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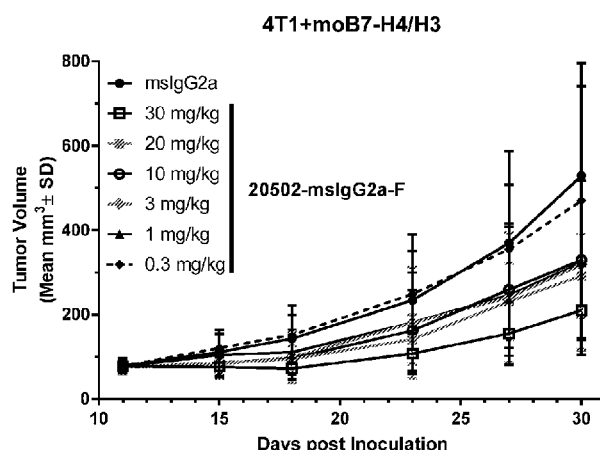
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(54) Title: B7-H4 ANTIBODIES AND METHODS OF USE THEREOF

FIG. 14A



(57) **Abstract:** The present disclosure provides antibodies and antigen-binding fragments thereof that specifically bind to human B7-H4 (and optionally cynomolgus monkey, mouse, and/or rat B7-H4) and compositions comprising such antibodies or antigen-binding fragments thereof. In a specific aspect, the antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 increase T cell proliferation, increase interferon-gamma production, and/or deplete B7-H4 expressing cells via ADCC activity. The present disclosure also provides methods for treating disorders, such as cancer, by administering an antibody or antigen-binding fragment thereof that specifically binds to human B7-H4.

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[0001] B7-H4 ANTIBODIES AND METHODS OF USE THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0002] This application claims the benefit of U.S. Provisional Application No. 62/550,173, filed August 25, 2017, U.S. Provisional Application No. 62/579,774, filed October 31, 2017, U.S. Provisional Application No. 62/607,810, filed December 19, 2017, and U.S. Provisional Application No. 62/656,789, filed April 12, 2018, which are each hereby incorporated in its entirety by reference.

REFERENCE TO A SEQUENCE LISTING SUBMITTED ELECTRONICALLY VIA EFS-WEB

[0003] The content of the electronically submitted sequence listing (Name: 3986.0090004_SL_ST25.txt; Size: 331,354 bytes; Date of Creation: August 3, 2018) is herein incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

Field

[0004] The present disclosure relates to antibodies that specifically bind to human B7-H4 compositions comprising such antibodies, and methods of producing and using antibodies that specifically bind to B7-H4.

Description of The Related Art

[0005] B7-H4 (also known as B7x, B7-S1, and VTCN1) is an immune regulatory molecule that shares homology with other B7 family members, include PD-L1. It is a type I transmembrane protein comprised of both IgV and IgC ectodomains. While B7-H4 expression in healthy tissues is relatively limited at the protein level, B7-H4 is expressed in several solid tumors such as gynecological carcinomas of the breast, ovary, and endometrium. Expression of B7-H4 in tumors tends to correlate with poor prognosis. The receptor for B7-H4 is unknown, but it is believed to be expressed on T cells. B7-H4 is believed to directly inhibit T cell activity.

[0006] Given the expression and function of B7-H4, provided herein are antibodies that specifically bind to B7-H4 and the use of these antibodies to modulate B7-H4 activity, including, e.g., in the treatment of cancer.

SUMMARY

[0007] Provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences selected from the group consisting of: SEQ ID NOs:5-10, respectively; SEQ ID NOs:15-20, respectively; SEQ ID NOs:25-30, respectively; SEQ ID NOs:35-40, respectively; SEQ ID NOs:458-463, respectively; SEQ ID NOs:45-50, respectively; SEQ ID NOs:55-60, respectively; SEQ ID NOs:65-70, respectively; SEQ ID NOs:75-80, respectively; SEQ ID NOs:85-90, respectively; SEQ ID NOs:95-100, respectively; SEQ ID NOs:105-110, respectively; SEQ ID NOs:115-120, respectively; SEQ ID NOs:125-130, respectively; SEQ ID NOs:135-140, respectively; SEQ ID NOs:145-150, respectively; SEQ ID NOs:155-160, respectively; SEQ ID NOs:165-170, respectively; SEQ ID NOs:175-180, respectively; SEQ ID NOs:185-190, respectively; and SEQ ID NOs:195-200, respectively.

[0008] In one embodiment, the antibody or antigen-binding fragment thereof comprises a VH comprising the amino acid sequence of SEQ ID NO:11, 21, 31, 41, 464, 51, 61, 71, 81, 91, 101, 111, 121, 131, 141, 151, 161, 171, 181, 191, or 201.

[0009] In one embodiment, the antibody or antigen-binding fragment thereof comprises a VL comprising the amino acid sequence of SEQ ID NO:12, 22, 32, 42, 52, 62, 72, 82, 92, 102, 112, 122, 132, 142, 152, 162, 172, 182, 192, or 202.

[0010] In one embodiment, the antibody or antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:11, 21, 31, 41, 464, 51, 61, 71, 81, 91, 101, 111, 121, 131, 141, 151, 161, 171, 181, 191, or 201.

[0011] Also provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO:12, 22, 32, 42, 52, 62, 72, 82, 92, 102, 112, 122, 132, 142, 152, 162, 172, 182, 192, or 202.

[0012] Also provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising a heavy chain variable region and a light chain variable region comprising the amino acid sequences of: SEQ ID NOs:11 and 12, respectively; SEQ ID NOs:21 and 22, respectively; SEQ ID NOs:31 and 32, respectively; SEQ ID NOs:41 and 42, respectively; SEQ ID NOs:464 and 42, respectively; SEQ ID NOs:51 and 52, respectively;

SEQ ID NOs:61 and 62, respectively; SEQ ID NOs:71 and 72, respectively; SEQ ID NOs:81 and 82, respectively; SEQ ID NOs:91 and 92, respectively; SEQ ID NOs:101 and 102, respectively; SEQ ID NOs:111 and 112, respectively; SEQ ID NOs:121 and 122, respectively; SEQ ID NOs:131 and 132, respectively; SEQ ID NOs:141 and 142, respectively; SEQ ID NOs:151 and 152, respectively; SEQ ID NOs:161 and 162, respectively; SEQ ID NOs:171 and 172, respectively; SEQ ID NOs:181 and 182, respectively; SEQ ID NOs:191 and 192, respectively; or SEQ ID NOs:201 and 202, respectively.

[0013] In one embodiment, the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region. In one embodiment, the heavy chain constant region is selected from the group consisting of human immunoglobulins IgG₁, IgG₂, IgG₃, IgG₄, IgA₁, and IgA₂ heavy chain constant regions.

[0014] In one embodiment, the antibody or antigen-binding fragment further comprises a light chain constant region. In one embodiment, the light chain constant region is selected from the group consisting of human immunoglobulins IgG κ and IgG λ light chain constant regions.

[0015] In one embodiment, the antibody or antigen-binding fragment further comprises a heavy chain constant region and a light chain constant region, wherein the heavy chain constant region is a human IgG₁ heavy chain constant region, and wherein the light chain constant region is a human IgG κ light chain constant region.

[0016] In one embodiment, the antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:13, 23, 33, 43, 469, 53, 63, 73, 83, 93, 103, 113, 123, 133, 143, 153, 163, 173, 183, 193, or 203.

[0017] In one embodiment, the antibody or antigen-binding fragment thereof comprises a light chain comprising the amino acid sequence of SEQ ID NO:14, 24, 34, 44, 54, 64, 74, 84, 94, 104, 114, 124, 134, 144, 154, 164, 174, 184, 194, or 204.

[0018] In one embodiment, the antibody or antigen-binding fragment thereof comprises a heavy chain and light chain comprising the amino acid sequences of: SEQ ID NOs:13 and 14, respectively; SEQ ID NOs:23 and 24, respectively; SEQ ID NOs:33 and 34, respectively; SEQ ID NOs:43 and 44, respectively; SEQ ID NOs:469 and 44, respectively; SEQ ID NOs:53 and 54, respectively; SEQ ID NOs:63 and 64, respectively; SEQ ID NOs:73 and 74, respectively; SEQ ID NOs:83 and 84, respectively; SEQ ID NOs:93 and 94, respectively; SEQ ID NOs:103 and 104, respectively; SEQ ID NOs:113 and 114, respectively; SEQ ID NOs:123 and 124, respectively; SEQ ID NOs:133 and 134, respectively; SEQ ID NOs:143 and 144, respectively; SEQ ID NOs:153 and 154, respectively; SEQ ID NOs:163 and 164, respectively; SEQ ID

NOs:173 and 174, respectively; SEQ ID NOs:183 and 184, respectively; SEQ ID NOs:193 and 194, respectively; or SEQ ID NOs:203 and 204, respectively.

[0019] Also provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, wherein the antibody or antigen-binding fragment thereof comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody selected from the group consisting of 15461, 20500, 20501, 20502, 20502.1, 22208, 15462, 22213, 15465, 20506, 15483, 20513, 22216, 15489, 20516, 15472, 15503, 15495, 15478, 15441, and 20496. In one embodiment, the CDRs are the Kabat-defined CDRs, the Chothia-defined CDRs, or the AbM-defined CDRs.

[0020] Also provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:458-463, respectively. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:464 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:469 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[0021] Also provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:35-40, respectively. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:41 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:43 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[0022] Also provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:65-70, respectively. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:71 and a variable light chain

region comprising the amino acid sequence of SEQ ID NO:72 or (ii) wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:73 and a light chain comprising the amino acid sequence of SEQ ID NO:74.

[0023] Also provided herein is an isolated antibody or antigen-binding fragment thereof that binds to the same epitope of human B7-H4 as the antibody or antigen-binding fragment thereof of any one of claims 1-20. In one embodiment, the antibody or antigen-binding fragment thereof binds to the same epitope of human B7-H4 as determined by SPR.

[0024] In one embodiment, the antibody or antigen-binding fragment thereof is a human antibody or antigen-binding fragment thereof. In one embodiment, the antibody or antigen-binding fragment thereof is a murine, humanized, or chimeric antibody or antigen-binding fragment thereof.

[0025] In one embodiment, the antibody or antigen-binding fragment thereof induces T cell proliferation. In one embodiment, the antibody or antigen-binding fragment increases T-cell proliferation by at least 21% as compared to treatment with a control antibody. In one embodiment, the antibody or antigen-binding fragment increases T-cell proliferation by about 5% to about 35% as compared to treatment with a control antibody. In one embodiment, the antibody or antigen-binding fragment thereof induces CD4⁺ T cell proliferation. In one embodiment, the antibody or antigen-binding fragment thereof increases CD4⁺ T cell proliferation by at least 9% as compared to treatment with a control antibody. In one embodiment, the antibody or antigen-binding fragment thereof increases CD4⁺ T cell proliferation by about 5% to about 15% as compared to treatment with a control antibody. In one embodiment, the antibody or antigen-binding fragment thereof induces CD8⁺ T cell proliferation. In one embodiment, the antibody or antigen-binding fragment thereof increases CD8⁺ T cell proliferation by at least 11% as compared to treatment with a control antibody. In one embodiment, the antibody or antigen-binding fragment thereof increases CD8⁺ T cell proliferation by about 5% to about 15% as compared to treatment with a control antibody.

[0026] In one embodiment, the antibody or antigen-binding fragment thereof induces interferon-gamma (IFN γ) production. In one embodiment, the antibody or antigen-binding fragment thereof is capable of increasing production of IFN γ by at least 2 fold, at least 3 fold, at least 4 fold, and at least 5 fold, at least 6 fold, at least 7 fold, at least 8 fold, about 2 fold to about 10 fold, or about 3 fold to about 10 fold.

[0027] In one embodiment, the antibody or antigen-binding fragment thereof is capable of inducing antibody dependent cell mediated cytotoxicity (ADCC) in a B7-H4-expressing cell. In

one embodiment, the antibody or antigen-binding fragment thereof induces specific lysis in at least 20%, at least 30%, at least 40%, about 20% to about 50%, or about 30% to about 50% of B7-H4 expressing cells.

[0028] In one embodiment, the antibody or antigen-binding fragment thereof inhibits tumor growth in a murine CT26 colorectal carcinoma model, a murine breast carcinoma 4T1 model, or a melanoma cell line B16-moB7-H4/H3 model. In one embodiment, the antibody or antigen-binding fragment thereof reduces tumor growth by at least 25%, at least 30%, at least 40%, at least 45%, or at least 50% as compared to treatment with a control antibody.

[0029] In one embodiment, the induction of T cell proliferation, the induction of CD4⁺ T cell proliferation, the induction of CD8⁺ T cell proliferation, the induction of IFN γ production, the ADCC activity, and/or in the inhibition of tumor growth is dose-dependent.

[0030] In one embodiment, the antibody or antigen-binding fragment thereof binds to cynomolgus monkey B7-H4. In one embodiment, the antibody or antigen-binding fragment thereof binds to rat B7-H4. In one embodiment, the antibody or antigen-binding fragment thereof binds to mouse B7-H4. In one embodiment, the antibody or antigen-binding fragment thereof binds to human B7-H4, cynomolgus monkey B7-H4, rat B7-H4 and mouse B7-H4.

[0031] In one embodiment, the antibody or antigen-binding fragment thereof binds to the IgV domain of human B7-H4.

[0032] In one embodiment, the antibody or antigen-binding fragment thereof is afucosylated.

[0033] In one embodiment, the antibody or antigen binding fragment thereof is a full length antibody. In one embodiment, the antibody or antigen binding fragment thereof is an antigen binding fragment. In one embodiment, the antigen binding fragment comprises a Fab, Fab', F(ab')₂, single chain Fv (scFv), disulfide linked Fv, V-NAR domain, IgNar, intrabody, IgG Δ CH2, minibody, F(ab')₃, tetrabody, triabody, diabody, single-domain antibody, DVD-Ig, Fcab, mAb², (scFv)₂, or scFv-Fc.

[0034] In one embodiment, the antibody or antigen-binding fragment thereof further comprises a detectable label.

[0035] Also provided herein is an isolated polynucleotide comprising a nucleic acid molecule encoding the heavy chain variable region or heavy chain of an antibody or antigen-binding fragment thereof provided herein. In one embodiment, the nucleic acid molecule encodes the VH of SEQ ID NO:11, 21, 31, 41, 464, 51, 61, 71, 81, 91, 101, 111, 121, 131, 141, 151, 161, 171, 181, 191, or 201 or the heavy chain of SEQ ID NO:13, 23, 33, 43, 469, 53, 63, 73, 83, 93, 103, 113, 123, 133, 143, 153, 163, 173, 183, 193, or 203. In one embodiment, the nucleic acid

molecule comprises the sequence of SEQ ID NO:213, 223, 233, 243, 470, 253, 263, 273, 283, 293, 303, 313, 323, 333, 343, 353, 363, 373, 383, 393, or 403. In one embodiment, the nucleic acid molecule comprises (i) the sequence of SEQ ID NO:213, 223, 233, 243, 470, 253, 263, 273, 283, 293, 303, 313, 323, 333, 343, 353, 363, 373, 383, 393, or 403 and (ii) the sequence of SEQ ID NO:408.

[0036] Also provided herein is an isolated polynucleotide comprising a nucleic acid molecule encoding the light chain variable region or light chain of an antibody or antigen-binding fragment thereof provided herein. In one embodiment, the nucleic acid molecule encodes the VL of SEQ ID NO:12, 22, 32, 42, 52, 62, 72, 82, 92, 102, 112, 122, 132, 142, 152, 162, 172, 182, 192, or 202 or the light chain of SEQ ID NO:14, 24, 34, 44, 54, 64, 74, 84, 94, 104, 114, 124, 134, 144, 154, 164, 174, 184, 194, or 204. In one embodiment, the nucleic acid molecule comprises the sequence of SEQ ID NO:214, 224, 234, 244, 254, 264, 274, 284, 294, 304, 314, 324, 334, 344, 354, 364, 374, 384, 394, or 404. In one embodiment, the nucleic acid molecule comprises (i) the sequence of SEQ ID NO:214, 224, 234, 244, 254, 264, 274, 284, 294, 304, 314, 324, 334, 344, 354, 364, 374, 384, 394, or 404 and (ii) the sequence of SEQ ID NO:406.

[0037] Also provided herein is an isolated polynucleotide comprising a nucleic acid molecule encoding the heavy chain variable region or heavy chain of an antibody or antigen-binding fragment provided herein and the light chain variable region or light chain of the antibody or antigen-binding fragment thereof.

[0038] Also provided herein is an isolated vector comprising a polynucleotide provided herein.

[0039] Also provided herein is a host cell comprising a polynucleotide provided herein, a vector provided herein, a first vector comprising one polynucleotide provided herein (e.g., a polynucleotide comprising a variable heavy chain or heavy chain encoding nucleic acid) and a second vector comprising another polynucleotide provided herein (e.g., a polynucleotide comprising variable light chain or light chain encoding nucleic acid). In one embodiment, the host cell is a cell selected from the group consisting of *E. coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, yeast, CHO, YB/20, NS0, PER-C6, HEK-293T, NIH-3T3, HeLa, BHK, Hep G2, SP2/0, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, BMT10 cell, plant cell, insect cell, and human cell in tissue culture. In one embodiment, the host cell is a CHO cell. In one embodiment, the host cell (e.g., a mammalian host cell, such as a CHO cell) lacks a functional alpha-1,6-fucosyltransferase gene (FUT8) gene.

[0040] Also provided herein is a method (e.g., an *in vitro* method) of producing an antibody

or antigen-binding fragment thereof that binds to human B7-H4 comprising culturing a host cell provided herein so that the nucleic acid molecule is expressed and the antibody or antigen-binding fragment thereof is produced.

[0041] Also provided herein is an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4 and is encoded by a polynucleotide provided herein.

