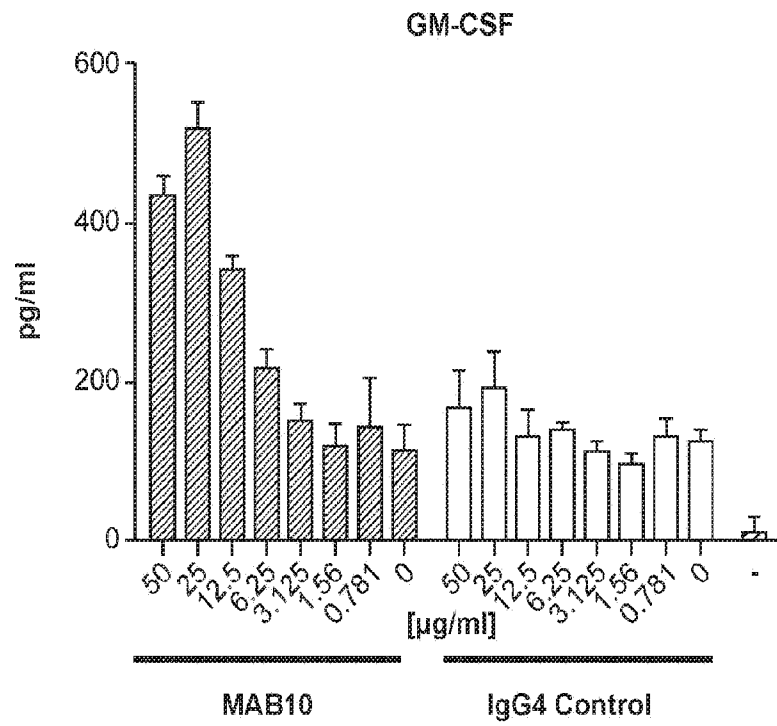


FIG. 7D

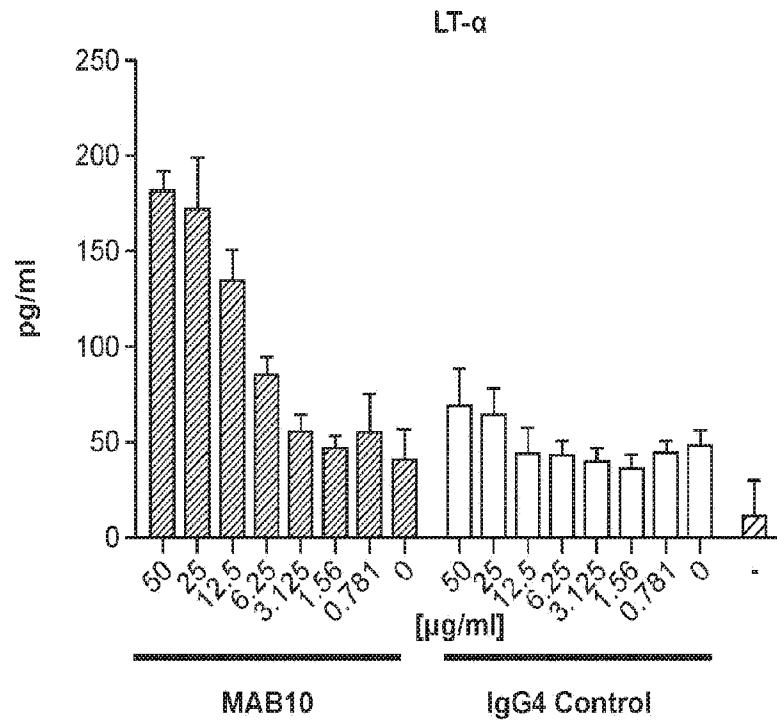


FIG. 7E

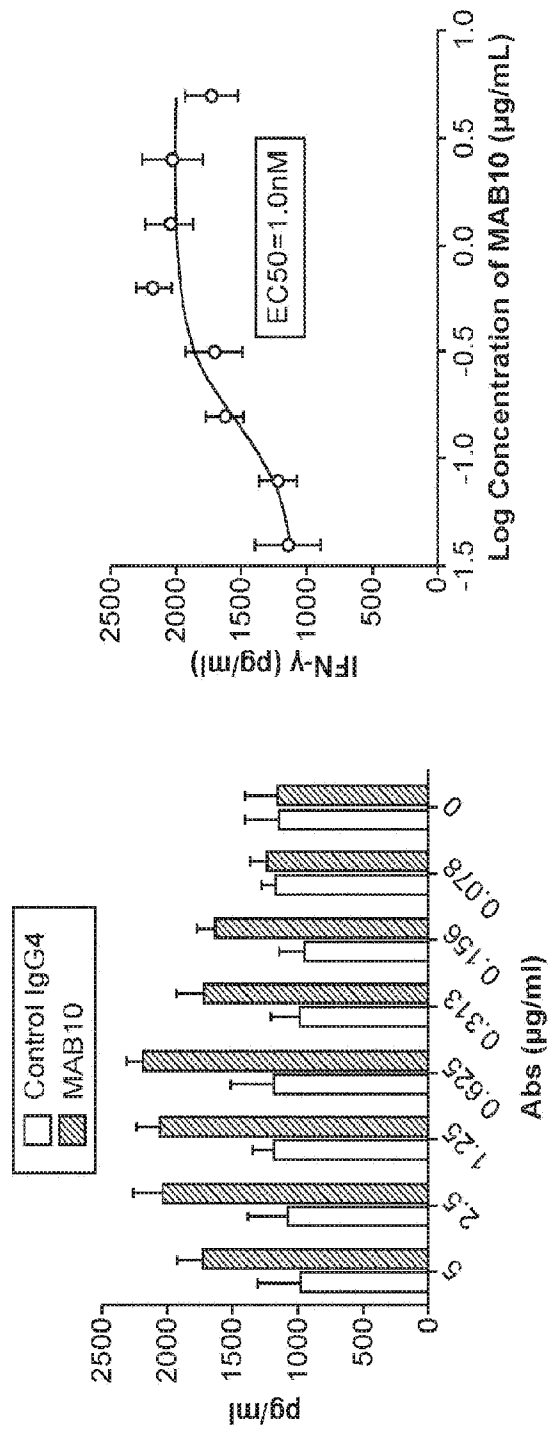


FIG. 8A