[0042] Also provided herein is a pharmaceutical composition comprising an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, or a host cell provided herein; and a pharmaceutically acceptable excipient.

[0043] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments provided herein and (ii) a pharmaceutically acceptable excipient, wherein at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% , or at least 99% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated.

[0044] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments provided herein and (ii) a pharmaceutically acceptable excipient, wherein at least 95% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated.

[0045] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:458-463, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% , or at least 99% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:464 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:469 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[0046] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs: 458-

463, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 95% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO: 464 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 469 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[0047] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:35-40, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% , or at least 99% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:41 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:43 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[0048] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:35-40, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 95% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:41 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:43 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[0049] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3

and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:65-70, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% , or at least 99% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:71 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:72 or (ii) wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:73 and a light chain comprising the amino acid sequence of SEQ ID NO:74.

[0050] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:65-70, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 95% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:71 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:72 or (ii) wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:73 and a light chain comprising the amino acid sequence of SEQ ID NO:74.

[0051] In one embodiment, fucosylation is undetectable in the composition.

[0052] Also provided herein is a method for inducing T cell proliferation comprising contacting a T cell with an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein. In one embodiment, T cell proliferation is reduced by at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, or at least 80% (e.g., as compared to treatment with a control antibody).

[0053] Also provided herein is a method for inducing CD4⁺ T cell proliferation comprising contacting a CD4⁺ T cell with an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein. In one embodiment, CD4⁺ T cell proliferation is reduced by at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, or at least 80% (e.g., as compared to treatment with a control antibody).

[0054] Also provided herein is a method for inducing CD8⁺ T cell proliferation comprising contacting a CD8⁺ T cell with an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein. In one embodiment, CD8⁺ T cell proliferation is reduced by at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, or at least 80% (e.g., as compared to treatment with a control antibody).

[0055] Also provided herein is a method for inducing interferon gamma production comprising contacting a T cell with an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein. In one embodiment, interferon gamma production is increased by at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, or at least 80% (e.g., as compared to treatment with a control antibody).

[0056] Also provided herein is a method for killing a cell expressing B7-H4 comprising contacting the cell with an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein.

[0057] Also provided herein is a method for depleting B7-H4-expressing cells from a population of cells comprising contacting the population of cells with an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein.

[0058] In one embodiment, the killing or depletion occurs via ADCC.

[0059] In one embodiment, the contacting is *in vitro*. In one embodiment, the contacting is in a subject.

[0060] Also provided herein is a method of treating cancer in a subject, the method comprising administering to the subject an effective amount of an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein. In one embodiment, the cancer is selected from the group consisting of breast cancer, such as triple negative breast cancer or invasive ductal carcinoma, endometrial carcinoma, ovarian cancer, non-small cell lung cancer, pancreatic cancer, thyroid cancer, kidney cancer and bladder cancer. In one embodiment, the breast cancer is triple negative breast cancer or wherein the non-small cell lung cancer is squamous cell carcinoma. In one embodiment, the non-small cell lung cancer is an adenocarcinoma. In one embodiment, the cancer is selected from the group consisting of head

and neck cancer, small cell lung cancer, gastric cancer, and melanoma. In one embodiment, the ovarian cancer is a serous adenocarcinoma. In one embodiment, the breast cancer is a ductal adenocarcinoma.

[0061] In one embodiment, the cancer is a PD-1 inhibitor inadequate responder and/or PD-L1 inhibitor inadequate responder. In one embodiment, the cancer expresses a low level of PD-L1.

[0062] In one embodiment, the subject is human.

[0063] Also provided herein is a method for detecting B7-H4 in a sample comprising contacting said sample with an antibody or antigen-binding fragment thereof provided herein. In one embodiment, the sample is obtained from a cancer in a human subject.

[0064] Also provided herein is a kit comprising an antibody or antigen-binding fragment thereof provided herein, a polynucleotide provided herein, a vector provided herein, a host cell provided herein, or a pharmaceutical composition provided herein and a) a detection reagent, b) a B7-H4 antigen, c) a notice that reflects approval for use or sale for human administration, or d) a combination thereof.

[0065] Also provided herein is an isolated antibody or antigen-binding fragment, wherein the antibody or antigen-binding fragment thereof inhibits T cell checkpoint blockade activity of B7-H4. In one embodiment, the T cell checkpoint blockade activity is measured by an increase in IL-2 production relative to control cells.

[0066] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments and (ii) a pharmaceutically acceptable excipient, wherein the antibodies or antigen-binding fragments inhibit T cell checkpoint blockade activity of B7-H4. In an embodiment, the T cell checkpoint blockade activity is measured by an increase in IL-2 production relative to control cells.

[0066A] The present invention provides an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising:

(a) a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 41 and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 42; or

(b) a VH comprising the amino acid sequence of SEQ ID NO: 464 and a VL comprising the amino acid sequence of SEQ ID NO: 42.

[0066B] The present invention provides an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, wherein the antibody or antigen-binding fragment thereof comprises the VH and the VL of an antibody selected from the group consisting of 20502 and 20502.1.

[0066C] The present invention provides an isolated polynucleotide comprising a nucleic acid

molecule encoding the heavy chain variable region or heavy chain of the antibody or antigen-binding fragment thereof as described herein, and wherein the nucleic acid molecule encodes the VH of SEQ ID NO: 41 or 464 or the heavy chain of SEQ ID NO: 43.

[0066D] The present invention provides an isolated polynucleotide comprising a nucleic acid molecule encoding the light chain variable region or light chain of the antibody or antigen-binding fragment thereof as described herein, and wherein the nucleic acid molecule encodes the VL of SEQ ID NO: 42 or the light chain of SEQ ID NO: 44.

[0066E] The present invention provides an isolated vector comprising a polynucleotide as described herein.

[0066F] The present invention provides a host cell comprising a polynucleotide as described herein, a vector as described herein, or a first vector comprising a polynucleotide as described herein and a second vector comprising a polynucleotide as described herein.

[0066G] The present invention provides a method of producing an antibody or antigen-binding fragment thereof that binds to human B7-H4 comprising culturing a host cell as described herein so that the nucleic acid molecule is expressed and the antibody or antigen-binding fragment thereof is produced.

[0066H] The present invention provides a pharmaceutical composition comprising an antibody or antigen-binding fragment thereof as described herein and a pharmaceutically acceptable excipient.

[0066I] The present invention provides a method for inducing T cell proliferation comprising contacting a T cell with an antibody or antigen-binding fragment thereof as described herein or a pharmaceutical composition as described herein.

[0066J] The present invention provides a method for inducing CD4⁺ T cell proliferation, CD8⁺ T cell proliferation, and/or interferon gamma production comprising contacting a CD4⁺ T cell or a CD8⁺ T cell with an antibody or antigen-binding fragment thereof as described herein or a pharmaceutical composition as described herein.

[0066K] The present invention provides a method for killing a cell expressing B7-H4 comprising contacting the cell with an antibody or antigen-binding fragment thereof as described herein or a pharmaceutical composition as described herein.

[0066L] The present invention provides the use of an antibody or antigen-binding fragment thereof as described herein or a pharmaceutical composition as described herein in the preparation of a medicament for the treatment of a B7-H4 expressing cancer.

[0066M] The present invention provides a method of treating a B7-H4 expressing cancer in a subject, the method comprising administering to the subject an effective amount of an antibody or

antigen-binding fragment thereof as described herein or a pharmaceutical composition as described herein.

[0066N] The present invention provides a method for detecting B7-H4 in a sample comprising contacting said sample with an antibody or antigen-binding fragment thereof as described herein.

[0066O] The present invention provides a kit comprising an antibody or antigen-binding fragment thereof as described herein or a pharmaceutical composition as described herein and a) a detection reagent, b) a B7-H4 antigen, c) a notice that reflects approval for use or sale for human administration, or d) a combination thereof.

[0066P] The present invention provides an isolated antibody or antigen-binding fragment thereof as described herein, wherein the antibody or antigen-binding fragment thereof inhibits T cell checkpoint blockade activity of B7-H4.

BRIEF DESCRIPTION OF THE FIGURES

[0067] **Fig. 1A** shows B7-H4 expression in a variety of tumor tissues. (See Example 1.)

[0068] **Fig. 1B** shows B7-H4 prevalence in various tumor types by IHC. (See Example 1.)

[0069] **Fig. 2A** shows the binding of B7-H4 antibodies to HEK293T cells expressing human, cynomolgus monkey, or mouse B7-H4. (See Example 6.)

[0070] **Fig. 2B** shows the binding of B7-H4 antibodies to SK-BR-3 cells and to HEK293T cells expressing mouse, cynomolgus monkey, or rat B7-H4. (See Example 6.)

[0071] **Fig. 3A** shows the effect of B7-H4 antibodies on CD4⁺, CD8⁺ or total T cell proliferation. (See Example 7.)

- [0072] **Fig. 3B** shows the effect of B7-H4 antibodies on interferon-gamma (IFN γ) production. (See Example 7.)
- [0073] **Fig. 3C** shows the effect of B7-H4 antibodies on CD4⁺, CD8⁺ or total T cell proliferation and on interferon-gamma (IFN γ) production. (See Example 7.)
- [0074] **Fig. 3D** shows the effect of various concentrations of B7-H4 antibodies on interferon-gamma (IFN γ) production. (See Example 7.)
- [0075] **Figs. 4A-4D** show the binding of fucosylated and afucosylated antibodies to B7-H4 on SK-BR-3 cells (Fig. 4A) and to HEK293T cells expressing mouse (Fig. 4B), cynomolgus monkey (Fig. 4C), or rat B7-H4 (Fig. 4D). (See Example 9.)
- [0076] **Figs. 5A and 5B** show the binding of afucosylated and fucosylated B7-H4 antibodies (respectively) to human Fc γ receptor IIIa (Fc γ RIIIa) V158 allele. (See Example 10.)
- [0077] **Fig. 6A** shows the T cell checkpoint blockade activity of fucosylated and afucosylated B7-H4 antibodies. (See Example 11.)
- [0078] **Fig. 6B** shows T cell checkpoint ligand activity of afucosylated B7-H4 antibodies compared to isotype control treated cells as measured by IL-2 production. (See Example 11.)
- [0079] **Fig. 7** shows the ADCC activity of fucosylated and afucosylated B7-H4 antibodies against a B7-H4 expressing cell line. (See Example 12.)
- [0080] **Fig. 8** shows the ADCC activity of fucosylated and afucosylated B7-H4 antibodies against cells with various B7-H4 expression levels. (See Example 13.)
- [0081] **Fig. 9A** shows the *in vivo* anti-tumor efficacy of the B7-H4 antibody 20502. (See Example 14.)
- [0082] **Fig. 9B** shows the *in vivo* anti-tumor efficacy of the B7-H4 antibody 22213. (See Example 14.)
- [0083] **Fig. 10** shows the *in vivo* anti-tumor efficacy of a murine version of the B7-H4 antibody 20502 in mice implanted with 4T1 (breast carcinoma) and B16 (melanoma) cells. (See Example 14.)
- [0084] **Fig. 11** shows the *in vivo* anti-tumor efficacy of afucosylated 20502 in an MX-1 human breast cancer xenograft model. The images show human B7-H4 expression in the MX-1 xenograft tumor (left) and murine B7-H4 expression in the 4T1 tumors (right). (See Example 14.)
- [0085] **Figs. 12A-12C** show the *in vivo* anti-tumor efficacy of 20502-msIgG2a-F administered on the same day as an anti-PD-1 antibody. (See Example 15.) * indicates $p < 0.05$; and **** indicates $p < 0.0001$.

[0086] **Fig. 13** shows that treatment with afucosylated 20502 (bottom panels) results in NK cell infiltration (left panels), T-cell infiltration (center panels), and PD-L1 up-regulation (right panels) as compared to treatment with a control antibody (top panels). (See Example 16.)

[0087] **Fig. 14A** shows that 20502-msIgG2a-F antibody significantly reduces tumor growth in 4T1 breast carcinoma cells in a dose dependent manner. (See Example 17.)

[0088] **Fig. 14B** shows that 20502-msIgG2a-F antibody significantly inhibits tumor growth at 30 mg/kg ($p = 0.0003$), 20 mg/kg ($p = 0.0103$), 10 mg/kg ($p = 0.0419$), 3 mg/kg ($p = 0.0277$), and 1 mg/kg ($p = 0.0333$) as assessed by OneWay ANOVA on Day 30. (See Example 17.)

[0089] **Fig. 15A** shows that 20502-msIgG2a-F antibody significantly reduces growth of B16 expressing B7-H4/H3. (See Example 17.)

[0090] **Fig. 15B** shows that 20502-msIgG2a-F antibody significantly inhibits tumor growth at 30 mg/kg ($p = 0.0085$), 20 mg/kg ($p = 0.0041$), 10 mg/kg ($p = 0.0017$), and 3 mg/kg ($p = 0.0420$) as assessed by OneWay ANOVA on Day 23. (See Example 17.)

DETAILED DESCRIPTION

[0091] Provided herein are antibodies (*e.g.*, monoclonal antibodies) and antigen-binding fragments thereof that specifically bind to B7-H4 (*e.g.*, human B7-H4). The anti-B7-H4 antibodies and antigen-binding fragments thereof can, for example, result in T cell checkpoint blockade activity (*e.g.*, as measured by an increase in interferon-gamma ($\text{IFN}\gamma$), CD4 T-cell proliferation, CD8 T-cell proliferation, and/or total T-cell proliferation) and/or have antibody-dependent cellular cytotoxicity (ADCC activity).

[0092] Also provided are isolated nucleic acids (polynucleotides), such as complementary DNA (cDNA), encoding such antibodies and antigen-binding fragments thereof. Further provided are vectors (*e.g.*, expression vectors) and cells (*e.g.*, host cells) comprising nucleic acids (polynucleotides) encoding such antibodies and antigen-binding fragments thereof. Also provided are methods of making such antibodies and antigen-binding fragments thereof. In other aspects, provided herein are methods for treating certain conditions, such as cancer. Related compositions (*e.g.*, pharmaceutical compositions), kits, and detection methods are also provided.

1.1 Terminology

[0093] As used herein, the term “B7-H4” refers to mammalian B7-H4 polypeptides including, but not limited to, native B7-H4 polypeptides and isoforms of B7-H4 polypeptides. “B7-H4” encompasses full-length, unprocessed B7-H4 polypeptides as well as forms of B7-H4

polypeptides that result from processing within the cell. As used herein, the term "human B7-H4" refers to a polypeptide comprising the amino acid sequence of SEQ ID NO:1. A "B7-H4 polynucleotide," "B7-H4 nucleotide," or "B7-H4 nucleic acid" refer to a polynucleotide encoding B7-H4.

[0094] The term "PD-1" as used herein, refers to mammalian PD-1 polypeptides, including, but not limited to, native PD-1 polypeptides and isoforms of PD-1 polypeptides. PD-1 is also referred to as Programmed death protein 1 or Programmed cell death protein 1. "PD-1" encompasses full-length, unprocessed PD-1 polypeptides as well as forms of PD-1 polypeptides that result from processing in the cell. As used herein, the term "human PD-1" refers to a polypeptide comprising the amino acid sequence of SEQ ID NO:439:

PGWFLDSPDR	PWNPPTFSPA	LLVVTEGDNA	TFTCSFSNTS	ESFVLNWYRM
SPSNQTDKLA	AFPEDRSQPG	QDCRFRVTQL	PNGRDFHMSV	VRARRNDSGT
YLCGAISLAP	KAQIKESLRA	ELRVTERRAE	VPTAHPSPSP	RPAGQFQTLV
VGTVGGLLGS	LVLVWVLAV	ICSRAARGTI	GARRTGQPLK	EDPSAVPVFS
VDYGELDFQW	REKTPEPPVP	CVPEQTEYAT	IVFPSGMGTS	SPARRGSADG

PRSAQPLRPE DGHCSWPL (SEQ ID NO:439) (mature human PD-1 without a signal sequence). A "PD-1 polynucleotide," "PD-1 nucleotide" or "PD-1 nucleic acid" refers to a polynucleotide encoding PD-1.

[0095] The term "antibody" means an immunoglobulin molecule that recognizes and specifically binds to a target, such as a protein, polypeptide, peptide, carbohydrate, polynucleotide, lipid, or combinations of the foregoing through at least one antigen recognition site within the variable region of the immunoglobulin molecule. As used herein, the term "antibody" encompasses intact polyclonal antibodies, intact monoclonal antibodies, chimeric antibodies, humanized antibodies, human antibodies, fusion proteins comprising an antibody, and any other modified immunoglobulin molecule so long as the antibodies exhibit the desired biological activity. An antibody can be of any the five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, or subclasses (isotypes) thereof (e.g. IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2), based on the identity of their heavy-chain constant domains referred to as alpha, delta, epsilon, gamma, and mu, respectively. The different classes of immunoglobulins have different and well known subunit structures and three-dimensional configurations. Antibodies can be naked or conjugated to other molecules such as toxins, radioisotopes, etc.

[0096] The term "antibody fragment" refers to a portion of an intact antibody. An "antigen-binding fragment," "antigen-binding domain," or "antigen-binding region," refers to a portion of

an intact antibody that binds to an antigen. An antigen-binding fragment can contain the antigenic determining regions of an intact antibody (e.g., the complementarity determining regions (CDR)). Examples of antigen-binding fragments of antibodies include, but are not limited to Fab, Fab', F(ab')₂, and Fv fragments, linear antibodies, and single chain antibodies. An antigen-binding fragment of an antibody can be derived from any animal species, such as rodents (e.g., mouse, rat, or hamster) and humans or can be artificially produced.