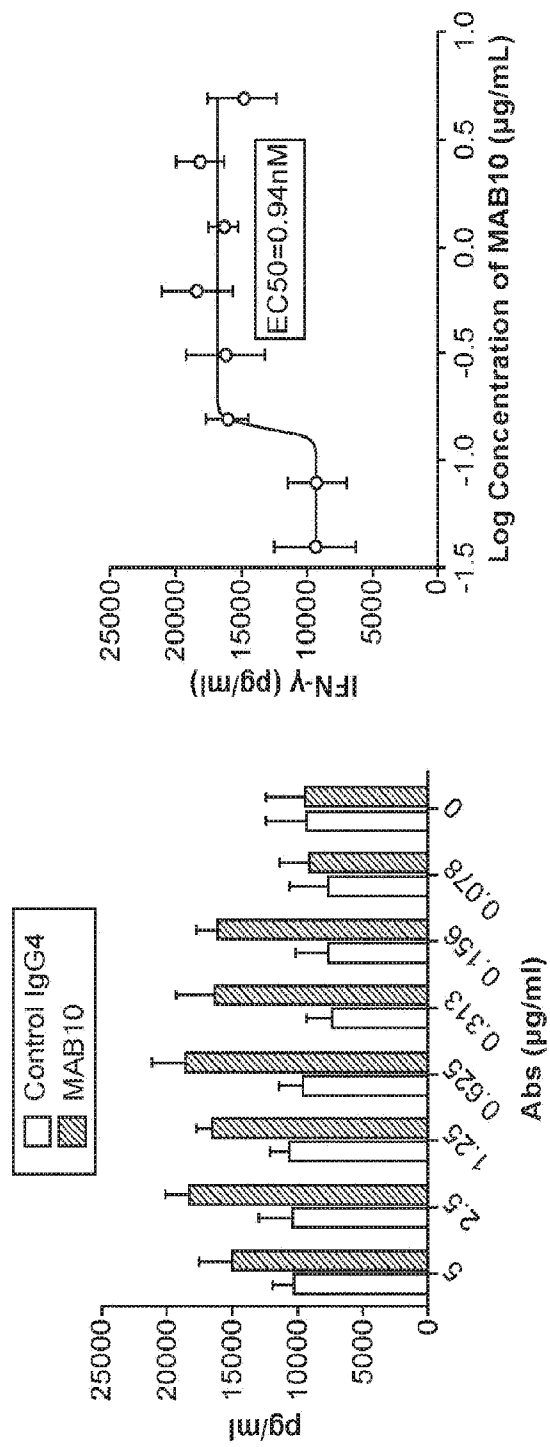


FIG. 8B

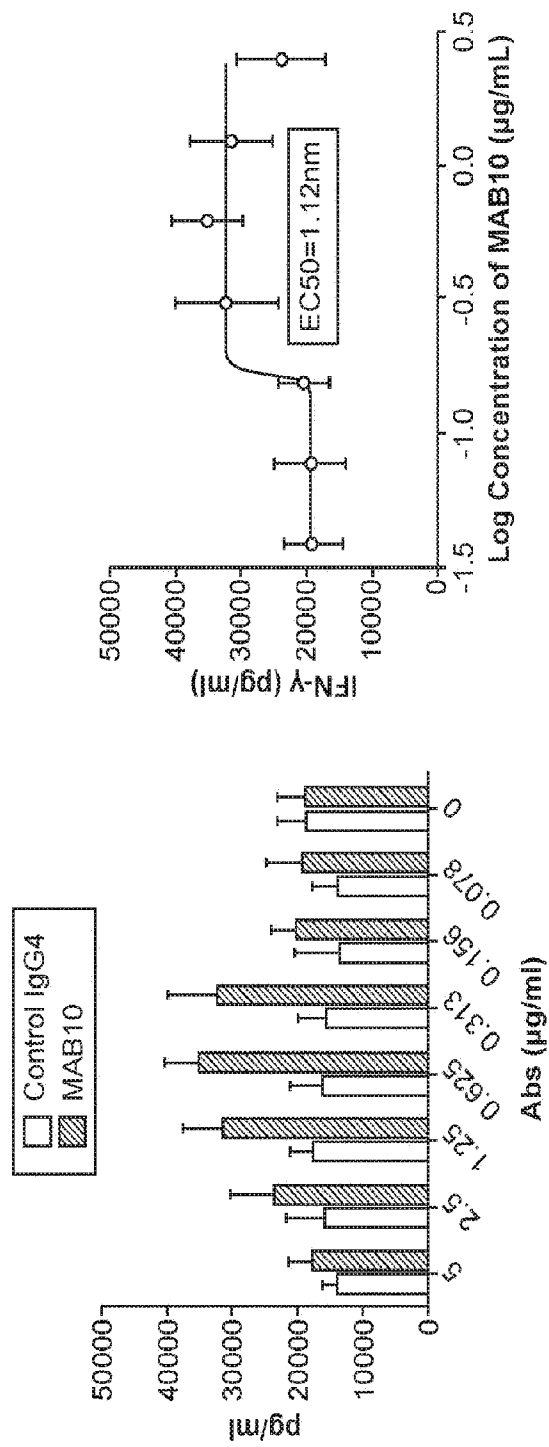


FIG. 8C

TIGIT/PD1 Assay, 1:1 Ratio Anti-TIGIT and Anti-PD-1

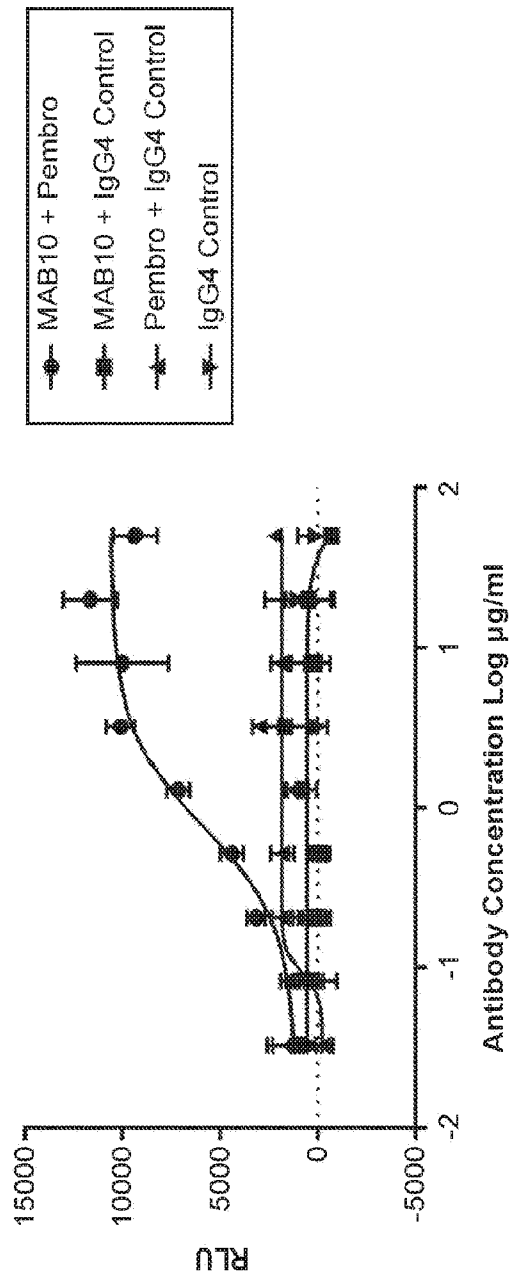


FIG. 9A

TIGIT/PD1, Fixed Concentration of Anti-PD-1

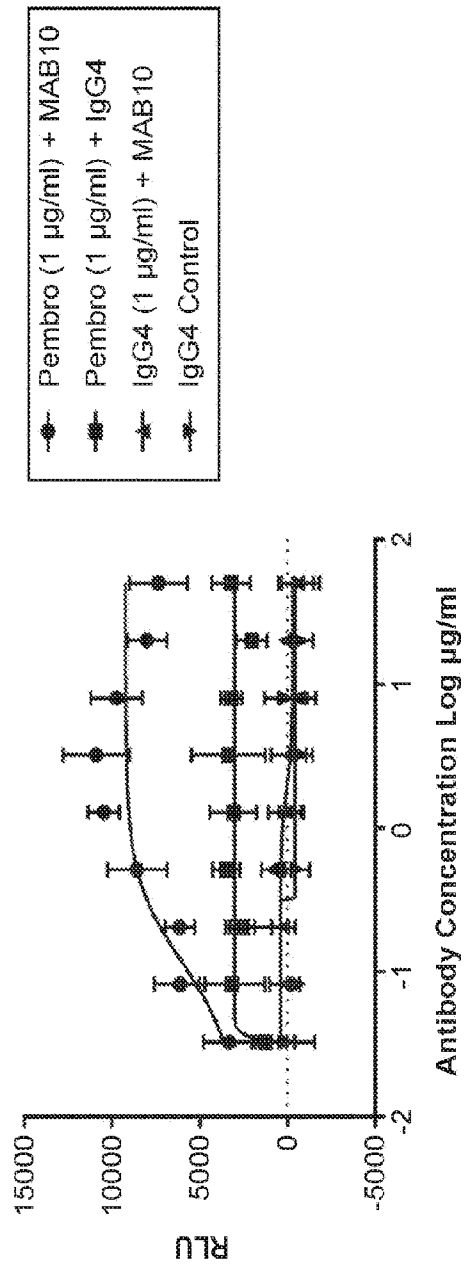


FIG. 9B

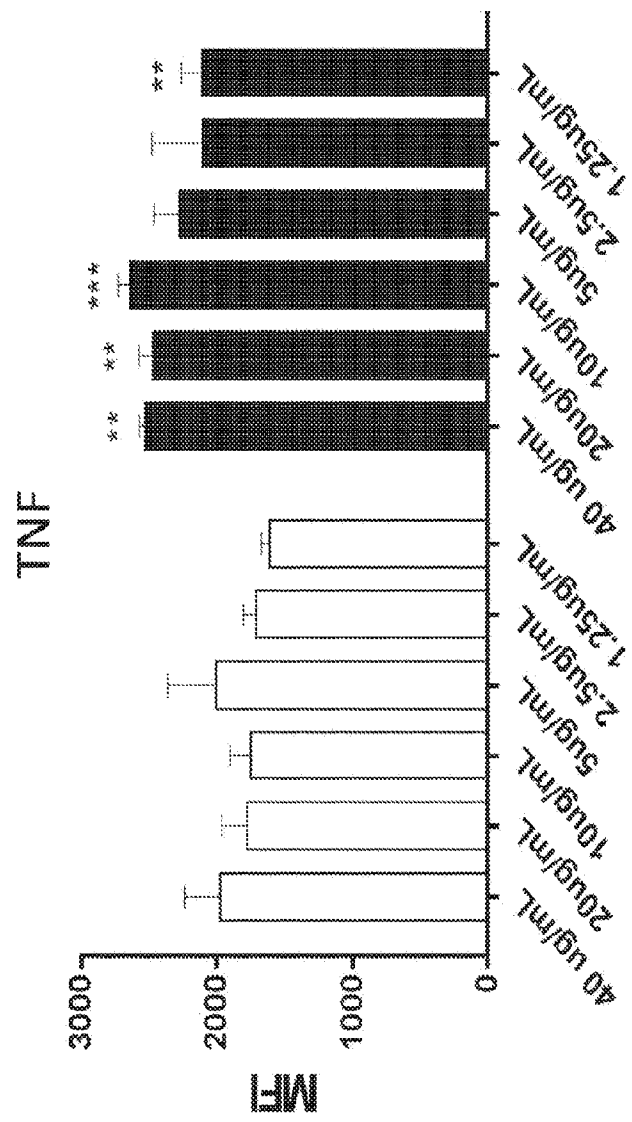