[0097] The terms "anti-B7-H4 antibody," "B7-H4 antibody" and "antibody that binds to B7-H4" refer to an antibody that is capable of binding B7-H4 with sufficient affinity such that the antibody is useful as a diagnostic and/or therapeutic agent in targeting B7-H4. The extent of binding of an anti-B7-H4 antibody to an unrelated, non-B7-H4 protein can be less than about 10% of the binding of the antibody to B7-H4 as measured, e.g., by a radioimmunoassay (RIA).

[0098] The terms "anti-PD-1 antibody," "PD-1 antibody" and "antibody that binds to PD-1" refer to an antibody that is capable of binding PD-1 with sufficient affinity such that the antibody is useful as a diagnostic and/or therapeutic agent in targeting PD-1. The extent of binding of an anti-PD-1 antibody to an unrelated, non-PD-1 protein can be less than about 10% of the binding of the antibody to PD-1 as measured, e.g., by a radioimmunoassay (RIA).

[0099] A "monoclonal" antibody or antigen-binding fragment thereof refers to a homogeneous antibody or antigen-binding fragment population involved in the highly specific recognition and binding of a single antigenic determinant, or epitope. This is in contrast to polyclonal antibodies that typically include different antibodies directed against different antigenic determinants. The term "monoclonal" antibody or antigen-binding fragment thereof encompasses both intact and full-length monoclonal antibodies as well as antibody fragments (such as Fab, Fab', F(ab')₂, Fv), single chain (scFv) mutants, fusion proteins comprising an antibody portion, and any other modified immunoglobulin molecule comprising an antigen recognition site. Furthermore, "monoclonal" antibody or antigen-binding fragment thereof refers to such antibodies and antigen-binding fragments thereof made in any number of manners including but not limited to by hybridoma, phage selection, recombinant expression, and transgenic animals.

[00100] As used herein, the terms "variable region" or "variable domain" are used interchangeably and are common in the art. The variable region typically refers to a portion of an antibody, generally, a portion of a light or heavy chain, typically about the amino-terminal 110 to 120 amino acids or 110 to 125 amino acids in the mature heavy chain and about 90 to 115 amino acids in the mature light chain, which differ extensively in sequence among antibodies and are

used in the binding and specificity of a particular antibody for its particular antigen. The variability in sequence is concentrated in those regions called complementarity determining regions (CDRs) while the more highly conserved regions in the variable domain are called framework regions (FR). Without wishing to be bound by any particular mechanism or theory, it is believed that the CDRs of the light and heavy chains are primarily responsible for the interaction and specificity of the antibody with antigen. In certain embodiments, the variable region is a human variable region. In certain embodiments, the variable region comprises rodent or murine CDRs and human framework regions (FRs). In particular embodiments, the variable region is a primate (*e.g.*, non-human primate) variable region. In certain embodiments, the variable region comprises rodent or murine CDRs and primate (*e.g.*, non-human primate) framework regions (FRs).

[00101] The terms “VL” and “VL domain” are used interchangeably to refer to the light chain variable region of an antibody.

[00102] The terms “VH” and “VH domain” are used interchangeably to refer to the heavy chain variable region of an antibody.

[00103] The term “Kabat numbering” and like terms are recognized in the art and refer to a system of numbering amino acid residues in the heavy and light chain variable regions of an antibody or an antigen-binding fragment thereof. In certain aspects, CDRs can be determined according to the Kabat numbering system (see, *e.g.*, Kabat EA & Wu TT (1971) *Ann NY Acad Sci* 190: 382-391 and Kabat EA *et al.*, (1991) *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242). Using the Kabat numbering system, CDRs within an antibody heavy chain molecule are typically present at amino acid positions 31 to 35, which optionally can include one or two additional amino acids, following 35 (referred to in the Kabat numbering scheme as 35A and 35B) (CDR1), amino acid positions 50 to 65 (CDR2), and amino acid positions 95 to 102 (CDR3). Using the Kabat numbering system, CDRs within an antibody light chain molecule are typically present at amino acid positions 24 to 34 (CDR1), amino acid positions 50 to 56 (CDR2), and amino acid positions 89 to 97 (CDR3). In a specific embodiment, the CDRs of the antibodies described herein have been determined according to the Kabat numbering scheme.

[00104] Chothia refers instead to the location of the structural loops (Chothia and Lesk, *J. Mol. Biol.* 196:901-917 (1987)). The end of the Chothia CDR-H1 loop when numbered using the Kabat numbering convention varies between H32 and H34 depending on the length of the loop (this is because the Kabat numbering scheme places the insertions at H35A and H35B; if neither

35A nor 35B is present, the loop ends at 32; if only 35A is present, the loop ends at 33; if both 35A and 35B are present, the loop ends at 34). The AbM hypervariable regions represent a compromise between the Kabat CDRs and Chothia structural loops, and are used by Oxford Molecular's AbM antibody modeling software.

Loop	Kabat	AbM	Chothia
L1	L24-L34	L24-L34	L24-L34
L2	L50-L56	L50-L56	L50-L56
L3	L89-L97	L89-L97	L89-L97
H1	H31-H35B	H26-H35B (Kabat Numbering)	H26-H32...34
H1	H31-H35	H26-H35 (Chothia Numbering)	H26-H32
H2	H50-H65	H50-H58	H52-H56
H3	H95-H102	H95-H102	H95-H102

[00105] As used herein, the term “constant region” or “constant domain” are interchangeable and have its meaning common in the art. The constant region is an antibody portion, *e.g.*, a carboxyl terminal portion of a light and/or heavy chain which is not directly involved in binding of an antibody to antigen but which can exhibit various effector functions, such as interaction with the Fc receptor. The constant region of an immunoglobulin molecule generally has a more conserved amino acid sequence relative to an immunoglobulin variable domain. In certain aspects, an antibody or antigen-binding fragment comprises a constant region or portion thereof that is sufficient for antibody-dependent cell-mediated cytotoxicity (ADCC).

[00106] As used herein, the term “heavy chain” when used in reference to an antibody can refer to any distinct type, *e.g.*, alpha (α), delta (δ), epsilon (ϵ), gamma (γ), and mu (μ), based on the amino acid sequence of the constant domain, which give rise to IgA, IgD, IgE, IgG, and IgM classes of antibodies, respectively, including subclasses of IgG, *e.g.*, IgG₁, IgG₂, IgG₃, and IgG₄. Heavy chain amino acid sequences are well known in the art. In specific embodiments, the heavy chain is a human heavy chain.

[00107] As used herein, the term “light chain” when used in reference to an antibody can refer to any distinct type, *e.g.*, kappa (κ) or lambda (λ) based on the amino acid sequence of the constant domains. Light chain amino acid sequences are well known in the art. In specific

embodiments, the light chain is a human light chain.

[00108] The term "chimeric" antibodies or antigen-binding fragments thereof refers to antibodies or antigen-binding fragments thereof wherein the amino acid sequence is derived from two or more species. Typically, the variable region of both light and heavy chains corresponds to the variable region of antibodies or antigen-binding fragments thereof derived from one species of mammals (e.g. mouse, rat, rabbit, etc.) with the desired specificity, affinity, and capability while the constant regions are homologous to the sequences in antibodies or antigen-binding fragments thereof derived from another (usually human) to avoid eliciting an immune response in that species.

[00109] The term "humanized" antibody or antigen-binding fragment thereof refers to forms of non-human (e.g. murine) antibodies or antigen-binding fragments that are specific immunoglobulin chains, chimeric immunoglobulins, or fragments thereof that contain minimal non-human (e.g., murine) sequences. Typically, humanized antibodies or antigen-binding fragments thereof are human immunoglobulins in which residues from the complementary determining region (CDR) are replaced by residues from the CDR of a non-human species (e.g. mouse, rat, rabbit, hamster) that have the desired specificity, affinity, and capability ("CDR grafted") (Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-327 (1988); Verhoeyen et al., *Science* 239:1534-1536 (1988)). In some instances, the Fv framework region (FR) residues of a human immunoglobulin are replaced with the corresponding residues in an antibody or fragment from a non-human species that has the desired specificity, affinity, and capability. The humanized antibody or antigen-binding fragment thereof can be further modified by the substitution of additional residues either in the Fv framework region and/or within the replaced non-human residues to refine and optimize antibody or antigen-binding fragment thereof specificity, affinity, and/or capability. In general, the humanized antibody or antigen-binding fragment thereof will comprise substantially all of at least one, and typically two or three, variable domains containing all or substantially all of the CDR regions that correspond to the non-human immunoglobulin whereas all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody or antigen-binding fragment thereof can also comprise at least a portion of an immunoglobulin constant region or domain (Fc), typically that of a human immunoglobulin. Examples of methods used to generate humanized antibodies are described in U.S. Pat. 5,225,539; Roguska et al., *Proc. Natl. Acad. Sci., USA*, 91(3):969-973 (1994), and Roguska et al., *Protein Eng.* 9(10):895-904 (1996). In some embodiments, a "humanized antibody" is a resurfaced antibody.

[00110] The term "human" antibody or antigen-binding fragment thereof means an antibody or antigen-binding fragment thereof having an amino acid sequence derived from a human immunoglobulin gene locus, where such antibody or antigen-binding fragment is made using any technique known in the art. This definition of a human antibody or antigen-binding fragment thereof includes intact or full-length antibodies and fragments thereof.

[00111] An "afucosylated" antibody or antigen-binding fragment thereof or an antibody or antigen-binding fragment thereof "lacking fucose" refers to an IgG1 or IgG3 isotype antibody or antigen-binding fragment thereof that lacks fucose in its constant region glycosylation. Glycosylation of human IgG1 or IgG3 occurs at Asn297 as core fucosylated biantennary complex oligosaccharide glycosylation terminated with up to 2 Gal residues. In some embodiments, an afucosylated antibody lacks fucose at Asn297. These structures are designated as G0, G1 (a 1,6 or a 1,3), or G2 glycan residues, depending on the amount of terminal Gal residues. See, e.g., Raju, T. S., *BioProcess Int.* 1: 44-53 (2003). CHO type glycosylation of antibody Fc is described, e.g., in Routier, F. FL, *Glycoconjugate J.* 14: 201-207 (1997).

[00112] Methods of measuring fucose include any methods known in the art. For purposes herein, fucose is detected by the method described in Example 1 of WO2015/017600, which is herein incorporated by reference in its entirety. Briefly, glycan analysis is performed by releasing glycans from the antibody (e.g., by enzymatic release), labeling the glycans with anthranilic acid (2-AA), and then purifying the labeled glycans. Normal phase HPLC with fluorescent detection is used to separate the glycans and measure the relative amount of each glycan in the antibody. The glycans may be positively identified as lacking or including fucose by mass spectrometry. In some embodiments, fucose is undetectable in a composition comprising a plurality of afucosylated antibodies or antigen-binding fragments thereof. In some embodiments, an afucosylated antibody or antigen-binding fragment thereof has enhanced ADCC activity, which may be measured by the assay provided in Example 12 herein. In some embodiments, an afucosylated antibody or antigen-binding fragment thereof has enhanced affinity for Fc gamma RIIIA. In some embodiments, an afucosylated antibody or antigen-binding fragment thereof has enhanced affinity for Fc gamma RIIIA(V158). In some embodiments, an afucosylated antibody or antigen-binding fragment thereof has enhanced affinity for Fc gamma RIIIA(F158). Affinity for Fc gamma RIIIA or its alleles may be measure by the assay provided in Example 10 herein.

[00113] "Binding affinity" generally refers to the strength of the sum total of non-covalent interactions between a single binding site of a molecule (e.g., an antibody or antigen-binding fragment thereof) and its binding partner (e.g., an antigen). Unless indicated otherwise, as used

herein, “binding affinity” refers to intrinsic binding affinity which reflects a 1:1 interaction between members of a binding pair (*e.g.*, antibody or antigen-binding fragment thereof and antigen). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (K_D). Affinity can be measured and/or expressed in a number of ways known in the art, including, but not limited to, equilibrium dissociation constant (K_D), and equilibrium association constant (K_A). The K_D is calculated from the quotient of k_{off}/k_{on} , whereas K_A is calculated from the quotient of k_{on}/k_{off} . k_{on} refers to the association rate constant of, *e.g.*, an antibody or antigen-binding fragment thereof to an antigen, and k_{off} refers to the dissociation of, *e.g.*, an antibody or antigen-binding fragment thereof from an antigen. The k_{on} and k_{off} can be determined by techniques known to one of ordinary skill in the art, such as BIAcore[®] or KinExA.

[00114] As used herein, an “epitope” is a term in the art and refers to a localized region of an antigen to which an antibody or antigen-binding fragment thereof can specifically bind. An epitope can be, for example, contiguous amino acids of a polypeptide (linear or contiguous epitope) or an epitope can, for example, come together from two or more non-contiguous regions of a polypeptide or polypeptides (conformational, non-linear, discontinuous, or non-contiguous epitope). In certain embodiments, the epitope to which an antibody or antigen-binding fragment thereof binds can be determined by, *e.g.*, NMR spectroscopy, X-ray diffraction crystallography studies, ELISA assays, hydrogen/deuterium exchange coupled with mass spectrometry (*e.g.*, liquid chromatography electrospray mass spectrometry), array-based oligo-peptide scanning assays, and/or mutagenesis mapping (*e.g.*, site-directed mutagenesis mapping). For X-ray crystallography, crystallization may be accomplished using any of the known methods in the art (*e.g.*, Giegé R *et al.*, (1994) *Acta Crystallogr D Biol Crystallogr* 50(Pt 4): 339-350; McPherson A (1990) *Eur J Biochem* 189: 1-23; Chayen NE (1997) *Structure* 5: 1269-1274; McPherson A (1976) *J Biol Chem* 251: 6300-6303). Antibody/antigen-binding fragment thereof:antigen crystals can be studied using well known X-ray diffraction techniques and can be refined using computer software such as X-PLOR (Yale University, 1992, distributed by Molecular Simulations, Inc.; *see, e.g.*, *Meth Enzymol* (1985) volumes 114 & 115, eds Wyckoff HW *et al.*,; U.S. 2004/0014194), and BUSTER (Bricogne G (1993) *Acta Crystallogr D Biol Crystallogr* 49(Pt 1): 37-60; Bricogne G (1997) *Meth Enzymol* 276A: 361-423, ed Carter CW; Roversi P *et al.*, (2000) *Acta Crystallogr D Biol Crystallogr* 56(Pt 10): 1316-1323). Mutagenesis mapping studies can be accomplished using any method known to one of skill in the art. *See, e.g.*, Champe M *et al.*, (1995) *J Biol Chem* 270: 1388-1394 and Cunningham BC & Wells JA (1989) *Science* 244: 1081-1085 for a description of mutagenesis techniques, including alanine scanning

mutagenesis techniques.

[00115] A B7-H4 antibody that “binds to the same epitope” as a reference B7-H4 antibody refers to an antibody that binds to the same B7-H4 amino acid residues as the reference B7-H4 antibody. The ability of a B7-H4 antibody to bind to the same epitope as a reference B7-H4 antibody is determined by a hydrogen/deuterium exchange assay (see Coales et al. *Rapid Commun. Mass Spectrom.* 2009; 23: 639–647).

[00116] As used herein, the terms “immunospecifically binds,” “immunospecifically recognizes,” “specifically binds,” and “specifically recognizes” are analogous terms in the context of antibodies or antigen-binding fragments thereof. These terms indicate that the antibody or antigen-binding fragment thereof binds to an epitope via its antigen-binding domain and that the binding entails some complementarity between the antigen binding domain and the epitope. Accordingly, an antibody that “specifically binds” to human B7-H4 (SEQ ID NO:1) may also bind to B7-H4 from other species (e.g., cynomolgous monkey, mouse, and/or rat B7-H4) and/or B7-H4 proteins produced from other human alleles, but the extent of binding to an un-related, non-B7-H4 protein (e.g., other B7 protein family members such as PD-L1) is less than about 10% of the binding of the antibody to B7-H4 as measured, e.g., by a radioimmunoassay (RIA).

[00117] In a specific embodiment, provided herein is an antibody or antigen-binding fragment thereof that binds to human, cynomolgus monkey, mouse, and rat B7-H4.

[00118] An antibody is said to “competitively inhibit” binding of a reference antibody to a given epitope if it preferentially binds to that epitope or an overlapping epitope to the extent that it blocks, to some degree, binding of the reference antibody to the epitope. Competitive inhibition may be determined by any method known in the art, for example, competition ELISA assays. An antibody may be said to competitively inhibit binding of the reference antibody to a given epitope by at least 90%, at least 80%, at least 70%, at least 60%, or at least 50%.

[00119] A polypeptide, antibody, polynucleotide, vector, cell, or composition which is “isolated” is a polypeptide, antibody, polynucleotide, vector, cell, or composition which is in a form not found in nature. Isolated polypeptides, antibodies, polynucleotides, vectors, cell or compositions include those which have been purified to a degree that they are no longer in a form in which they are found in nature. In some embodiments, an antibody, polynucleotide, vector, cell, or composition which is isolated is substantially pure. As used herein, “substantially pure” refers to material which is at least 50% pure (i.e., free from contaminants), at least 90% pure, at least 95% pure, at least 98% pure, or at least 99% pure.

[00120] The terms "polypeptide," "peptide," and "protein" are used interchangeably herein to refer to polymers of amino acids of any length. The polymer can be linear or branched, it can comprise modified amino acids, and it can be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation or modification, such as conjugation with a labeling component. Also included within the definition are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, etc.), as well as other modifications known in the art. It is understood that, because the polypeptides of this invention are based upon antibodies, in certain embodiments, the polypeptides can occur as single chains or associated chains.

[00121] "Percent identity" refers to the extent of identity between two sequences (e.g., amino acid sequences or nucleic acid sequences). Percent identity can be determined by aligning two sequences, introducing gaps to maximize identity between the sequences. Alignments can be generated using programs known in the art. For purposes herein, alignment of nucleotide sequences can be performed with the blastn program set at default parameters, and alignment of amino acid sequences can be performed with the blastp program set at default parameters (see National Center for Biotechnology Information (NCBI) on the worldwide web, ncbi.nlm.nih.gov).