FIG. 10A

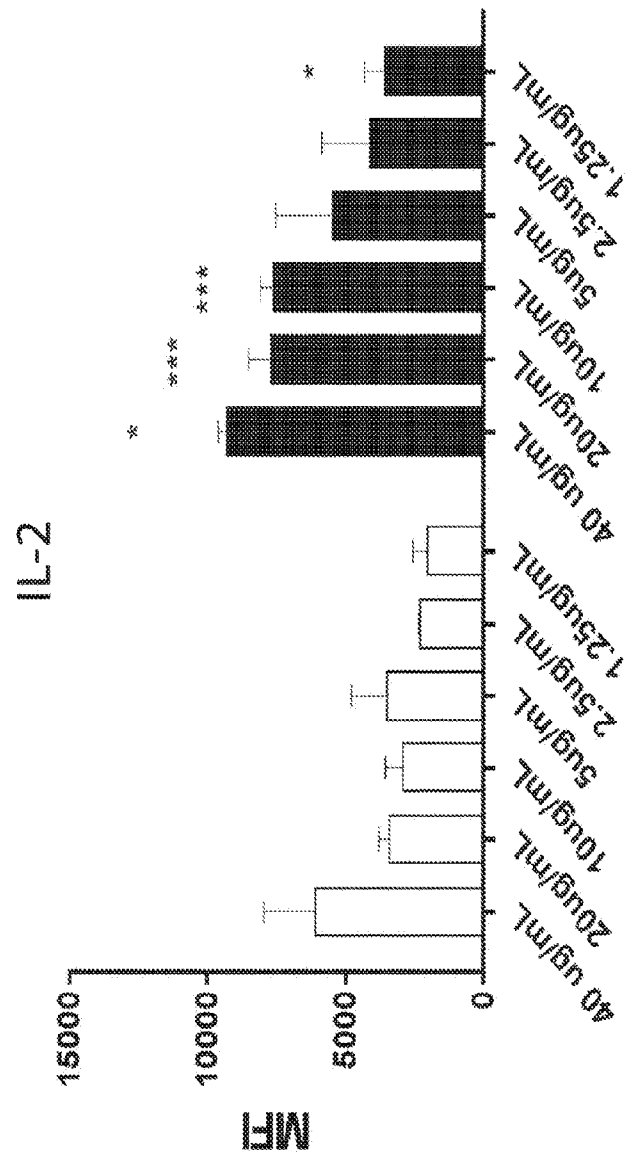


FIG. 10B

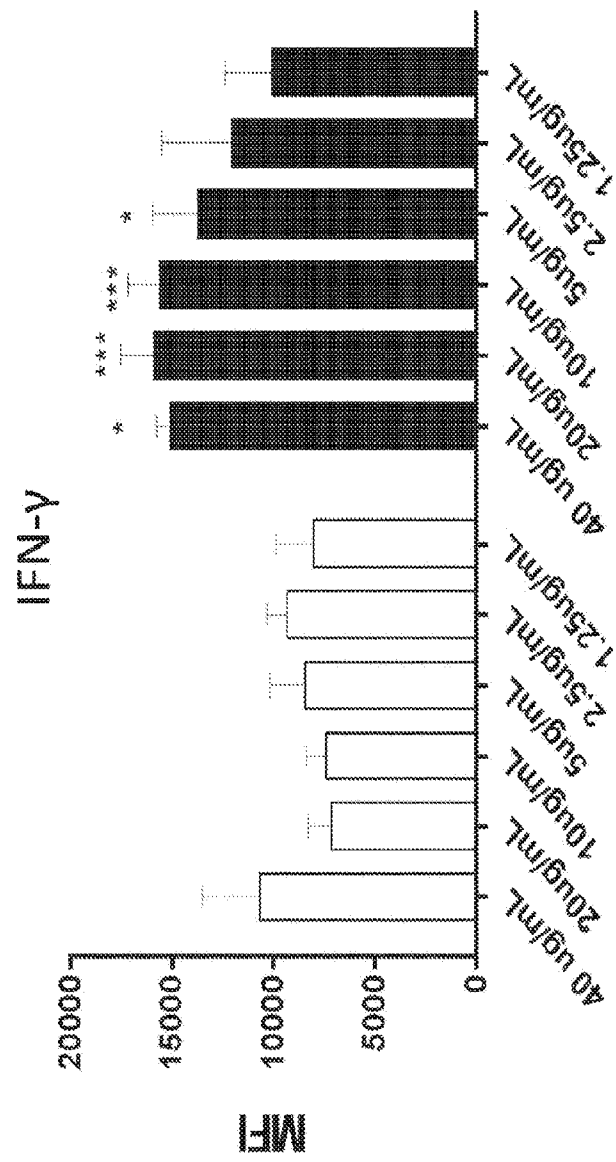


FIG. 10C

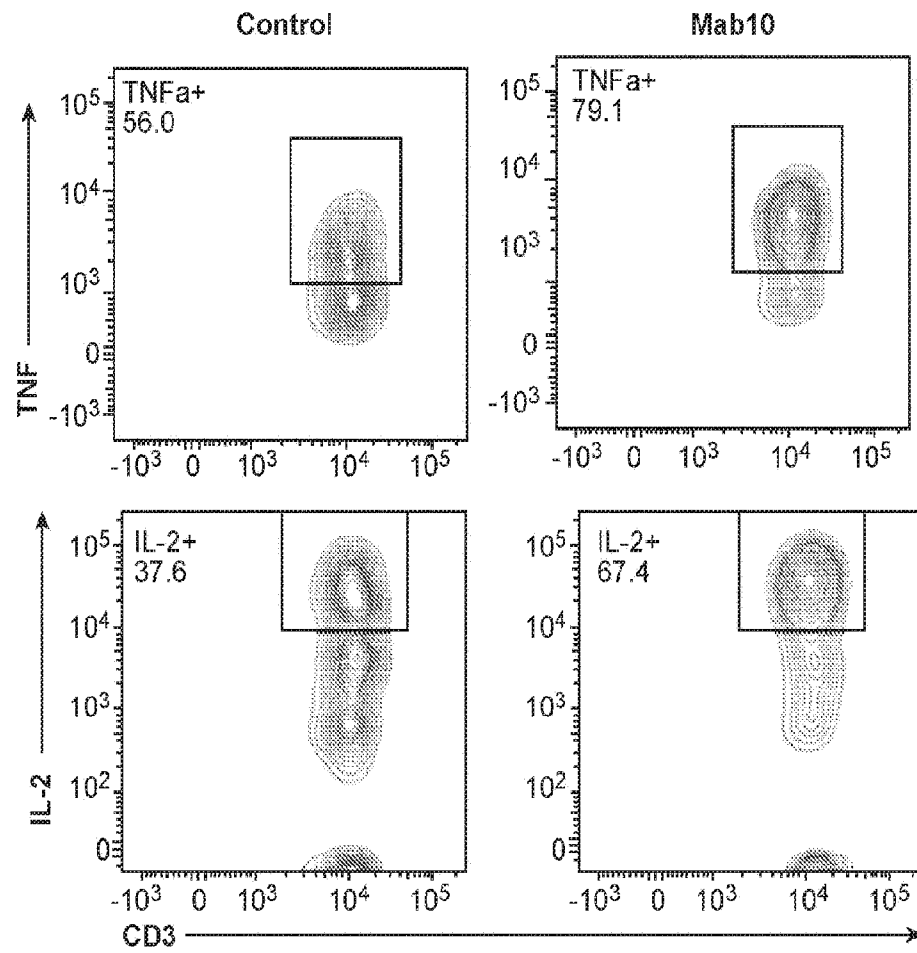


FIG. 10D

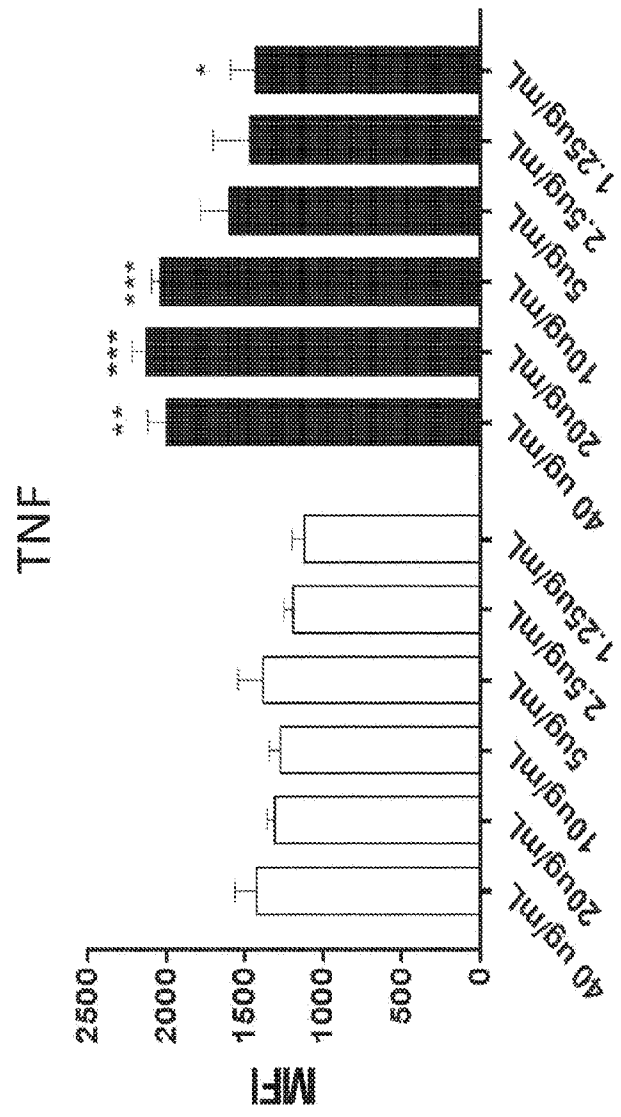


FIG. 11A

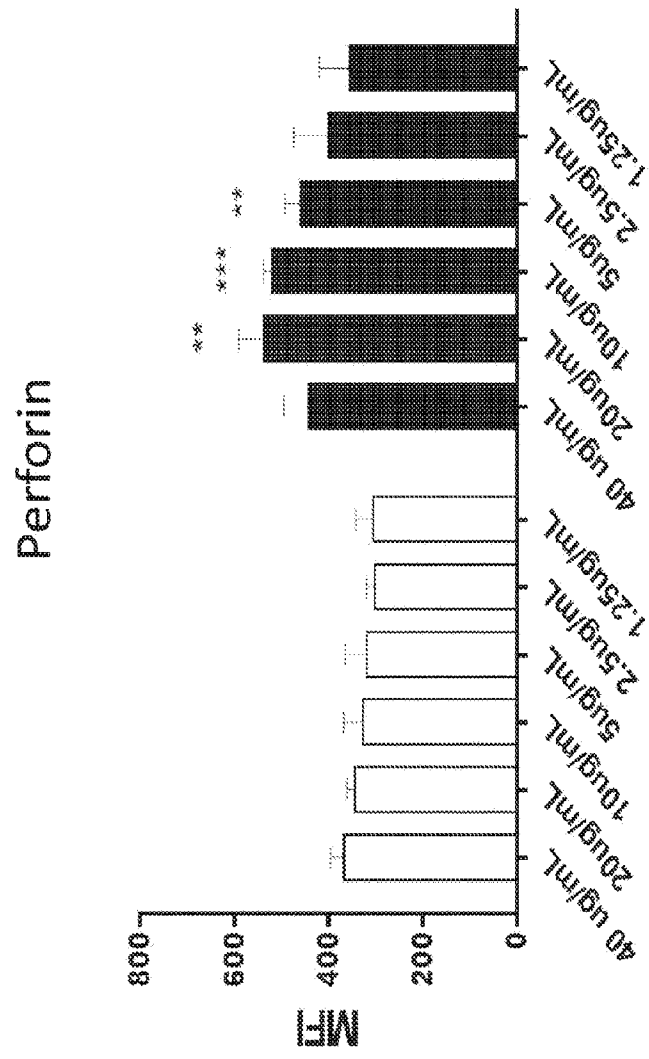


FIG. 11B

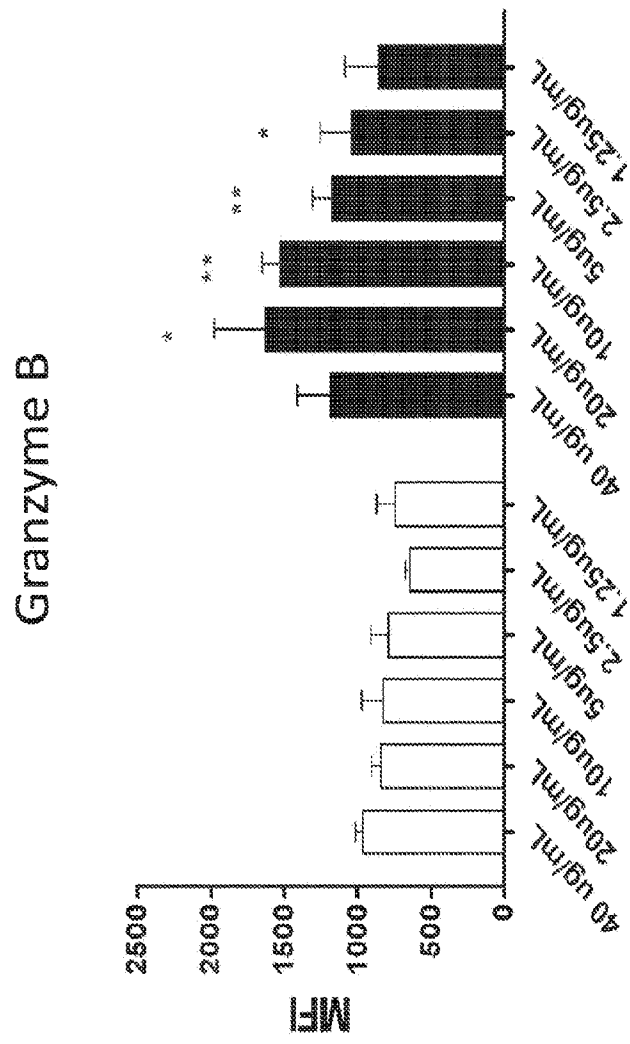