[00122] As used herein, the term "host cell" can be any type of cell, e.g., a primary cell, a cell in culture, or a cell from a cell line. In specific embodiments, the term "host cell" refers to a cell transfected with a nucleic acid molecule and the progeny or potential progeny of such a cell. Progeny of such a cell may not be identical to the parent cell transfected with the nucleic acid molecule, e.g., due to mutations or environmental influences that may occur in succeeding generations or integration of the nucleic acid molecule into the host cell genome.

[00123] The term "pharmaceutical formulation" refers to a preparation which is in such form as to permit the biological activity of the active ingredient to be effective, and which contains no additional components which are unacceptably toxic to a subject to which the formulation would be administered. The formulation can be sterile.

[00124] The terms "administer", "administering", "administration", and the like, as used herein, refer to methods that may be used to enable delivery of a drug, e.g., an anti-B7-H4 antibody or antigen-binding fragment thereof to the desired site of biological action (e.g., intravenous administration). Administration techniques that can be employed with the agents

and methods described herein are found in e.g., Goodman and Gilman, The Pharmacological Basis of Therapeutics, current edition, Pergamon; and Remington's, Pharmaceutical Sciences, current edition, Mack Publishing Co., Easton, Pa.

[00125] Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) or consecutive administration in any order.

[00126] The combination therapy can provide "synergy," i.e., the effect achieved when the active agents used together is greater than the sum of the effects that result from using the active agents separately. A synergistic effect can be attained when the active agents are: (1) co-formulated and administered or delivered simultaneously in a combined, unit dosage formulation; (2) delivered serially, by alternation, or in parallel as separate formulations; or (3) by some other regimen. When delivered in alternation therapy, a synergistic effect can be attained when the active agents are administered or delivered sequentially, e.g., by different injections in separate syringes. A "synergistic combination" produces an effect that is greater than the sum of the effects of the individual active agents of the combination.

[00127] The combination therapy can provide an "additive" effect, i.e., the effect achieved when the active agents used together is equal to the sum of the effects the result from using the active agents separately.

[00128] As used herein, the terms "subject" and "patient" are used interchangeably. The subject can be an animal. In some embodiments, the subject is a mammal such as a non-human animal (e.g., cow, pig, horse, cat, dog, rat, mouse, monkey or other primate, etc.). In some embodiments, the subject is a cynomolgus monkey. In some embodiments, the subject is a human.

[00129] The term "therapeutically effective amount" refers to an amount of a drug, e.g., an anti-B7-H4 antibody or antigen-binding fragment thereof effective to treat a disease or disorder in a subject. In the case of cancer, the therapeutically effective amount of the drug can reduce the number of cancer cells; reduce the tumor size or burden; inhibit (i.e., slow to some extent and in a certain embodiment, stop) cancer cell infiltration into peripheral organs; inhibit (i.e., slow to some extent and in a certain embodiment, stop) tumor metastasis; inhibit, to some extent, tumor growth; relieve to some extent one or more of the symptoms associated with the cancer; and/or result in a favorable response such as increased progression-free survival (PFS), disease-free survival (DFS), or overall survival (OS), complete response (CR), partial response (PR), or, in some cases, stable disease (SD), a decrease in progressive disease (PD), a reduced time to progression (TTP), or any combination thereof. To the extent the drug can prevent growth and/or

kill existing cancer cells, it can be cytostatic and/or cytotoxic.

[00130] Terms such as "treating" or "treatment" or "to treat" or "alleviating" or "to alleviate" refer to therapeutic measures that cure, slow down, lessen symptoms of, and/or halt progression of a diagnosed pathologic condition or disorder. Thus, those in need of treatment include those already diagnosed with or suspected of having the disorder. In certain embodiments, a subject is successfully "treated" for cancer according to the methods of the present invention if the patient shows one or more of the following: a reduction in the number of or complete absence of cancer cells; a reduction in the tumor size; inhibition of or an absence of cancer cell infiltration into peripheral organs including, for example, the spread of cancer into soft tissue and bone; inhibition of or an absence of tumor metastasis; inhibition or an absence of tumor growth; relief of one or more symptoms associated with the specific cancer; reduced morbidity and mortality; improvement in quality of life; reduction in tumorigenicity, tumorigenic frequency, or tumorigenic capacity, of a tumor; reduction in the number or frequency of cancer stem cells in a tumor; differentiation of tumorigenic cells to a non-tumorigenic state; increased progression-free survival (PFS), disease-free survival (DFS), or overall survival (OS), complete response (CR), partial response (PR), stable disease (SD), a decrease in progressive disease (PD), a reduced time to progression (TTP), or any combination thereof.

[00131] The terms "cancer" and "cancerous" refer to or describe the physiological condition in mammals in which a population of cells are characterized by unregulated cell growth. Examples of cancer include, but are not limited to, gynecological cancers (e.g., breast cancer (including triple negative breast cancer, ductal carcinoma), ovarian cancer, and endometrial cancer), non-small cell lung cancer, pancreatic cancer, thyroid cancer, kidney cancer (e.g., renal cell carcinoma), and bladder cancer (e.g., urothelial cell carcinoma). A non-small cell lung cancer can be e.g., an adenocarcinoma. Additional examples of cancer include, e.g., head and neck cancer, small cell lung cancer, gastric cancer, melanoma, cholangiocarcinoma, glioblastoma or glioblastoma multiforme (GBM), and merkel cell carcinoma. In one embodiment, the ovarian cancer is a serous adenocarcinoma. In one embodiment, the breast cancer is a ductal adenocarcinoma. The cancer can be a "cancer that expresses B7-H4" or a "B7-H4 expressing cancer." Such terms refer to a cancer comprising cells that express B7-H4. The cancer may be a primary tumor or may be advanced or metastatic cancer.

[00132] A "refractory" cancer is one that progresses even though an anti-tumor treatment, such as a chemotherapy, is administered to the cancer patient.

[00133] A "recurrent" cancer is one that has regrown, either at the initial site or at a distant

site, after a response to initial therapy.

[00134] A “relapsed” patient is one who has signs or symptoms of cancer after remission. Optionally, the patient has relapsed after adjuvant or neoadjuvant therapy.

[00135] “T cell checkpoint blockade activity” refers to blocking or inhibition of a T cell checkpoint activity or response. T cell checkpoint blockade activity can be measured in an artificial antigen presenting cells (aAPC) assay based on changes in IFN γ production. Primary human T cells can be enriched from PBMCs using a T cell enrichment kit (such as an EasySep™ Human T Cell Enrichment Kit or similar kit). Enriched T cells are incubated with beads (e.g., anti-CD3/anti-CD28 beads). After a period of time, the beads are magnetically removed, and T cells are washed and incubated. Next, T cells are washed and incubated along with artificial antigen presenting cells (aAPCs) in the presence of B7-H4 antibody dose titration. aAPCs can be treated with Mitomycin C and then thoroughly washed prior to adding to the T cell co-culture. After co-culture of T cells, aAPCs, and B7-H4 antibodies, plates can be centrifuged, and supernatants can be harvested and assessed for IFN γ production by ELISA. IFN γ production can be plotted vs. antibody concentration, and the EC50 potency can be calculated using nonlinear regression curve fit. Results can be measured as EC50 +/- STD in nM. T cell checkpoint blockade activity by B7-H4 antibodies can be demonstrated by an increase in IFN γ production. “T cell checkpoint blockade activity” can also be measured in an assay using cells that endogenously express B7-H4. Primary human T cells can be enriched from HLA-A2+ donor PBMCs using a T cell isolation kit (e.g., Human Pan T Cell Isolation Kit). MART-I TCR expressing T cells can be generated by first activating enriched Pan T cells with beads (e.g., anti-CD3/anti-CD28 Dynabeads), IL-2 and IL-7 for 48 hours. Activated T cells can then be transduced with MART-I TCR lentiviral particles in the presence of IL-2, IL-7 and polybrene. After transduction, MART-I TCR+ Pan T cells can be expanded over a period of time in the presence of IL-2 and IL-7. To generate HLA-A2 expressing target cell lines, the endogenous B7-H4 expressing cancer cell lines can be transduced with HLA-A2 lentiviral particles for a period of time (e.g., 48 hours). Furthermore, B7-H4 can be knocked-out of the HLA-A2+ cell line. Then, MART-I TCR+ Pan T cells can be co-cultured in the presence of the various target cell lines at a 1:1 E:T ratio, MART-I peptide and a B7-H4 antibody or a human isotype control. After co-incubation, plates can be centrifuged, and supernatants can be harvested and assessed for IL-2 production. IL-2 production can be measured by a standard immunoassay kit (such as an AlphaLISA assay or similar assay).

[00136] As used in the present disclosure and claims, the singular forms "a," "an," and "the" include plural forms unless the context clearly dictates otherwise.

[00137] It is understood that wherever embodiments are described herein with the language "comprising," otherwise analogous embodiments described in terms of "consisting of" and/or "consisting essentially of" are also provided. In this disclosure, "comprises," "comprising," "containing" and "having" and the like can have the meaning ascribed to them in U.S. Patent law and can mean "includes," "including," and the like; "consisting essentially of" or "consists essentially" likewise has the meaning ascribed in U.S. Patent law and the term is open-ended, allowing for the presence of more than that which is recited so long as basic or novel characteristics of that which is recited is not changed by the presence of more than that which is recited, but excludes prior art embodiments

[00138] Unless specifically stated or obvious from context, as used herein, the term "or" is understood to be inclusive. The term "and/or" as used in a phrase such as "A and/or B" herein is intended to include both "A and B," "A or B," "A," and "B." Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following embodiments: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[00139] As used herein, the terms "about" and "approximately," when used to modify a numeric value or numeric range, indicate that deviations of 5% to 10% above and 5% to 10% below the value or range remain within the intended meaning of the recited value or range.

[00139A] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each of the appended claims.

[00140] Any compositions or methods provided herein can be combined with one or more of any of the other compositions and methods provided herein.

1.1 Antibodies

[00141] In a specific aspect, provided herein are antibodies (e.g., monoclonal antibodies, such as chimeric, humanized, or human antibodies) and antigen-binding fragments thereof which specifically bind to B7-H4 (e.g., human B7-H4). The amino acid sequences for human, cynomolgus monkey, murine, and rat B7-H4 are known in the art and also provided herein as represented by SEQ ID NOs:1-4, respectively.

Human B7-H4:

MASLGQILFWSIISIILLAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDIKLSDIVI
QWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASRLKKNVQLTDA

GTYKCYIITSKGKGANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWAS
QVDQGANFSEVSNTSFELNSENVTMKVVSVLNVNTINNTYSCMIENDIAKATGDIKVTES
EIKRRSHLQLLNSKASLCVSSFFAISWALLPLSPYMLK (SEQ ID NO:1)

Cynomolgus monkey B7-H4:

MASLGQILFWSIISIIFILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDIKLS
D
IVIQWLKEGVIGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASRLKKNVQLTDA
GTYKCYIITSKGKGANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWAS
QVDQGANFSEVSNTSFELNSENVTMKVVSVLNVNTINNTYSCMIENDIAKATGDIKVTES
EIKRRSHLQLLNSKASLCVSSFLAISWALLPLAPYMLK (SEQ ID NO:2)

Murine B7-H4

MASLGQIIFWSIINIILAGAIALIIGFGISGKHFITVTTFTSAGNIGEDGTLSCTFEPDIKLN
G
IVIQWLKEGIKGLVHEFKEGKDDLSSQHEMFRGRTAVFADQVVVGNASRLKKNVQLTD
AGTYTCYIRTSKGKGANLEYKTGAFSMPEINVDYNASSESLRCEAPRWFPQPTVAWAS
QVDQGANFSEVSNTSFELNSENVTMKVVSVLNVNTINNTYSCMIENDIAKATGDIKVTD
SEVKRRSQLQLLNSGSPCVFSSAFVAGWALLSLSCCLMLR (SEQ ID NO:3)

Rat B7-H4

MASLGQIIFWSIINVIIILAGAIIVLIIGFGISGKHFITVTTFTSAGNIGEDGTLSCTFEPDIKLN
G
GIVIQWLKEGIKGLVHEFKEGKDDLSSQHEMFRGRTAVFADQVVVGNASRLKKNVQLT
DAGTYTCYIHTSKGKGANLEYKTGAFSMPEINVDYNASSESLRCEAPRWFPQPTVAW
ASQVDQGANFSEVSNTSFELNSENVTMKVVSVLNVNTINNTYSCMIENDIAKATGDIKV
TDSEVKRRSQLLELLNSGSPCVSSVSAAGWALLSLSCCLMLR (SEQ ID NO:4)

[00142] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof binds to human and cynomolgus monkey B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof binds to human, murine, and rat B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof binds to human, cynomolgus monkey, murine, and rat B7-H4.

[00143] B7-H4 contains an IgC ectodomain (amino acids 153-241 of SEQ ID NO:1) and an IgV domain (amino acids 35-146 of SEQ ID NO:1).

[00144] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to the IgV domain of human B7-H4. Accordingly, provided herein are antibodies and antigen-binding fragments thereof that bind to a polypeptide consisting of amino acids 35-146 of SEQ ID NO:1.

[00145] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2).

Table 1. VH CDR Amino Acid Sequences ¹

Anti-body	VH CDR1 (SEQ ID NO:)	VH CDR2 (SEQ ID NO:)	VH CDR3 (SEQ ID NO:)
15461	GSISSSSYWYG (SEQ ID NO:5)	NIYYSGSTYYNPSLKS (SEQ ID NO:6)	AREGSYPNWFDP (SEQ ID NO:7)
20500	GSIKSGSHYWG (SEQ ID NO:15)	NIYYSGSTYYNPSLRS (SEQ ID NO:16)	AREGSYPNWFDP (SEQ ID NO:17)
20501	GSIKSGSHYWG (SEQ ID NO:25)	NIYYSGSTYYNPSLKS (SEQ ID NO:26)	AREGSYPNWLDP (SEQ ID NO:27)
20502	GSIKSGSYWYG (SEQ ID NO:458)	NIYYSGSTYYNPSLRS (SEQ ID NO:459)	AREGSYPNQFDP (SEQ ID NO:460)
20502 .1	GSIKSGSYWYG (SEQ ID NO:35)	NIYYSGSTYYNPSLKS (SEQ ID NO:36)	AREGSYPNQFDP (SEQ ID NO:37)
22208	GSIKSGSHYWG (SEQ ID NO:45)	NIYYSGSTYYNPSLKS (SEQ ID NO:46)	AREGSYPNWFDP (SEQ ID NO:47)
15462	GSISSSSYWYG (SEQ ID NO:55)	NIYYSGSTYYNPSLKS (SEQ ID NO:56)	AREGSYTTVLNV (SEQ ID NO:57)
22213	GSIGRGSYWYG (SEQ ID NO:65)	NIYYSGSTYYNPSLKS (SEQ ID NO:66)	AREGSYTTVLNV (SEQ ID NO:67)
15465	GSISSGGYYWS (SEQ ID NO:75)	NIYYSGSTYYNPSLKS (SEQ ID NO:76)	ARESSTISADFDL (SEQ ID NO:77)
20506	GSISHGGYYWS (SEQ ID NO:85)	NIYYSGSTYYNPSLKS (SEQ ID NO:86)	ARESSTISADFDL (SEQ ID NO:87)
15483	GSISSGGYYWS (SEQ ID NO:95)	NIYYSGSTYYNPSLKS (SEQ ID NO:96)	ARGLSTIDEAFDP (SEQ ID NO:97)
20513	GSISDGSYYWS (SEQ ID NO:105)	NIYYSGSTYYNPSLRS (SEQ ID NO:106)	ARGLSTIDEAFDP (SEQ ID NO:107)
22216	GSISDGSYYWS (SEQ ID NO:115)	NIYYSGSTYYNPSLRS (SEQ ID NO:116)	ARGLSTIDEAFDP (SEQ ID NO:117)
15489	GSISSYYWS (SEQ ID NO:125)	YIYSSGSTNYNPSLKS (SEQ ID NO:126)	ARGSGQYAAPDYGMD V (SEQ ID NO:127)
20516	GSIISSYYWG (SEQ ID NO:135)	YIYSSGSTSYNPSLKS (SEQ ID NO:136)	ARGSGLYAAPDYGLDV (SEQ ID NO:137)
15472	FTFSSYAMS (SEQ ID NO:145)	TISGSGGSTYYADSVKG (SEQ ID NO:146)	ARGAGHYDLVGRY (SEQ ID NO:147)
15503	FTFSSYAMS (SEQ ID NO:155)	AISGSGGSTYYADSVKG (SEQ ID NO:156)	ARVGFRALNY (SEQ ID NO:157)

15495	GTFSSY AIS (SEQ ID NO:165)	GIPIFGTASYAQKFQG (SEQ ID NO:166)	ARQQYDGRRYFGL (SEQ ID NO:167)
15478	GTFSSY AIS (SEQ ID NO:175)	GIPIFGTANYAQKFQG (SEQ ID NO:176)	ARGGPWFDP (SEQ ID NO:177)
15441	FTFSSYAMS (SEQ ID NO:185)	AISGSGGSTSYADSVKG (SEQ ID NO:186)	AKPSLATMLAFDI (SEQ ID NO:187)
20496	GSISSSVYYWS (SEQ ID NO:195)	SILVSGSTYYNPSLKS (SEQ ID NO:196)	ARAVSFLDV (SEQ ID NO:197)

¹The VH CDRs in Table 1 are determined according to Kabat.