FIG. 11C

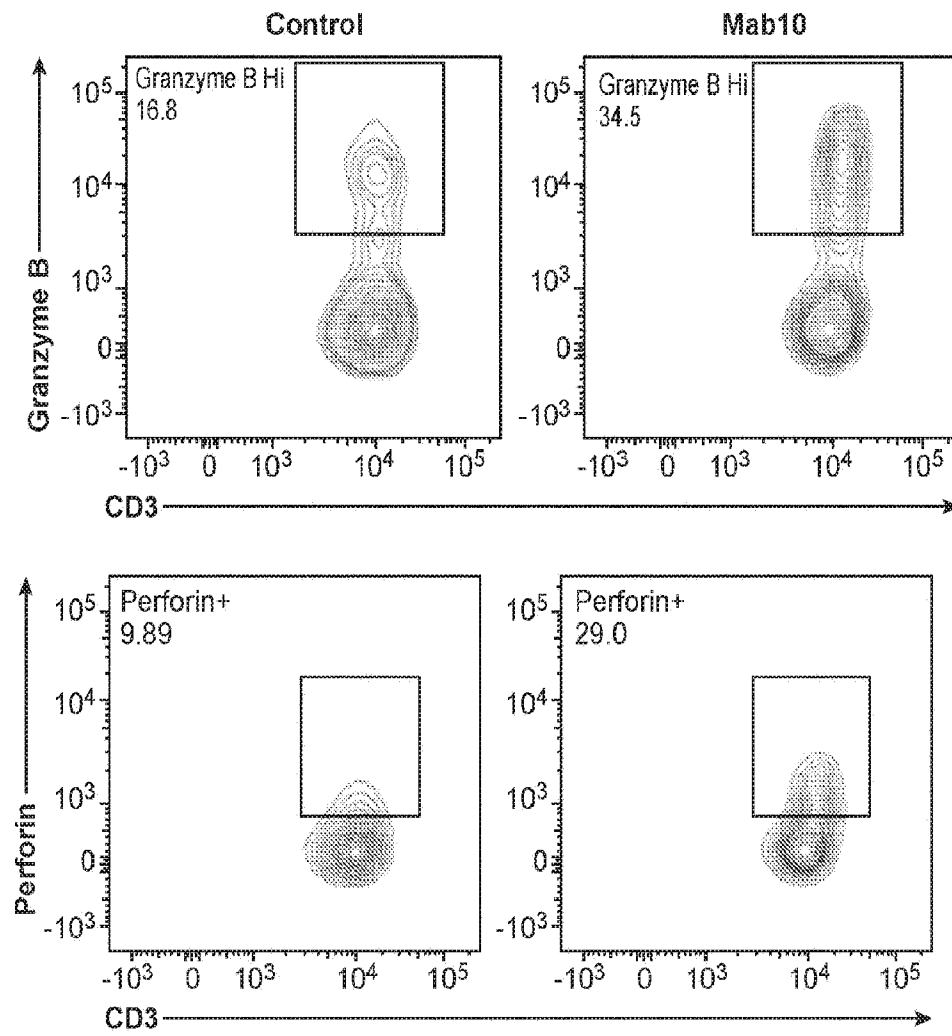


FIG. 11D

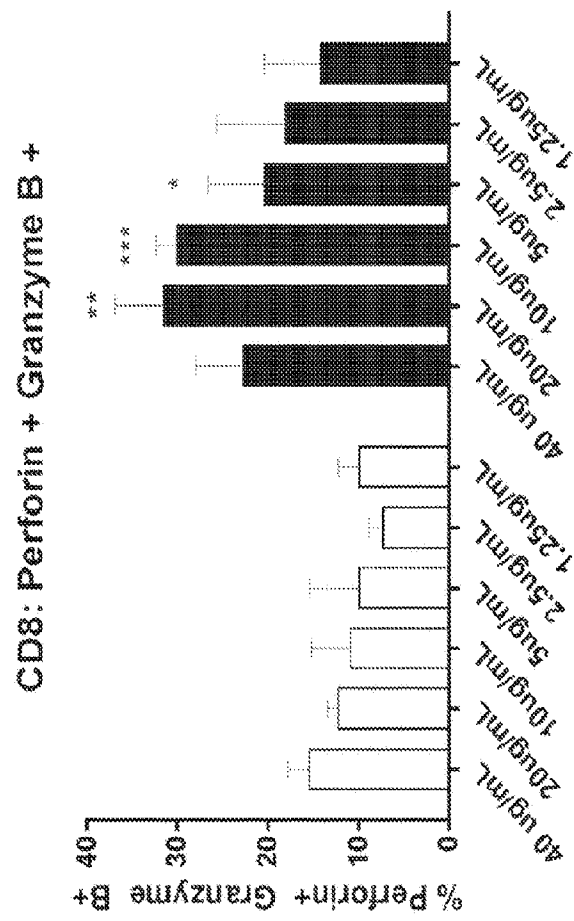


FIG. 12A

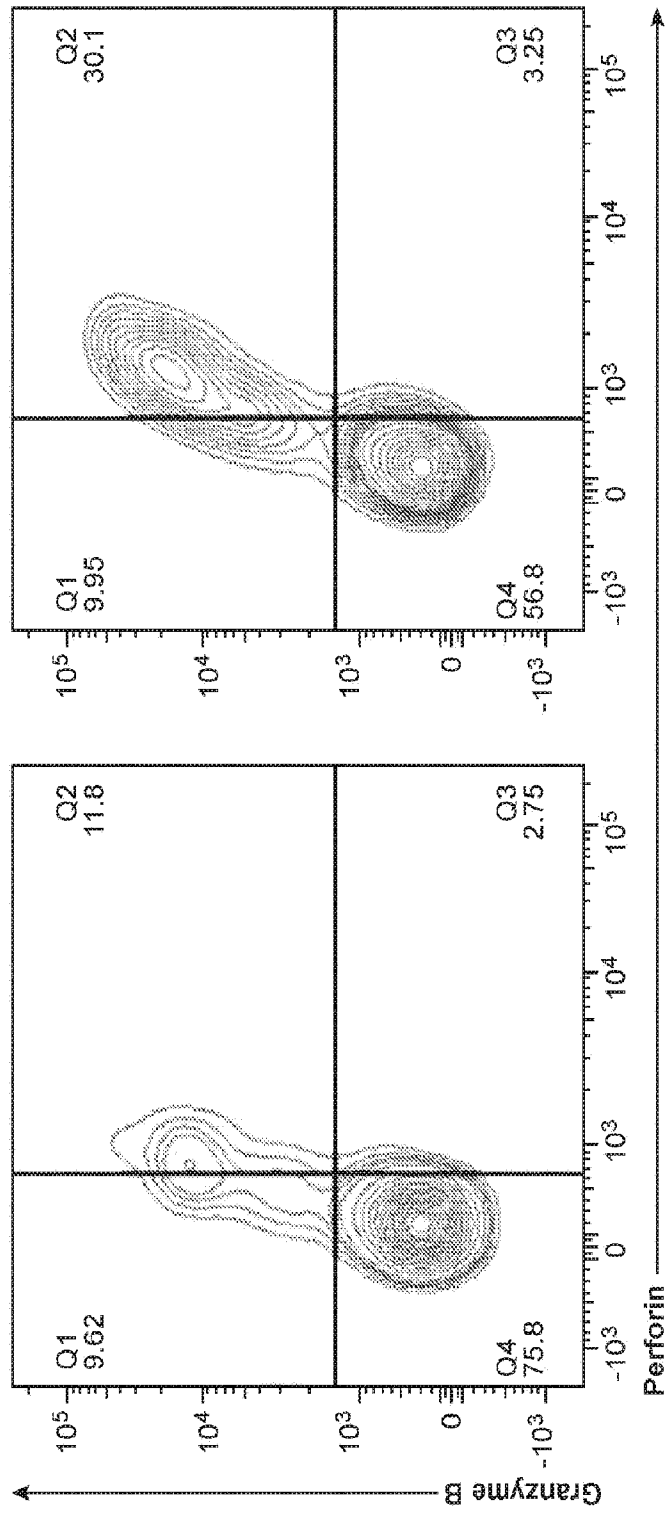