Table 2. VL CDR Amino Acid Sequences ²

Antibody	VL CDR1 (SEQ ID NO:)	VL CDR2 (SEQ ID NO:)	VL CDR3 (SEQ ID NO:)
15461	RASQSVSSNLA (SEQ ID NO:8)	GASTRAT (SEQ ID NO:9)	QQYHSFPFT (SEQ ID NO:10)
20500	RASQSVSSNLA (SEQ ID NO:18)	GASTRAT (SEQ ID NO:19)	QQYHSFPFT (SEQ ID NO:20)
20501	RASQSVSSNLA (SEQ ID NO:28)	GASTRAT (SEQ ID NO:29)	QQYHSFPFT (SEQ ID NO:30)
20502	RASQSVSSNLA (SEQ ID NO:461)	GASTRAT (SEQ ID NO:462)	QQYHSFPFT (SEQ ID NO:463)
20502.1	RASQSVSSNLA (SEQ ID NO:38)	GASTRAT (SEQ ID NO:39)	QQYHSFPFT (SEQ ID NO:40)
22208	RASQSVSTNLA (SEQ ID NO:48)	DASARVT (SEQ ID NO:49)	QQYHSFPFT (SEQ ID NO:50)
15462	RASQSVSSSYLA (SEQ ID NO:58)	GASSRAT (SEQ ID NO:59)	QQAASYPLT (SEQ ID NO:60)
22213	RASQSVASSHLA (SEQ ID NO:68)	DAVSRAT (SEQ ID NO:69)	QQAASYPLT (SEQ ID NO:70)
15465	RASQGISRWLA (SEQ ID NO:78)	AASSLQS (SEQ ID NO:79)	QQAHTFPYT (SEQ ID NO:80)
20506	RASQGISRWLA (SEQ ID NO:88)	AASSLQS (SEQ ID NO:89)	QQAHTFPYT (SEQ ID NO:90)
15483	RASQSISSWLA (SEQ ID NO:98)	KASSLES (SEQ ID NO:99)	QQDNSYPYT (SEQ ID NO:100)
20513	RASQSISSWLA (SEQ ID NO:108)	KASSLES (SEQ ID NO:109)	QQDNSYPYT (SEQ ID NO:110)
22216	RASKSISSWLA (SEQ ID NO:118)	EASSLHS (SEQ ID NO:119)	QQDNSYPYT (SEQ ID NO:120)

15489	RASQSISSWLA (SEQ ID NO:128)	KASSLES (SEQ ID NO:129)	QQDNSFPFT (SEQ ID NO:130)
20516	RASQSISSWLA (SEQ ID NO:138)	KASSLES (SEQ ID NO:139)	QQDNSFPFT (SEQ ID NO:140)
15472	RASQSISSYLN (SEQ ID NO:148)	AASSLQS (SEQ ID NO:149)	QQLYSLPPT (SEQ ID NO:150)
15503	RASQDISSWLA (SEQ ID NO:158)	AASSLQS (SEQ ID NO:159)	QQATSYPPWT (SEQ ID NO:160)
15495	RASQSVSSNLA (SEQ ID NO:168)	SASTRAT (SEQ ID NO:169)	QQVNVWPPT (SEQ ID NO:170)
15478	RASQSISSWLA (SEQ ID NO:178)	KASSLES (SEQ ID NO:179)	QQYNSYPPFT (SEQ ID NO:180)
15441	RASQSISSWLA (SEQ ID NO:188)	DASSLES (SEQ ID NO:189)	QQSKSYPRP (SEQ ID NO:190)
20496	RASQSISSYLN (SEQ ID NO: 198)	GASSLQS (SEQ ID NO: 199)	QQSYDPPWT (SEQ ID NO: 200)

[00146] ²The VL CDRs in Table 2 are determined according to Kabat.

[00147] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the VH of an antibody listed in Table 3.

Table 3: Variable Heavy Chain (VH) Amino Acid Sequences

Antibody	VH Amino Acid Sequence (SEQ ID NO)
15461	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYY CAREGSYPNWFDPWGQGTLTVSS (SEQ ID NO: 11)
20500	QLQLQESGPGLVKPSETLSLTCTVSGGSISGSHYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLRSRTISVDTSKNQFSLKLSSVTAADTAVYY CAREGSYPNWFDPWGQGTLTVSS (SEQ ID NO:21)
20501	QLQLQESGPGLVKPSETLSLTCTVSGGSISGSHYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYY CAREGSYPNWLDPWGQGTLTVSS (SEQ ID NO:31)
20502	QLQLQESGPGLVKPSETLSLTCTVSGGSISGSHYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLRSRTISVDTSKNQFSLKLSSVTAADTAVYY CAREGSYPNQFDPWGQGTLTVSS (SEQ ID NO:464)
20502.1	QLQLQESGPGLVKPSETLSLTCTVSGGSISGSHYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYY CAREGSYPNQFDPWGQGLTVSS (SEQ ID NO:41)
22208	QLQLQESGPGLVKPSETLSLTCTVSGGSISGSHYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLKSRTTMSVDTSKNQFSLKLSSVTAADTAVY YCAREGSYPNWFDPWGQGTLTVSS (SEQ ID NO:51)
15462	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYY CAREGSYTTVLNVWGQGTMTVSS (SEQ ID NO:61)
22213	QLQLQESGPGLVKPSETLSLTCTVSGGSIGRGSYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYY

	CAREGSYTTVLNVWGQGTMTVTVSS (SEQ ID NO:71)
15465	QVQLQESGPGLVKPSQTLSTCTVSGGSISGGYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVY YCARESSTISADFDLWGRGTLVTVSS (SEQ ID NO:81)
20506	QLQLQESGPGLVKPSETLSLTCTASGGSSISHGGYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLKSRTMSVDTSKNQFSLKLSSVTAADTAV YYCARESSTISADFDLWGRGTLVTVSS (SEQ ID NO:91)
15483	QVQLQESGPGLVKPSQTLSTCTVSGGSISGGYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVY YCARGLSTIDEAFDPWGQGTTLVTVSS (SEQ ID NO:101)
20513	QLQLQESGPGLVKPSETLSLTCTVSGGSISDGSYYWSWIRQHPGKGL WIGNIYYSGSTYYNPSLRSRTMSVDTSKNQFSLKLSSVTAADTAVY YCARGLSTIDEAFDPWGQGTTLVTVSS (SEQ ID NO:111)
22216	QVQLQESGPGLVKPSQTLSTCTVSGGSISDGSYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLRSRTMSVDTSKNQFSLKLSSVTAADTAV YYCARGLSTIDEAFDPWGQGTTLVTVSS (SEQ ID NO:121)
15489	QVQLQESGPGLVKPSETLSLTCTVSGGSISYYWSWIRQPPGKGLEWI GYIYSSGSTNYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RGSGQYAAPDYGMVDVWGQGTTLVTVSS (SEQ ID NO:131)
20516	QVQLQESGPGLVKPSETLSLTCTVSGGSISYYWGWIRQPPGKGLEWI GYIYSSGSTSYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RGSGLYAAPDYGLDVWGQGTTLVTVSS (SEQ ID NO:141)
15472	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLE WVSTISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAV YYCARGAGHYDLVGRYWGQGTTLVTVSS (SEQ ID NO:151)
15503	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLE WVSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAV YYCARVGFRALNYWGQGTTLVTVSS (SEQ ID NO:161)
15495	QVQLVQSGAEVKKPGSSVKVCKASGGTFSSYAISWVRQAPGQGLE WMGGIPIFGTASYAQKFQGRVTITADESTSTAYMELSSLRSED TAVY YCARQQYDGRRYFGLWGRGTLVTVSS (SEQ ID NO:171)
15478	QVQLVQSGAEVKKPGSSVKVCKASGGTFSSYAISWVRQAPGQGLE WMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSED TAVY YCARGGPWFDPWGQGTTLVTVSS (SEQ ID NO:181)
15441	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLE WVSAISGSGGSTSYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAV YYCAKPSLATMLAFDIWGQGTMTVTVSS (SEQ ID NO:191)
20496	QLQLQESGPGLVKPSETLSLTCTVSGGSISVVYYWSWIRQPPGKGLE WIGSILVSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYY CARAVSFLDVWGQGTMTVIVSS (SEQ ID NO:201)

[00148] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the VL of an antibody listed in Table 4.

Table 4: Variable Light Chain (VL) Amino Acid Sequences

Antibody	VL Amino Acid Sequence (SEQ ID NO)

15461	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLI YGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFT FGGGTKVEIK (SEQ ID NO:12)
20500	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLI YGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFT FGGGTKVEIK (SEQ ID NO:22)
20501	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLI YGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFT FGGGTKVEIK (SEQ ID NO:32)
20502 and 20502.1	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLI YGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFT FGGGTKVEIK (SEQ ID NO:42)
22208	EIVMTQSPATLSVSPGERATLSCRASQSVSTNLAWYQQKPGQAPRLLI YDASARVTGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFT FGGGTKVEIK (SEQ ID NO:52)
15462	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLI YGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASYPLT FGGGTKVEIK (SEQ ID NO:62)
22213	EIVLTQSPGTLSLSPGERATLSCRASQSVASSHLAWYQQKPGQAPRLL IYDAVSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASYPL TFGGGTKVEIK (SEQ ID NO:72)
15465	DIQMTQSPSSVSASVGDRVITITCRASQGISRWLAWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFPYT FGGGTKVEIK (SEQ ID NO:82)
20506	DIQMTQSPSSVSASVGDRVITITCRASQGISRWLAWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFPYT FGGGTKVEIK (SEQ ID NO:92)
15483	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAPKLLI YKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYT FGGGTKVEIK (SEQ ID NO:102)
20513	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAPKLLI YKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYT FGGGTKVEIK (SEQ ID NO:112)
22216	DIQMTQSPSTLSASVGDRVITITCRASKSISSWLAWYQQKPGKAPKLLI YEASSLHSGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYT FGGGTKVEIK (SEQ ID NO:122)
15489	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAPKLLI YKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPFT FGGGTKVEIK (SEQ ID NO:132)
20516	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAPKLLI YKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPFT FGGGTKVEIK (SEQ ID NO:142)
15472	DIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQLYSLPPT FGGGTKVEIK (SEQ ID NO:152)
15503	DIQLTQSPSSVSASVGDRVITITCRASQDISSWLAWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQATSYP WTFGGGTKVEIK (SEQ ID NO:162)

15495	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLI YSASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQVNVWPP TFGGGTKVEIK (SEQ ID NO:172)
15478	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLI YKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYNSYPPF TFGGGTKVEIK (SEQ ID NO:182)
15441	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLI YDASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSKSYPR TFGGGTKVEIK (SEQ ID NO:192)
20496	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLI YGASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYDPPW TFGGGTKVEIK (SEQ ID NO:202)

[00149] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the VH and the VL of an antibody listed in Tables 3 and 4 (i.e., the VH of the antibody listed in Table 3 and the VL of the same antibody listed in Table 4).

[00150] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the VH framework regions of an antibody listed in Table 5.

Table 5. VH FR Amino Acid Sequences⁴

Anti-body	VH FR1 (SEQ ID NO:)	VH FR2 (SEQ ID NO:)	VH FR3 (SEQ ID NO:)	VH FR4 (SEQ ID NO:)
15461	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:205)	WIRQPPGKGLE WIG (SEQ ID NO:206)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:207)	WGQGTLLVT VSS (SEQ ID NO:208)
20500	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:215)	WIRQPPGKGLE WIG (SEQ ID NO:216)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:217)	WGQGTLLVT VSS (SEQ ID NO:218)
20501	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:225)	WIRQPPGKGLE WIG (SEQ ID NO:226)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:227)	WGQGTLLVT VSS (SEQ ID NO:228)
20502	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:465)	WIRQPPGKGLE WIG (SEQ ID NO:466)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:467)	WGQGTLLVT VSS (SEQ ID NO:468)
20502.1	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:235)	WIRQPPGKGLE WIG (SEQ ID NO:236)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:237)	WGQGILVT VSS (SEQ ID NO:238)
22208	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:245)	WIRQPPGKGLE WIG (SEQ ID NO:246)	RVTMSVDTSKNQFS LKLSSVTAADTAVY YC (SEQ ID NO:247)	WGQGTLLVT VSS (SEQ ID NO:248)
15462	QLQLQESGPGLVK PSETLSLTCTVSG	WIRQPPGKGLE WIG (SEQ ID	RVTISVDTSKNQFSL KLSSVTAADTAVYY	WGQGTMTVT VSS (SEQ ID

	(SEQ ID NO:255)	NO:256)	C (SEQ ID NO:257)	NO:258)
22213	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:265)	WIRQPPGKGLE WIG (SEQ ID NO:266)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:267)	WGQGTMTVT VSS (SEQ ID NO:268)
15465	QVQLQESGPGLVK PSQTLSLTCTVSG (SEQ ID NO:275)	WIRQHPGKGLE WIG (SEQ ID NO:276)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:277)	WGRGTLVT VSS (SEQ ID NO:278)
20506	QLQLQESGPGLVK PSETLSLTCTASG (SEQ ID NO:285)	WIRQHPGKGLE WIG (SEQ ID NO:286)	RVTMSVDTSKNQFS LKLSSVTAADTAVY YC (SEQ ID NO:287)	WGRGTLVT VSS (SEQ ID NO:288)
15483	QVQLQESGPGLVK PSQTLSLTCTVSG (SEQ ID NO:295)	WIRQHPGKGLE WIG (SEQ ID NO:296)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:297)	WGQGTMTVT VSS (SEQ ID NO:298)
20513	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:305)	WIRQHPGKGLE WIG (SEQ ID NO:306)	RVTMSVDTSKNQFS LKLSSVTAADTAVY YC (SEQ ID NO:307)	WGQGTMTVT VSS (SEQ ID NO:308)
22216	QVQLQESGPGLVK PSQTLSLTCTVSG (SEQ ID NO:315)	WIRQHPGKGLE WIG (SEQ ID NO:316)	RVTMSVDTSKNQFS LKLSSVTAADTAVY YC (SEQ ID NO:317)	WGQGTMTVT VSS (SEQ ID NO:318)
15489	QVQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:325)	WIRQPPGKGLE WIG (SEQ ID NO:326)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:327)	WGQGTMTVT VSS (SEQ ID NO:328)
20516	QVQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:335)	WIRQPPGKGLE WIG (SEQ ID NO:336)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:337)	WGQGTMTVT VSS (SEQ ID NO:338)
15472	EVQLLES GGGLVQ PGGSLRLSCAASG (SEQ ID NO:345)	WVRQAPGKGL EWVS (SEQ ID NO:346)	RFTISRDN SKNTLYL QMNSLRAEDTAVY YC (SEQ ID NO:347)	WGQGTMTVT VSS (SEQ ID NO:348)
15503	EVQLLES GGGLVQ PGGSLRLSCAASG (SEQ ID NO:355)	WVRQAPGKGL EWVS (SEQ ID NO:356)	RFTISRDN SKNTLYL QMNSLRAEDTAVY YC (SEQ ID NO:357)	WGQGTMTVT VSS (SEQ ID NO:358)
15495	QVQLVQSGAEVK KPGSSVKV SCKAS G (SEQ ID NO:365)	WVRQAPGQGL EWMG (SEQ ID NO:366)	RVTITADESTSTAY MELSSLRSED TAVY YC (SEQ ID NO:367)	WGRGTLVT VSS (SEQ ID NO:368)
15478	QVQLVQSGAEVK KPGSSVKV SCKAS G (SEQ ID NO:375)	WVRQAPGQGL EWMG (SEQ ID NO:376)	RVTITADESTSTAY MELSSLRSED TAVY YC (SEQ ID NO:377)	WGQGTMTVT VSS (SEQ ID NO:378)
15441	EVQLLES GGGLVQ PGGSLRLSCAASG (SEQ ID NO:385)	WVRQAPGKGL EWVS (SEQ ID NO:386)	RFTISRDN SKNTLYL QMNSLRAEDTAVY YC (SEQ ID NO:387)	WGQGTMTVT VSS (SEQ ID NO:388)
20496	QLQLQESGPGLVK PSETLSLTCTVSG (SEQ ID NO:395)	WIRQPPGKGLE WIG (SEQ ID NO:396)	RVTISVDTSKNQFSL KLSSVTAADTAVYY C (SEQ ID NO:397)	WGQGTMTVI VSS (SEQ ID NO:398)

⁴The VH framework regions described in Table 5 are determined based upon the boundaries of the Kabat numbering system for CDRs. In other words, the VH CDRs are determined by Kabat and the framework regions are the amino acid residues surrounding the CDRs in the variable region in the format FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

[00151] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the VL framework regions of an antibody listed in Table 6.