FIG. 12B

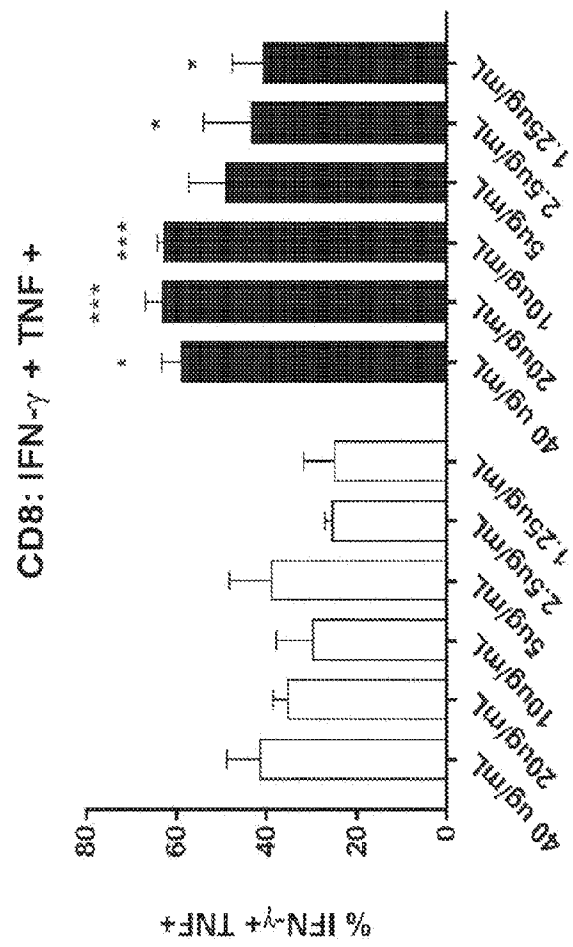


FIG. 12C

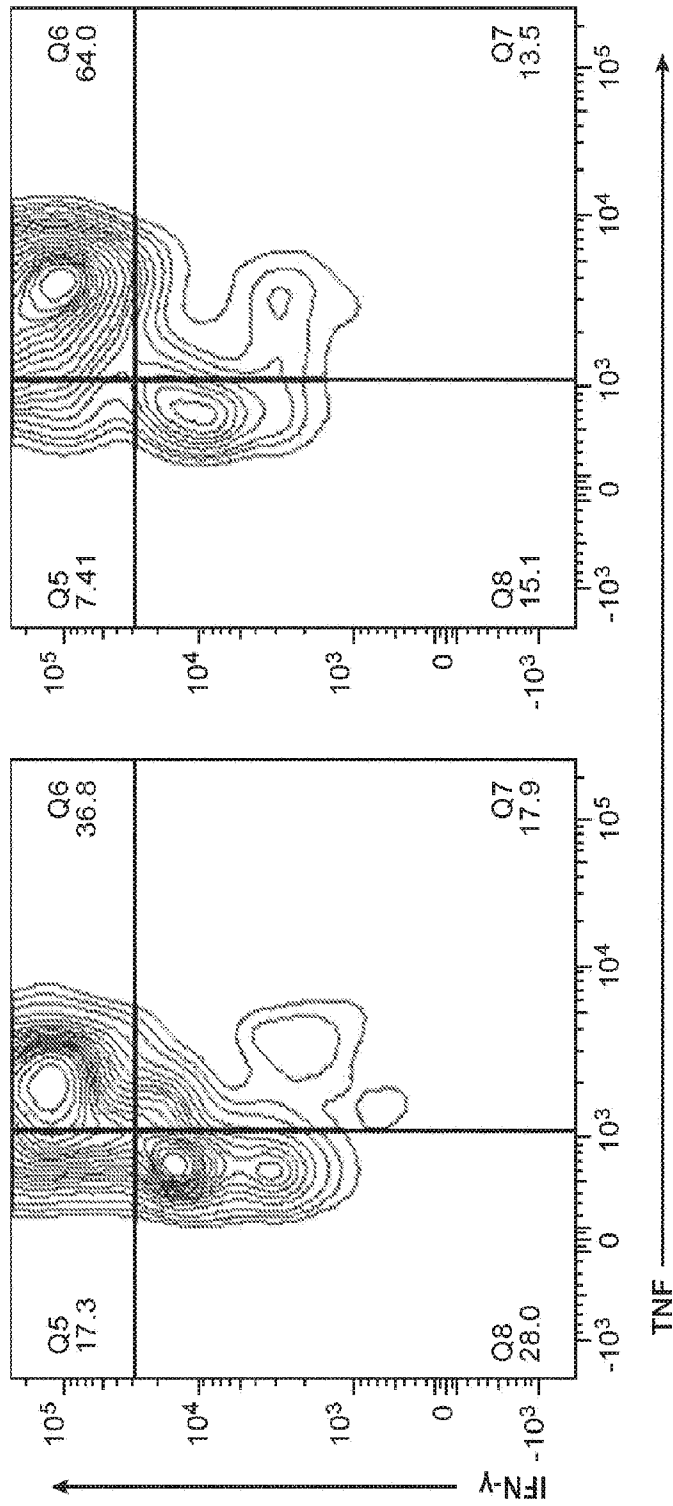


FIG. 12D

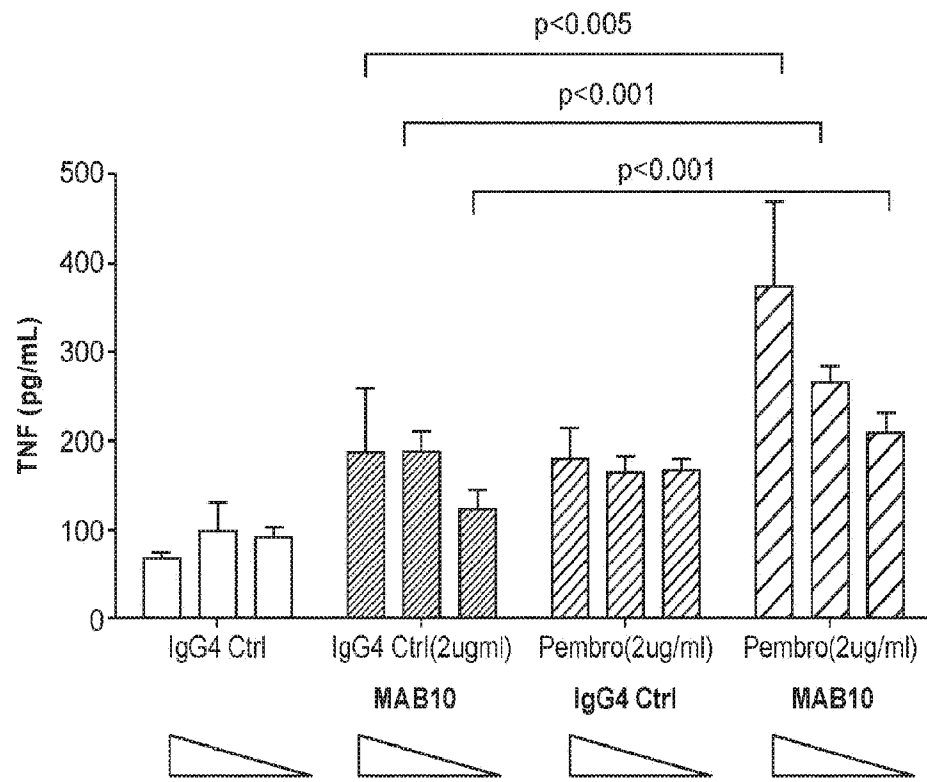