Table 6. VL FR Amino Acid Sequences³

Anti-body	VL FR1 (SEQ ID NO:)	VL FR2 (SEQ ID NO:)	VL FR3 (SEQ ID NO:)	VL FR4 (SEQ ID NO:)
15461	EIVMTQSPATLSVS PGERATLSC (SEQ ID NO:209)	WYQQKPGQAP RLLIY (SEQ ID NO:210)	GIPARFSGSGSGT EFTLTISLQSEDF AVYYC (SEQ ID	FGGGTKVEI K (SEQ ID NO:212)
20500	EIVMTQSPATLSVS PGERATLSC (SEQ ID NO:219)	WYQQKPGQAP RLLIY (SEQ ID NO:220)	GIPARFSGSGSGT EFTLTISLQSEDF AVYYC (SEQ ID NO:221)	FGGGTKVEI K (SEQ ID NO:222)
20501	EIVMTQSPATLSVS PGERATLSC (SEQ ID NO:229)	WYQQKPGQAP RLLIY (SEQ ID NO:230)	GIPARFSGSGSGT EFTLTISLQSEDF AVYYC (SEQ ID NO:231)	FGGGTKVEI K (SEQ ID NO:232)
20502 and 20502.1	EIVMTQSPATLSVS PGERATLSC (SEQ ID NO:239)	WYQQKPGQAP RLLIY (SEQ ID NO:240)	GIPARFSGSGSGT EFTLTISLQSEDF AVYYC (SEQ ID NO:241)	FGGGTKVEI K (SEQ ID NO:242)
22208	EIVMTQSPATLSVS PGERATLSC (SEQ ID NO: 249)	WYQQKPGQAP RLLIY (SEQ ID NO:250)	GIPARFSGSGSGT EFTLTISLQSEDF AVYYC (SEQ ID NO:251)	FGGGTKVEI K (SEQ ID NO:252)
15462	EIVLTQSPGTLTSL PGERATLSC (SEQ ID NO:259)	WYQQKPGQAP RLLIY (SEQ ID NO:260)	GIPDRFSGSGSGT DFTLTISRLEPEDF AVYYC (SEQ ID NO:261)	FGGGTKVEI K (SEQ ID NO:262)
22213	EIVLTQSPGTLTSL PGERATLSC (SEQ ID NO:269)	WYQQKPGQAP RLLIY (SEQ ID NO:270)	GIPDRFSGSGSGT DFTLTISRLEPEDF AVYYC (SEQ ID NO:271)	FGGGTKVEI K (SEQ ID NO:272)
15465	DIQMTQSPSSVSAS VGDRVITC (SEQ ID NO:279)	WYQQKPGKAP KLLIY (SEQ ID NO:280)	GVPSRFSGSGSGT DFTLTISLQPEDF ATYYC (SEQ ID NO:281)	FGGGTKVEI K (SEQ ID NO:282)
20506	DIQMTQSPSSVSAS VGDRVITC (SEQ ID NO:289)	WYQQKPGKAP KLLIY (SEQ ID NO:290)	GVPSRFSGSGSGT DFTLTISLQPEDF ATYYC (SEQ ID NO:291)	FGGGTKVEI K (SEQ ID NO:292)

15483	DIQMTQSPSTLSAS VGDRVITC (SEQ ID NO:299)	WYQQKPGKAP KLLIY (SEQ ID NO:300)	GVPSRFSGSGSGT EFTLTISLQPDFF ATYYC (SEQ ID NO:301)	FGGGTKVEI K (SEQ ID NO:302)
20513	DIQMTQSPSTLSAS VGDRVITC (SEQ ID NO:309)	WYQQKPGKAP KLLIY (SEQ ID NO:310)	GVPSRFSGSGSGT EFTLTISLQPDFF ATYYC (SEQ ID NO:311)	FGGGTKVEI K (SEQ ID NO:312)
22216	DIQMTQSPSTLSAS VGDRVITC (SEQ ID NO:319)	WYQQKPGKAP KLLIY (SEQ ID NO:320)	GVPSRFSGSGSGT EFTLTISLQPDFF ATYYC (SEQ ID NO:321)	FGGGTKVEI K (SEQ ID NO:322)
15489	DIQMTQSPSTLSAS VGDRVITC (SEQ ID NO:329)	WYQQKPGKAP KLLIY (SEQ ID NO:330)	GVPSRFSGSGSGT EFTLTISLQPDFF ATYYC (SEQ ID NO:331)	FGGGTKVEI K (SEQ ID NO:332)
20516	DIQMTQSPSTLSAS VGDRVITC (SEQ ID NO:339)	WYQQKPGKAP KLLIY (SEQ ID NO:340)	GVPSRFSGSGSGT EFTLTISLQPDFF ATYYC (SEQ ID NO:341)	FGGGTKVEI K (SEQ ID NO:342)
15472	DIQMTQSPSSLSAS VGDRVITC (SEQ ID NO:349)	WYQQKPGKAP KLLIY (SEQ ID NO:350)	GVPSRFSGSGSGT DFTLTISLQPEDF ATYYC (SEQ ID NO:351)	FGGGTKVEI K (SEQ ID NO:352)
15503	DIQLTQSPSSVSAS VGDRVITC (SEQ ID NO:359)	WYQQKPGKAP KLLIY (SEQ ID NO:360)	GVPSRFSGSGSGT DFTLTISLQPEDF ATYYC (SEQ ID NO:361)	FGGGTKVEI K (SEQ ID NO:362)
15495	EIVMTQSPATLSVS PGERATLSC (SEQ ID NO:369)	WYQQKPGQAP RLLIY (SEQ ID NO:370)	GIPARFSGSGSGT EFTLTISLQSEDF AVYYC (SEQ ID NO:371)	FGGGTKVEI K (SEQ ID NO:372)
15478	DIQMTQSPSTLSAS VGDRVITC (SEQ ID NO:379)	WYQQKPGKAP KLLIY (SEQ ID NO:380)	GVPSRFSGSGSGT EFTLTISLQPDFF ATYYC (SEQ ID NO:381)	FGGGTKVEI K (SEQ ID NO:382)
15441	DIQMTQSPSTLSAS VGDRVITC (SEQ ID NO:389)	WYQQKPGKAP KLLIY (SEQ ID NO:390)	GVPSRFSGSGSGT EFTLTISLQPDFF ATYYC (SEQ ID NO:391)	FGGGTKVEI K (SEQ ID NO:392)

20496	DIQMTQSPSSLSAS VGDRVITC (SEQ ID NO:399)	WYQQKPGKAP KLLIY (SEQ ID NO:400)	GVPSRFSGSGSGT DFTLTISLQPEDF ATYYC (SEQ ID NO:401)	FGGGTKVEI K (SEQ ID NO:402)

³The VL framework regions described in Table 6 are determined based upon the boundaries of the Kabat numbering system for CDRs. In other words, the VL CDRs are determined by Kabat and the framework regions are the amino acid residues surrounding the CDRs in the variable region in the format FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

[00152] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the four VH framework regions and the four VL framework regions of an antibody listed in Tables 5 and 6 (i.e., the four VH framework regions of the antibody listed in Table 5 and the four VL framework regions of the same antibody listed in Table 6.)

[00153] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the heavy chain sequence of an antibody listed in Table 7.

Table 7: Full-length heavy chain amino acid sequences

Antibody	Full-Length Heavy Chain Amino Acid Sequence (SEQ ID NO)
15461	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGKGLE WIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVY YCAREGSYPNWFDPWGQGT LVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:13)
20500	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGL EWIGNIYYSGSTYYNPSLRSRTISVDTSKNQFSLKLSSVTAADTAVY YCAREGSYPNWFDPWGQGT LVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:23)
20501	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGL EWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAV YYCAREGSYPNWLDPWGQGT LVTVSSASTKGPSVFPLAPSSKSTSG

	GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:33)
20502	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGKGL EWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVY YCAREGSYPNQFDPWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:469)
20502.1	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGKGL EWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAV YYCAREGSYPNQFDPWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:43)
22208	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGL EWIGNIYYSGSTYYNPSLRSRVTMSVDTSKNQFSLKLSSVTAADTAV YYCAREGSYPNWFDPWGQGTLLTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:53)
15462	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSYWGWIRQPPGKGL WIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVY YCAREGSYTTVLNVWGQGTMTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:63)
22213	QLQLQESGPGLVKPSETLSLTCTVSGGSIGRGSYWGWIRQPPGKGL

	EWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAV YYCAREGSYTTVLNVWGQGTMTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:73)
15465	QVQLQESGPGLVKPSQTLSTCTVSGGSISSGGYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAV YYCARESSSTISADFDLWGRGTLTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:83)
20506	QLQLQESGPGLVKPSETLSLTCTASGGSISSGGYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLKSRTMSVDTSKNQFSLKLSSVTAADTAV YYCARESSSTISADFDLWGRGTLTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:93)
15483	QVQLQESGPGLVKPSQTLSTCTVSGGSISSGGYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAV YYCARGLSTIDEAFDPWGQGTMTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:103)
20513	QLQLQESGPGLVKPSETLSLTCTVSGGISDGSYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLRSRTMSVDTSKNQFSLKLSSVTAADTAV YYCARGLSTIDEAFDPWGQGTMTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

	QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:113)
22216	QVQLQESGPGLVKPSQTLSTCTVSGGSISDGSYYWSWIRQHPGKGL EWIGNIYYSGSTYYNPSLRSRVTMSVDTSKNQFSLKLSSVTAADTAV YYCARGLSTIDEAFDPWGQGTLLTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:123)
15489	QVQLQESGPGLVKPSETLSLTCTVSGGSISYYWSWIRQPPGKGLEW IGYIYSSGSTNYPNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYC ARGSGQYAAPDYGMDVWGQGTTLTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:133)
20516	QVQLQESGPGLVKPSETLSLTCTVSGGSIISSYYWGWRQPPGKGLEWI GYIYSSGSTSYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RGSGLYAAPDYGLDVWGQGTTLTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:143)
15472	EVQLLES GGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLE WVSTISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTA VYYCARGAGHYDLVGRYWGQGTLLTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:153)
15503	EVQLLES GGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLE WVSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTA VYYCARVGFRALNYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSLSSLTGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV

	NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:163)
15495	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLE WMGGIPIFGTASYAQKFQGRVTITADESTSTAYMELSSLRSED TAVYYCARQQYDGRRYFGLWGRGTLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:173)
15478	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLE WMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSED TAVYYCARGGPWFDPWGQGTLLTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:183)
15441	EVQLLESGGGLVQPGGSLRLSCAASGTFSSYAMSWVRQAPGKGLE WVSAISGSGGSTSYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTA VYYCAKPSLATMLAFDIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:193)
20496	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSVYYWSWIRQPPGKGLE WIGSILVSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYY CARAVSFLDVWGQGTMTVIVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:203)

[00154] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the light chain sequence of an antibody listed in Table 8.

Table 8: Full-length light chain amino acid sequences

Antibody	Full-Length Light Chain Amino Acid Sequence (SEQ ID NO)
15461	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLL IYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPF TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:14)
20500	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLL IYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPF TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:24)
20501	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLL IYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPF TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:34)
20502 and 20502.1	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLL IYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPF TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:44)
22208	EIVMTQSPATLSVSPGERATLSCRASQSVSTNLAWYQQKPGQAPRLL IYDASARVTGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPF TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:54)
15462	EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLL IYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASYP LTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKH KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:64)
22213	EIVLTQSPGTLSSLSPGERATLSCRASQSVASSHLAWYQQKPGQAPRL LIYDAVSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASY PLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEK HKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:74)
15465	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAPKL LIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFP YTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKH KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:84)
20506	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAPKL LIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFP YTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLTLSKADYEKH KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:94)
15483	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLL IYKASSLESQVPSRFSGSGSGTEFTLTISSLQPDFAVYYCQQDNSYP

	YTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:104)
20513	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLL IYKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYP YTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:114)
22216	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLL IYEASSLHSGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYP YTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:124)
15489	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLL IYKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPF TFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:134)
20516	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLL IYKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPF TFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:144)
15472	DIQMTQSPSSLASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQLYSLPP TFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:154)
15503	DIQLTQSPSSVSASVGDRVTITCRASQDISSWLAWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQATSYP WTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEK HKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:164)
15495	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLL IYSASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQVNVWP PTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:174)
15478	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLL IYKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYNSYPP FTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK KVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:184)
15441	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLL IYDASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQSKSYPR TFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:194)

20496	DIQMTQSPSSLSASVGDRVITTCRASQSISSYLNWYQQKPGKAPKLLI YGASSLQSGVPSRFSGSGSGTDFLTISLQPEDFATYYCQQSYDPPW TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:204)

[00155] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4 and comprises the heavy chain sequence and the light chain sequence of an antibody listed in Tables 7 and 8 (i.e., the heavy chain sequence of the antibody listed in Table 7 and the light chain sequence of the same antibody listed in Table 8).

[00156] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 80% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 80% identical to the VL sequence of the same antibody in Table 4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 85% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 85% identical to the VL sequence of the same antibody in Table 4.

[00157] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 90% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 90% identical to the VL sequence of the same antibody in Table 4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 95% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 95% identical to the VL sequence of the same antibody in Table 4.

[00158] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 96% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 96% identical to the VL sequence of the same antibody in Table 4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 97% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 97% identical to the VL sequence of the same antibody in Table 4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 98% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 98% identical to the VL sequence of the same antibody in Table 4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), and comprises a VH comprising a sequence at least 99% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 99% identical to the VL sequence of the same antibody in Table 4.

[00159] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 80% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 80% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least

85% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 85% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4.

[00160] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 90% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 90% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 95% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 95% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4.

[00161] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 96% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 96% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 97% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 97% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 98% identical to the VH sequence of the same antibody in Table 3

and a VL comprising a sequence at least 98% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 99% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 99% identical to the VL sequence of the same antibody in Table 4, and binds to human, cynomolgus monkey, rat, and/or mouse B7-H4.

[00162] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 80% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 80% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and mediates ADCC activity against B7-H4-expressing cells. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 85% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 85% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and mediates ADCC activity against B7-H4-expressing cells.

[00163] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 90% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 90% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and/or mediates ADCC activity against B7-H4-expressing cells. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in

Table 2), comprises a VH comprising a sequence at least 95% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 95% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and mediates ADCC activity against B7-H4-expressing cells.

[00164] In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 96% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 96% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and mediates ADCC activity against B7-H4-expressing cells. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 97% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 97% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and mediates ADCC activity against B7-H4-expressing cells. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 98% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 98% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and mediates ADCC activity against B7-H4-expressing cells. In certain embodiments, an antibody or antigen-binding fragment thereof described herein binds to human B7-H4, comprises the six CDRs of an antibody listed in Tables 1 and 2 (i.e., the three VH CDRs of the antibody listed in Table 1 and the three VL CDRs of the same antibody listed in Table 2), comprises a VH comprising a sequence at least 99% identical to the VH sequence of the same antibody in Table 3 and a VL comprising a sequence at least 99% identical to the VL sequence of the same antibody in Table 4, increases T cell proliferation, increases IFN γ production, and mediates ADCC activity against B7-H4-expressing cells.

[00165] In certain aspects, an antibody or antigen-binding fragment thereof described herein

may be described by its VL domain alone, or its VH domain alone, or by its 3 VL CDRs alone, or its 3 VH CDRs alone. See, for example, Rader C et al., (1998) PNAS 95: 8910-8915, which is incorporated herein by reference in its entirety, describing the humanization of the mouse anti- $\alpha\beta 3$ antibody by identifying a complementing light chain or heavy chain, respectively, from a human light chain or heavy chain library, resulting in humanized antibody variants having affinities as high or higher than the affinity of the original antibody. See also Clackson T et al., (1991) Nature 352: 624-628, which is incorporated herein by reference in its entirety, describing methods of producing antibodies that bind a specific antigen by using a specific VL domain (or VH domain) and screening a library for the complementary variable domains. The screen produced 14 new partners for a specific VH domain and 13 new partners for a specific VL domain, which were strong binders, as determined by ELISA. See also Kim SJ & Hong HJ, (2007) J Microbiol 45: 572-577, which is incorporated herein by reference in its entirety, describing methods of producing antibodies that bind a specific antigen by using a specific VH domain and screening a library (e.g., human VL library) for complementary VL domains; the selected VL domains in turn could be used to guide selection of additional complementary (e.g., human) VH domains.

[00166] In certain aspects, the CDRs of an antibody or antigen-binding fragment thereof can be determined according to the Chothia numbering scheme, which refers to the location of immunoglobulin structural loops (see, e.g., Chothia C & Lesk AM, (1987), J Mol Biol 196: 901-917; Al-Lazikani B et al., (1997) J Mol Biol 273: 927-948; Chothia C et al., (1992) J Mol Biol 227: 799-817; Tramontano A et al., (1990) J Mol Biol 215(1): 175-82; and U.S. Patent No. 7,709,226). Typically, when using the Kabat numbering convention, the Chothia CDR-H1 loop is present at heavy chain amino acids 26 to 32, 33, or 34, the Chothia CDR-H2 loop is present at heavy chain amino acids 52 to 56, and the Chothia CDR-H3 loop is present at heavy chain amino acids 95 to 102, while the Chothia CDR-L1 loop is present at light chain amino acids 24 to 34, the Chothia CDR-L2 loop is present at light chain amino acids 50 to 56, and the Chothia CDR-L3 loop is present at light chain amino acids 89 to 97. The end of the Chothia CDR-H1 loop when numbered using the Kabat numbering convention varies between H32 and H34 depending on the length of the loop (this is because the Kabat numbering scheme places the insertions at H35A and H35B; if neither 35A nor 35B is present, the loop ends at 32; if only 35A is present, the loop ends at 33; if both 35A and 35B are present, the loop ends at 34).

[00167] In certain aspects, provided herein are antibodies and antigen-binding fragments thereof that specifically bind to B7-H4 (e.g., human B7-H4) and comprise the Chothia VH and

VL CDRs of an antibody listed in Tables 3 and 4. In certain embodiments, antibodies or antigen-binding fragments thereof that specifically bind to B7-H4 (e.g., human B7-H4) comprise one or more CDRs, in which the Chothia and Kabat CDRs have the same amino acid sequence. In certain embodiments, provided herein are antibodies and antigen-binding fragments thereof that specifically bind to B7-H4 (e.g., human B7-H4) and comprise combinations of Kabat CDRs and Chothia CDRs.

[00168] In certain aspects, the CDRs of an antibody or antigen-binding fragment thereof can be determined according to the IMGT numbering system as described in Lefranc M-P, (1999) *The Immunologist* 7: 132-136 and Lefranc M-P et al., (1999) *Nucleic Acids Res* 27: 209-212. According to the IMGT numbering scheme, VH-CDR1 is at positions 26 to 35, VH-CDR2 is at positions 51 to 57, VH-CDR3 is at positions 93 to 102, VL-CDR1 is at positions 27 to 32, VL-CDR2 is at positions 50 to 52, and VL-CDR3 is at positions 89 to 97. In a particular embodiment, provided herein are antibodies and antigen-binding fragments thereof that specifically bind to B7-H4 (e.g., human B7-H4) and comprise the IMGT VH and VL CDRs of an antibody listed in Tables 3 and 4, for example, as described in Lefranc M-P (1999) *supra* and Lefranc M-P et al., (1999) *supra*.

[00169] In certain aspects, the CDRs of an antibody or antigen-binding fragment thereof can be determined according to MacCallum RM et al., (1996) *J Mol Biol* 262: 732-745. See also, e.g., Martin A. "Protein Sequence and Structure Analysis of Antibody Variable Domains," in *Antibody Engineering*, Kontermann and Dübel, eds., Chapter 31, pp. 422-439, Springer-Verlag, Berlin (2001). In a particular embodiment, provided herein are antibodies or antigen-binding fragments thereof that specifically bind to B7-H4 (e.g., human B7-H4) and comprise VH and VL CDRs of an antibody listed in Tables 3 and 4 as determined by the method in MacCallum RM et al.

[00170] In certain aspects, the CDRs of an antibody or antigen-binding fragment thereof can be determined according to the AbM numbering scheme, which refers AbM hypervariable regions which represent a compromise between the Kabat CDRs and Chothia structural loops, and are used by Oxford Molecular's AbM antibody modeling software (Oxford Molecular Group, Inc.). In a particular embodiment, provided herein are antibodies or antigen-binding fragments thereof that specifically bind to B7-H4 (e.g., human B7-H4) and comprise VH and VL CDRs of an antibody listed in Tables 3 and 4 as determined by the AbM numbering scheme.

[00171] In specific aspects, provided herein are antibodies that comprise a heavy chain and a light chain. With respect to the heavy chain, in a specific embodiment, the heavy chain of an

antibody described herein can be an alpha (α), delta (δ), epsilon (ϵ), gamma (γ) or mu (μ) heavy chain. In another specific embodiment, the heavy chain of an antibody described can comprise a human alpha (α), delta (δ), epsilon (ϵ), gamma (γ) or mu (μ) heavy chain. In a particular embodiment, an antibody described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises a heavy chain wherein the amino acid sequence of the VH domain comprises an amino acid sequence set forth in Table 3 and wherein the constant region of the heavy chain comprises the amino acid sequence of a human gamma (γ) heavy chain constant region. In a specific embodiment, an antibody described herein, which specifically binds to B7-H4 (e.g., human B7-H4), comprises a heavy chain wherein the amino acid sequence of the VH domain comprises a sequence set forth in Table 3, and wherein the constant region of the heavy chain comprises the amino acid of a human heavy chain described herein or known in the art. Non-limiting examples of human constant region sequences have been described in the art, e.g., see U.S. Patent No. 5,693,780 and Kabat EA et al., (1991) *supra*.

[00172] With respect to the light chain, in a specific embodiment, the light chain of an antibody described herein is a kappa light chain. The constant region of a human kappa light chain can comprise the following amino acid sequence:

[00173] RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
ID NO:405).

[00174] The constant region of a human kappa light chain can be encoded by the following nucleotide sequence:

[00175] CGGACCGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAG
TTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAG
GCCAAAGTACAGTGGAAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAG
TGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCCTGACGC
TGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAG
GGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT (SEQ ID NO:406).

[00176] In another specific embodiment, the light chain of an antibody described herein is a lambda light chain. In yet another specific embodiment, the light chain of an antibody described herein is a human kappa light chain or a human lambda light chain. In a particular embodiment, an antibody described herein, which immunospecifically binds to a B7-H4 polypeptide (e.g., human B7-H4) comprises a light chain wherein the amino acid sequence of the VL domain comprises a sequence set forth in Table 4, and wherein the constant region of the light chain

comprises the amino acid sequence of a human kappa light chain constant region. In another particular embodiment, an antibody described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) comprises a light chain wherein the amino acid sequence of the VL domain comprises a sequence set forth in Table 4 and wherein the constant region of the light chain comprises the amino acid sequence of a human lambda light chain constant region. In a specific embodiment, an antibody described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) comprises a light chain wherein the amino acid sequence of the VL domain comprises a sequence set forth in Table 4 and wherein the constant region of the light chain comprises the amino acid sequence of a human kappa or lambda light chain constant region. Non-limiting examples of human constant region sequences have been described in the art, e.g., see U.S. Patent No. 5,693,780 and Kabat EA et al., (1991) *supra*.

[00177] In a specific embodiment, an antibody described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) comprises a VH domain and a VL domain comprising any amino acid sequence described herein, and wherein the constant regions comprise the amino acid sequences of the constant regions of an IgG, IgE, IgM, IgD, IgA, or IgY immunoglobulin molecule, or a human IgG, IgE, IgM, IgD, IgA, or IgY immunoglobulin molecule. In another specific embodiment, an antibody described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) comprises a VH domain and a VL domain comprising any amino acid sequence described herein, and wherein the constant regions comprise the amino acid sequences of the constant regions of an IgG, IgE, IgM, IgD, IgA, or IgY immunoglobulin molecule, any class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2), or any subclass (e.g., IgG2a and IgG2b) of immunoglobulin molecule. In a particular embodiment, the constant regions comprise the amino acid sequences of the constant regions of a human IgG, IgE, IgM, IgD, IgA, or IgY immunoglobulin molecule, any class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2), or any subclass (e.g., IgG2a and IgG2b) of immunoglobulin molecule.

[00178] The constant region of a human IgG1 heavy chain can comprise the following amino acid sequence:

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:407).

[00179] The constant region of a human IgG₁ heavy chain can be encoded by the following nucleotide sequence:

GCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCTCCTCCAAGAGCACCTCT
GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGAC
GGTGTCTGTGGAACCTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCT
ACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTT
GGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGG
ACAAGAAAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCCACCGTGCCCA
GCACCTGAACTCCTGGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCCAAGGAC
ACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCAC
GAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGC
CAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCC
TCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCC
AACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCC
CCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACC
AGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGT
GGGAGAGCAATGGGCAGCCGGAGAACAACCTACAAGACCACGCCTCCCGTGCTGGAC
TCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG
CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACG
CAGAAGAGCCTCTCCCTGTCTCCGGGTAAA. (SEQ ID NO:408)

[00180] Non-limiting examples of human constant regions are described in the art, *e.g.*, see Kabat EA *et al.*, (1991) *supra*.

[00181] In certain embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into the Fc region of an antibody or antigen-binding fragment thereof described herein (*e.g.*, CH2 domain (residues 231-340 of human IgG₁) and/or CH3 domain (residues 341-447 of human IgG₁) and/or the hinge region, with numbering according to the Kabat numbering system (*e.g.*, the EU index in Kabat)) to alter one or more functional properties of the antibody or antigen-binding fragment thereof, such as serum half-life, complement fixation, Fc receptor binding, and/or antigen-dependent cellular cytotoxicity.

[00182] In certain embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into the hinge region of the Fc region (CH1 domain) such that the number of cysteine residues in the hinge region are altered (*e.g.*, increased or decreased) as described in, *e.g.*, U.S. Patent No. 5,677,425. The number of cysteine residues in the hinge region of the CH1

domain may be altered to, *e.g.*, facilitate assembly of the light and heavy chains, or to alter (*e.g.*, increase or decrease) the stability of the antibody or antigen-binding fragment thereof.

[00183] In some embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into the Fc region of an antibody or antigen-binding fragment thereof described herein (*e.g.*, CH2 domain (residues 231-340 of human IgG1) and/or CH3 domain (residues 341-447 of human IgG1) and/or the hinge region, with numbering according to the Kabat numbering system (*e.g.*, the EU index in Kabat)) to increase or decrease the affinity of the antibody or antigen-binding fragment thereof for an Fc receptor (*e.g.*, an activated Fc receptor) on the surface of an effector cell. Mutations in the Fc region that decrease or increase affinity for an Fc receptor and techniques for introducing such mutations into the Fc receptor or fragment thereof are known to one of skill in the art. Examples of mutations in the Fc receptor that can be made to alter the affinity of the antibody or antigen-binding fragment thereof for an Fc receptor are described in, *e.g.*, Smith P et al., (2012) PNAS 109: 6181-6186, U.S. Patent No. 6,737,056, and International Publication Nos. WO 02/060919; WO 98/23289; and WO 97/34631, which are incorporated herein by reference.

[00184] In a specific embodiment, one, two, or more amino acid mutations (*i.e.*, substitutions, insertions or deletions) are introduced into an IgG constant domain, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc domain fragment) to alter (*e.g.*, decrease or increase) half-life of the antibody or antigen-binding fragment thereof *in vivo*. See, *e.g.*, International Publication Nos. WO 02/060919; WO 98/23289; and WO 97/34631; and U.S. Patent Nos. 5,869,046, 6,121,022, 6,277,375 and 6,165,745 for examples of mutations that will alter (*e.g.*, decrease or increase) the half-life of an antibody or antigen-binding fragment thereof *in vivo*. In some embodiments, one, two or more amino acid mutations (*i.e.*, substitutions, insertions, or deletions) are introduced into an IgG constant domain, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc domain fragment) to decrease the half-life of the antibody or antigen-binding fragment thereof *in vivo*. In other embodiments, one, two or more amino acid mutations (*i.e.*, substitutions, insertions or deletions) are introduced into an IgG constant domain, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc domain fragment) to increase the half-life of the antibody or antigen-binding fragment thereof *in vivo*. In a specific embodiment, the antibodies or antigen-binding fragments thereof may have one or more amino acid mutations (*e.g.*, substitutions) in the second constant (CH2) domain (residues 231-340 of human IgG1) and/or the third constant (CH3) domain (residues 341-447 of human IgG1), with numbering according to the EU index in Kabat (Kabat EA et al., (1991) *supra*). In a specific embodiment,

the constant region of the IgG1 comprises a methionine (M) to tyrosine (Y) substitution in position 252, a serine (S) to threonine (T) substitution in position 254, and a threonine (T) to glutamic acid (E) substitution in position 256, numbered according to the EU index as in Kabat. See U.S. Patent No. 7,658,921, which is incorporated herein by reference. This type of mutant IgG, referred to as “YTE mutant” has been shown to display fourfold increased half-life as compared to wild-type versions of the same antibody (see Dall’Acqua WF et al., (2006) J Biol Chem 281: 23514-24). In certain embodiments, an antibody or antigen-binding fragment thereof comprises an IgG constant domain comprising one, two, three or more amino acid substitutions of amino acid residues at positions 251-257, 285-290, 308-314, 385-389, and 428-436, numbered according to the EU index as in Kabat.

[00185] In a further embodiment, one, two, or more amino acid substitutions are introduced into an IgG constant domain Fc region to alter the effector function(s) of the antibody or antigen-binding fragment thereof. For example, one or more amino acids selected from amino acid residues 234, 235, 236, 237, 297, 318, 320 and 322, numbered according to the EU index as in Kabat, can be replaced with a different amino acid residue such that the antibody or antigen-binding fragment thereof has an altered affinity for an effector ligand but retains the antigen-binding ability of the parent antibody. The effector ligand to which affinity is altered can be, for example, an Fc receptor or the C1 component of complement. This approach is described in further detail in U.S. Patent Nos. 5,624,821 and 5,648,260. In some embodiments, the deletion or inactivation (through point mutations or other means) of a constant region domain may reduce Fc receptor binding of the circulating antibody or antigen-binding fragment thereof thereby increasing tumor localization. See, e.g., U.S. Patent Nos. 5,585,097 and 8,591,886 for a description of mutations that delete or inactivate the constant domain and thereby increase tumor localization. In certain embodiments, one or more amino acid substitutions can be introduced into the Fc region to remove potential glycosylation sites on Fc region, which may reduce Fc receptor binding (see, e.g., Shields RL et al., (2001) J Biol Chem 276: 6591-604).

[00186] In certain embodiments, one or more amino acids selected from amino acid residues 329, 331, and 322 in the constant region, numbered according to the EU index as in Kabat, can be replaced with a different amino acid residue such that the antibody or antigen-binding fragment thereof has altered C1q binding and/or reduced or abolished complement dependent cytotoxicity (CDC). This approach is described in further detail in U.S. Patent No. 6,194,551 (Idusogie et al). In some embodiments, one or more amino acid residues within amino acid positions 231 to 238 in the N-terminal region of the CH2 domain are altered to thereby alter the

ability of the antibody to fix complement. This approach is described further in International Publication No. WO 94/29351. In certain embodiments, the Fc region is modified to increase the ability of the antibody or antigen-binding fragment thereof to mediate antibody dependent cellular cytotoxicity (ADCC) and/or to increase the affinity of the antibody or antigen-binding fragment thereof for an Fc γ receptor by mutating one or more amino acids (e.g., introducing amino acid substitutions) at the following positions: 238, 239, 248, 249, 252, 254, 255, 256, 258, 265, 267, 268, 269, 270, 272, 276, 278, 280, 283, 285, 286, 289, 290, 292, 293, 294, 295, 296, 298, 301, 303, 305, 307, 309, 312, 315, 320, 322, 324, 326, 327, 328, 329, 330, 331, 333, 334, 335, 337, 338, 340, 360, 373, 376, 378, 382, 388, 389, 398, 414, 416, 419, 430, 434, 435, 437, 438, or 439, numbered according to the EU index as in Kabat. This approach is described further in International Publication No. WO 00/42072.

[00187] In certain embodiments, an antibody or antigen-binding fragment thereof described herein comprises the constant domain of an IgG1 with a mutation (e.g., substitution) at position 267, 328, or a combination thereof, numbered according to the EU index as in Kabat. In certain embodiments, an antibody or antigen-binding fragment thereof described herein comprises the constant domain of an IgG1 with a mutation (e.g., substitution) selected from the group consisting of S267E, L328F, and a combination thereof. In certain embodiments, an antibody or antigen-binding fragment thereof described herein comprises the constant domain of an IgG1 with a S267E/L328F mutation (e.g., substitution). In certain embodiments, an antibody or antigen-binding fragment thereof described herein comprising the constant domain of an IgG1 with a S267E/L328F mutation (e.g., substitution) has an increased binding affinity for Fc γ RIIA, Fc γ RIIB, or Fc γ RIIA and Fc γ RIIB.

[00188] Antibodies with reduced fucose content have been reported to have an increased affinity for Fc receptors, such as, e.g., Fc γ RIIA. Accordingly, in certain embodiments, an antibody or antigen-binding fragment thereof described herein has reduced fucose content or lacks fucose (i.e., is “afucosylated”). Such antibodies or antigen-binding fragments thereof can be produced using techniques known to one skilled in the art. For example, they can be expressed in cells deficient or lacking the ability to fucosylate. In a specific example, cell lines with a knockout of both alleles of α 1,6-fucosyltransferase can be used to produce antibodies or antigen-binding fragments thereof with reduced fucose content. The Potelligent® system (Lonza) is an example of such a system that can be used to produce antibodies and antigen-binding fragments thereof with reduced fucose content. Alternatively, antibodies or antigen-

binding fragments thereof with reduced fucose content or no fucose content can be produced by, e.g.: (i) culturing cells under conditions which prevent or reduce fucosylation; (ii) posttranslational removal of fucose (e.g., with a fucosidase enzyme); (iii) post-translational addition of the desired carbohydrate, e.g., after recombinant expression of a non-glycosylated glycoprotein; or (iv) purification of the glycoprotein so as to select for antibodies or antigen-binding fragments thereof which are not fucosylated. See, e.g., Longmore GD & Schachter H (1982) *Carbohydr Res* 100: 365-92 and Imai-Nishiya H et al., (2007) *BMC Biotechnol.* 7: 84 for methods for producing antibodies thereof with no fucose content or reduced fucose content. See also Example 8 herein describing the production of afucosylated B7-H4 antibodies.

[00189] In some embodiments, the B7-H4 antibody or antigen-binding fragment thereof has enhanced ADCC activity in vitro compared to fucosylated B7-H4 antibodies or antigen-binding fragments thereof having the same amino acid sequence. In some embodiments, the afucosylated B7-H4 antibodies or antigen-binding fragments thereof cause specific lysis that is at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 60, at least 65, at least 70, or at least 75 percentage points greater than specific lysis with fucosylated B7-H4 antibodies.

[00190] In some embodiments, the B7-H4 antibody or antigen-binding fragment thereof has enhanced affinity for Fc gamma RIIIA compared to fucosylated B7-H4 antibodies or antigen-binding fragments thereof having the same amino acid sequence. In some embodiments, the afucosylated B7-H4 antibodies or antigen-binding fragments thereof bind to Fc gamma RIIIA with at least 2-fold, at least 3-fold, at least 4-fold, at least 5-fold, at least 7-fold, at least 10-fold, at least 12-fold, at least 15-fold, at least 17-fold, or at least 20-fold greater affinity than fucosylated B7-H4 antibodies or antigen-binding fragments thereof. In some embodiments, affinity for Fc gamma RIIIA is determined using surface plasmon resonance. In some embodiments, Fc gamma RIIIA is selected from Fc gamma RIIIA(V158) and Fc gamma RIIIA(F158). In some embodiments, Fc gamma RIIIA is Fc gamma RIIIA(V158).

[00191] In some embodiments, the presence of fucose can be determined by a method comprising high performance liquid chromatography (HPLC), capillary electrophoresis, or MALDI-TOF mass spectrometry.

[00192] In specific embodiments, an antibody or antigen-binding fragment thereof (i) comprises the CDR sequences of 20502 (e.g., the amino acid sequences of SEQ ID NOs:458-463), the VH and VL sequences of 20502 (the amino acid sequences of SEQ ID NOs:464 and 42, respectively), or the heavy and light chain sequences of 20502 (the amino acid sequences of SEQ

ID NOs:469 and 44, respectively) and (ii) is afucosylated.

[00193] In specific embodiments, a composition comprises antibodies or antigen-binding fragments thereof that (i) comprises the CDR sequences of 20502 (e.g., the amino acid sequences of SEQ ID NOs:458-463), the VH and VL sequences of 20502 (the amino acid sequences of SEQ ID NOs:464 and 42, respectively), or the heavy and light chain sequences of 20502 (the amino acid sequences of SEQ ID NOs:469 and 44, respectively) and (ii) are afucosylated, e.g., wherein at least 95% of the antibodies in the composition are afucosylated or wherein fucosylation is undetectable in the composition.