FIG. 13

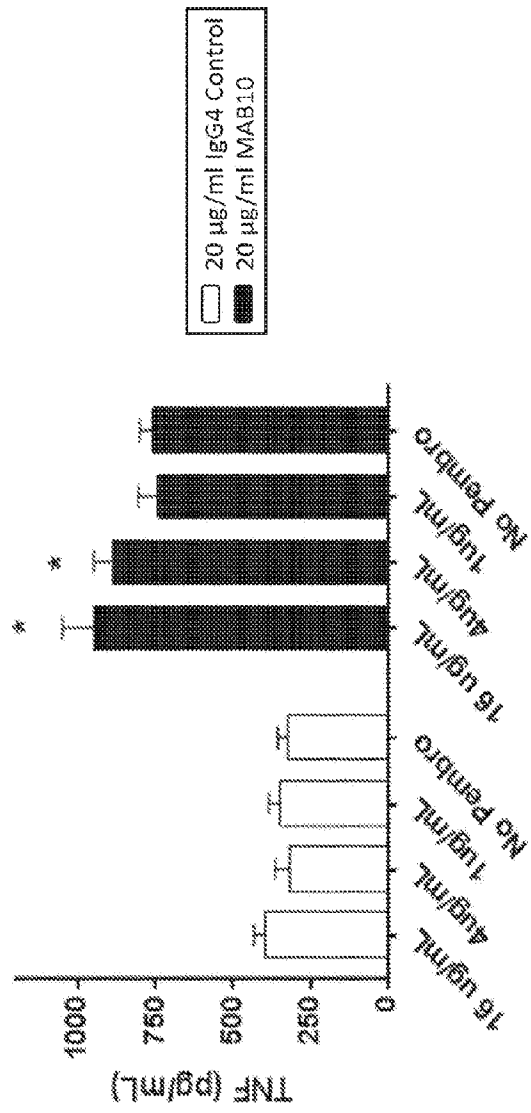


FIG. 14A

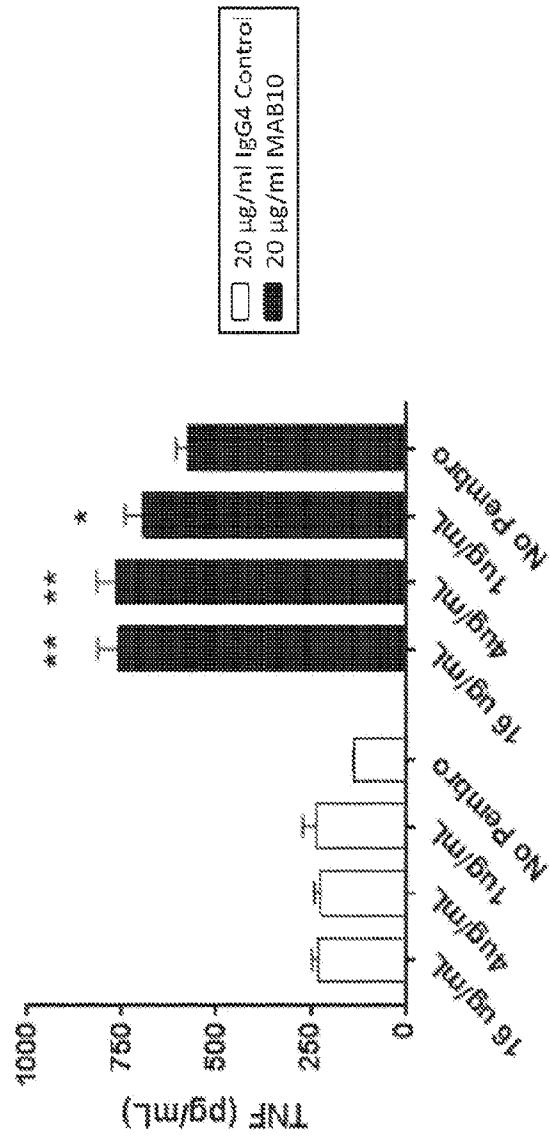


FIG. 14B

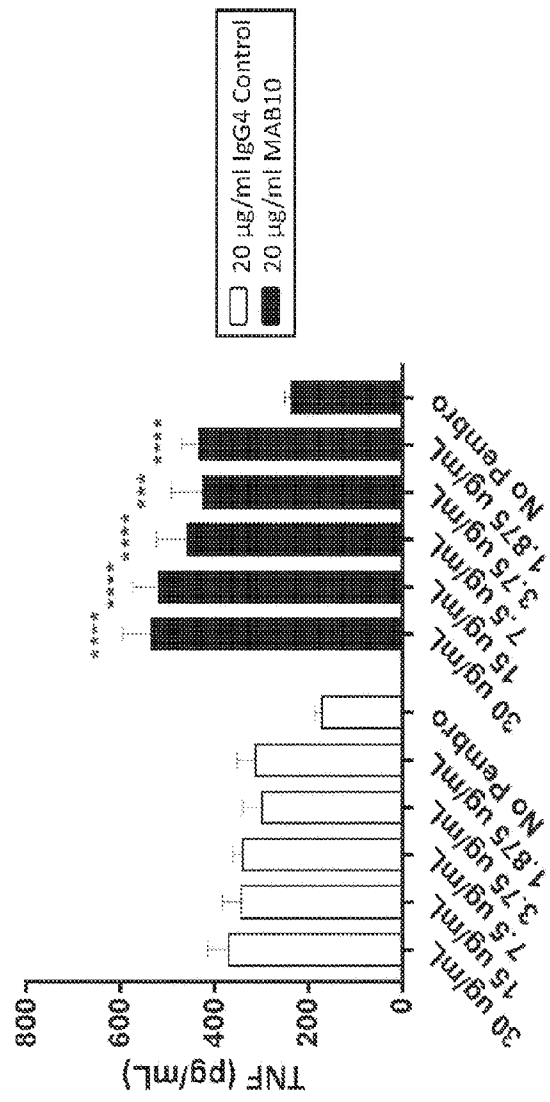


FIG. 14C