[00194] In specific embodiments, an antibody or antigen-binding fragment thereof (i) comprises the CDR sequences of 20502.1 (e.g., the amino acid sequences of SEQ ID NOs:35-40), the VH and VL sequences of 20502.1 (the amino acid sequences of SEQ ID NOs:41 and 42, respectively), or the heavy and light chain sequences of 20502.1 (the amino acid sequences of SEQ ID NOs:43 and 44, respectively) and (ii) is afucosylated.

[00195] In specific embodiments, a composition comprises antibodies or antigen-binding fragments thereof that (i) comprises the CDR sequences of 20502.1 (e.g., the amino acid sequences of SEQ ID NOs:35-40), the VH and VL sequences of 20502.1 (the amino acid sequences of SEQ ID NOs:41 and 42, respectively), or the heavy and light chain sequences of 20502.1 (the amino acid sequences of SEQ ID NOs:43 and 44, respectively) and (ii) are afucosylated, e.g., wherein at least 95% of the antibodies in the composition are afucosylated or wherein fucosylation is undetectable in the composition.

[00196] In specific embodiments, an antibody or antigen-binding fragment thereof (i) comprises the CDR sequences of 22213 (e.g., the amino acid sequences of SEQ ID NOs:65-70), the VH and VL sequences of 22213 (the amino acid sequences of SEQ ID NOs:71 and 72, respectively), or the heavy and light chain sequences of 22213 (the amino acid sequences of SEQ ID NOs:73 and 74, respectively) and (ii) is afucosylated.

[00197] In specific embodiments, a composition comprises antibodies or antigen-binding fragments thereof that (i) comprises the CDR sequences of 22213 (e.g., the amino acid sequences of SEQ ID NOs:65-70), the VH and VL sequences of 22213 (the amino acid sequences of SEQ ID NOs:71 and 72, respectively), or the heavy and light chain sequences of 22213 (the amino acid sequences of SEQ ID NOs:73 and 74, respectively) and (ii) are afucosylated, e.g., wherein at least 95% of the antibodies in the composition are afucosylated or wherein fucosylation is undetectable in the composition.

[00198] Engineered glycoforms may be useful for a variety of purposes, including but not

limited to enhancing or reducing effector function. Methods for generating engineered glycoforms in an antibody or antigen-binding fragment thereof described herein include but are not limited to those disclosed, e.g., in Umaña P et al., (1999) *Nat Biotechnol* 17: 176-180; Davies J et al., (2001) *Biotechnol Bioeng* 74: 288-294; Shields RL et al., (2002) *J Biol Chem* 277: 26733-26740; Shinkawa T et al., (2003) *J Biol Chem* 278: 3466-3473; Niwa R et al., (2004) *Clin Cancer Res* 1: 6248-6255; Presta LG et al., (2002) *Biochem Soc Trans* 30: 487-490; Kanda Y et al., (2007) *Glycobiology* 17: 104-118; U.S. Patent Nos. 6,602,684; 6,946,292; and 7,214,775; U.S. Patent Publication Nos. US 2007/0248600; 2007/0178551; 2008/0060092; and 2006/0253928; International Publication Nos. WO 00/61739; WO 01/292246; WO 02/311140; and WO 02/30954; Potillegent™ technology (Biowa, Inc. Princeton, N.J.); and GlycoMAb® glycosylation engineering technology (Glycart biotechnology AG, Zurich, Switzerland). See also, e.g., Ferrara C et al., (2006) *Biotechnol Bioeng* 93: 851-861; International Publication Nos. WO 07/039818; WO 12/130831; WO 99/054342; WO 03/011878; and WO 04/065540.

[00199] In certain embodiments, any of the constant region mutations or modifications described herein can be introduced into one or both heavy chain constant regions of an antibody or antigen-binding fragment thereof described herein having two heavy chain constant regions.

[00200] In another particular embodiment, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises a heavy chain and a light chain, wherein (i) the heavy chain comprises a VH domain comprising the VH CDR1, VL CDR2, and VL CDR3 amino acid sequences of an antibody listed in Table 1 (e.g., SEQ ID NOs:458-460, 35-37, or 65-67); (ii) the light chain comprises a VL domain comprising the VL CDR1, VH CDR2, and VH CDR3 amino acid sequences of the same antibody listed in Table 2 (e.g., SEQ ID NOs:461-463, 38-40, or 68-70); (iii); and the heavy chain further comprises a constant heavy chain domain comprising the amino acid sequence of the constant domain of a human IgG1 heavy chain (iv); the light chain further comprises a constant light chain domain comprising the amino acid sequence of the constant domain of a human kappa light chain.

[00201] In another particular embodiment, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises a heavy chain and a light chain, wherein (i) the heavy chain comprises a VH domain comprising the amino acid sequence of an antibody listed in Table 3 (e.g., SEQ ID NO:464, 41, or 71); (ii) the light chain comprises a VL domain comprising the amino acid sequence of the same antibody listed in Table 4 (e.g., SEQ ID NO:42 or 73); (iii); and the heavy chain further comprises a

constant heavy chain domain comprising the amino acid sequence of the constant domain of a human IgG1 heavy chain (iv); the light chain further comprises a constant light chain domain comprising the amino acid sequence of the constant domain of a human kappa light chain.

[00202] In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) exhibits T cell checkpoint blockade activity. Exemplary methods of measuring T cell checkpoint blockade activity are provided herein in Examples 7 and 11. In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) increases interferon-gamma (IFN γ) production in T cells. Exemplary methods of measuring IFN γ production are provided herein in Examples 7 and 11. In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) increases T cell proliferation. Exemplary methods of measuring T-cell proliferation are provided herein in Example 7. In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) increases CD4⁺ T cell proliferation. Exemplary methods of measuring CD4⁺ T-cell proliferation are provided herein in Example 7. In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) increases CD8⁺ T cell proliferation. Exemplary methods of measuring CD8⁺ T-cell proliferation are provided herein in Example 7.

[00203] In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) exhibits antibody-dependent cellular cytotoxicity (ADCC) activity. In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) exhibits antibody-dependent cellular cytotoxicity (ADCC) activity on cell lines with at least 300,000 cell surface B7-H4 molecules (e.g., SK-BR-3 cells). In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) exhibits antibody-dependent cellular cytotoxicity (ADCC) activity on cell lines with at least 100,000 cell surface B7-H4 molecules (e.g., HCC 1569 cells). In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) exhibits antibody-dependent cellular cytotoxicity (ADCC) activity on cell lines with at least 50,000 cell surface B7-H4 molecules (e.g., ZR-75-1 cells). In specific embodiments, an antibody

or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) exhibits antibody-dependent cellular cytotoxicity (ADCC) activity on cell lines with at least 30,000 cell surface B7-H4 molecules (e.g., MDA-MB-468 cells). In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4) exhibits antibody-dependent cellular cytotoxicity (ADCC) activity on cell lines with at least 15,000 cell surface B7-H4 molecules (e.g., HCC1964 cells). Exemplary methods of measuring ADCC activity are provided herein in Example 13.

[00204] In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises framework regions (e.g., framework regions of the VH domain and/or VL domain) that are human framework regions or derived from human framework regions. Non-limiting examples of human framework regions are described in the art, e.g., see Kabat EA et al., (1991) *supra*). In certain embodiment, an antibody or antigen-binding fragment thereof described herein comprises framework regions (e.g., framework regions of the VH domain and/or VL domain) that are primate (e.g., non-human primate) framework regions or derived from primate (e.g., non-human primate) framework regions.

[00205] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which specifically binds to B7-H4 (e.g., human B7-H4), comprises one, two, or more VH framework regions (FRs) having the amino acid sequences described herein for an antibody set forth in Table 5, *supra* (e.g., SEQ ID NOs: 465, 466, 467, and/or 469; SEQ ID NOs:235, 236, 237 and/or 238; or SEQ ID NOs:265, 266, 267, and/or 268). In some embodiments, an antibody or antigen-binding fragment thereof described herein, which specifically binds to B7-H4 (e.g., human B7-H4), comprises one, two, or more VL framework regions (FRs) having the amino acid sequences described herein for an antibody set forth in Table 6, *supra* (e.g., SEQ ID NOs:239, 240, 241, and/or 242 or SEQ ID NOs:269, 270, 271, and/or 272). In specific embodiments, an antibody or antigen-binding fragment thereof described herein, which specifically binds to B7-H4 (e.g., human B7-H4), comprises one, two, or more VH framework regions having the amino acid sequences described herein for an antibody set forth in Table 5, *supra*, and one, two, or more VL framework regions having the amino acid sequences described herein for the same antibody set forth in Table 6, *supra* (e.g., (i) SEQ ID NOs: 465, 466, 467, and/or 469 and SEQ ID NOs:239, 240, 241, and/or 242; (ii) SEQ ID NOs:235, 236, 237 and/or 238 and SEQ ID NOs:239, 240, 241, and/or 242 or (iii) SEQ ID NOs:265, 266, 267, and/or 268 and SEQ ID

NOs:269, 270, 271, and/or 272).

[00206] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which specifically binds to B7-H4 (e.g., human B7-H4), comprises VH framework regions (FRs) having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the VH framework regions described herein in Table 5, supra. In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which specifically binds to B7-H4 (e.g., human B7-H4), comprises VL framework regions (FRs) having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the VL framework regions described herein Table 6, supra. In some embodiments, an antibody or antigen-binding fragment thereof described herein, which specifically binds to B7-H4 (e.g., human B7-H4), comprises VH framework regions (FRs) having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the VH framework regions described herein Table 5, supra, and VL framework regions (FRs) having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the VL framework regions described herein Table 6, supra.

[00207] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises a VH domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VH domain of 20502 or 22213 (e.g., SEQ ID NO:464 or 71), wherein the antibody comprises VH CDRs that are identical to the VH CDRs of 20502 or 22213 (e.g., SEQ ID NOs:458-460 or 65-67).

[00208] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises a VL domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VL domain of 20502 or 22213 (e.g., SEQ ID NO:42 or 72), wherein the antibody or antigen-binding fragment thereof comprises VL CDRs that are identical to the VL CDRs of 20502 or 22213 (e.g., SEQ ID NO:461-463 or 68-70).

[00209] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises: (i) a VH domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VH domain of 20502 or

22213 (e.g., SEQ ID NO:464 or 71),; and (ii) a VL domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VL domain of 20502 or 22213 (e.g., SEQ ID NO:42 or 72), wherein the antibody comprises VH CDRs and VL CDRs that are identical to the VH CDRs and VL CDRs of 20502 or 22213 (e.g., SEQ ID NOs:458-463 or SEQ ID NOs:65-70).

[00210] In another aspect, provided herein are antibodies or antigen-binding fragments thereof that bind the same epitope of B7-H4 (e.g., an epitope of human B7-H4) as an antibody or antigen-binding fragment thereof described herein (e.g., 20502 or 22213).

[00211] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises a VH domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VH domain of 20502.1 or 22213 (e.g., SEQ ID NO:41 or 71), wherein the antibody comprises VH CDRs that are identical to the VH CDRs of 20502.1 or 22213 (e.g., SEQ ID NOs: 35-37 or 65-67).

[00212] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises a VL domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VL domain of 20502.1 or 22213 (e.g., SEQ ID NO:42 or 72), wherein the antibody or antigen-binding fragment thereof comprises VL CDRs that are identical to the VL CDRs of 20502.1 or 22213 (e.g., SEQ ID NO:38-40 or 68-70).

[00213] In certain embodiments, an antibody or antigen-binding fragment thereof described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), comprises: (i) a VH domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VH domain of 20502.1 or 22213 (e.g., SEQ ID NO:41 or 71),; and (ii) a VL domain having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to the amino acid sequence of the VL domain of 20502.1 or 22213 (e.g., SEQ ID NO:42 or 72), wherein the antibody comprises VH CDRs and VL CDRs that are identical to the VH CDRs and VL CDRs of 20502.1 or 22213 (e.g., SEQ ID NOs:35-40 or SEQ ID NOs:65-70).

[00214] In another aspect, provided herein are antibodies or antigen-binding fragments thereof that bind the same epitope of B7-H4 (e.g., an epitope of human B7-H4) as an antibody or antigen-binding fragment thereof described herein (e.g., 20502.1 or 22213).

[00215] Competition binding assays can be used to determine whether two antibodies bind to overlapping epitopes. Competitive binding can be determined in an assay in which the immunoglobulin under test inhibits specific binding of a reference antibody to a common antigen, such as B7-H4. Numerous types of competitive binding assays are known, for example: solid phase direct or indirect radioimmunoassay (RIA), solid phase direct or indirect enzyme immunoassay (EIA), sandwich competition assay (see Stahli C et al., (1983) *Methods Enzymol* 9: 242-253); solid phase direct biotin-avidin EIA (see Kirkland TN et al., (1986) *J Immunol* 137: 3614-9); solid phase direct labeled assay, solid phase direct labeled sandwich assay (see Harlow E & Lane D, (1988) *Antibodies: A Laboratory Manual*, Cold Spring Harbor Press); solid phase direct label RIA using I-125 label (see Morel GA et al., (1988) *Mol Immunol* 25(1): 7-15); solid phase direct biotin-avidin EIA (Cheung RC et al., (1990) *Virology* 176: 546-52); and direct labeled RIA. (Moldenhauer G et al., (1990) *Scand J Immunol* 32: 77-82). Typically, such an assay involves the use of purified antigen (e.g., B7-H4 such as human B7-H4) bound to a solid surface or cells bearing either of these, an unlabeled test immunoglobulin and a labeled reference immunoglobulin. Competitive inhibition can be measured by determining the amount of label bound to the solid surface or cells in the presence of the test immunoglobulin. Usually the test immunoglobulin is present in excess. Usually, when a competing antibody is present in excess, it will inhibit specific binding of a reference antibody to a common antigen by at least 50-55%, 55-60%, 60-65%, 65-70%, 70-75% or more. A competition binding assay can be configured in a large number of different formats using either labeled antigen or labeled antibody. In a common version of this assay, the antigen is immobilized on a 96-well plate. The ability of unlabeled antibodies to block the binding of labeled antibodies to the antigen is then measured using radioactive or enzyme labels. For further details see, for example, Wagener C et al., (1983) *J Immunol* 130: 2308-2315; Wagener C et al., (1984) *J Immunol Methods* 68: 269-274; Kuroki M et al., (1990) *Cancer Res* 50: 4872-4879; Kuroki M et al., (1992) *Immunol Invest* 21: 523-538; Kuroki M et al., (1992) *Hybridoma* 11: 391-407 and *Antibodies: A Laboratory Manual*, Ed Harlow E & Lane D editors supra, pp. 386-389.

[00216] In one embodiment, a competition assay is performed using surface plasmon resonance (BIAcore®), e.g., by an 'in tandem approach' such as that described by Abdiche YN et al., (2009) *Analytical Biochem* 386: 172-180, whereby B7-H4 antigen is immobilized on the chip surface, for example, a CM5 sensor chip and the anti-B7-H4 antibodies are then run over the chip. To determine if an antibody or antigen-binding fragment thereof competes with an anti-B7-H4 antibody described herein, the anti-B7-H4 antibody is first run over the chip surface to

achieve saturation and then the potential, competing antibody is added. Binding of the competing antibody or antigen-binding fragment thereof can then be determined and quantified relative to a non-competing control.

[00217] In one embodiment, Fortebio Octet competition binding (e.g., as described in Example 2 below) is used to determine that a B7-H4 antibody or antigen-binding fragment thereof competitively inhibits the binding of another B7-H4 antibody or antigen-binding fragment thereof to B7-H4.

[00218] In another aspect, provided herein are antibodies that competitively inhibit (e.g., in a dose dependent manner) an antibody or antigen-binding fragment thereof described herein (e.g., 20502, 20502.1 or 22213) from binding to B7-H4 (e.g., human B7-H4), as determined using assays known to one of skill in the art or described herein (e.g., ELISA competitive assays, or suspension array or surface plasmon resonance assay).

[00219] In specific aspects, provided herein is an antibody or antigen-binding fragment which competitively inhibits (e.g., in a dose dependent manner) binding to B7-H4 (e.g., human B7-H4), of an antibody comprising a VH domain having the amino acid sequence set forth in SEQ ID NO:464, and a VL domain having the amino acid sequence set forth in SEQ ID NO:42.

[00220] In specific aspects, provided herein is an antibody or antigen-binding fragment which competitively inhibits (e.g., in a dose dependent manner) binding to B7-H4 (e.g., human B7-H4), of an antibody comprising a VH domain having the amino acid sequence set forth in SEQ ID NO:41, and a VL domain having the amino acid sequence set forth in SEQ ID NO:42.

[00221] In specific aspects, provided herein is an antibody or antigen-binding fragment which competitively inhibits (e.g., in a dose dependent manner) binding to B7-H4 (e.g., human B7-H4), of an antibody comprising a VH domain having the amino acid sequence set forth in SEQ ID NO:71, and a VL domain having the amino acid sequence set forth in SEQ ID NO:72.

[00222] In specific aspects, provided herein is an antibody or antigen-binding fragment thereof which competitively inhibits (e.g., in a dose dependent manner) binding to B7-H4 (e.g., human B7-H4), with an antibody comprising (i) a VH domain comprising a VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of the VH CDRs listed in Table 1; and (ii) a VL domain comprising a VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of the CDRs listed in Table 2.

[00223] In specific aspects, provided herein is an antibody or antigen-binding fragment thereof, which immunospecifically binds to the same B7-H4 (e.g., human B7-H4) epitope as that of 20502, 20502.1, or 22213.

[00224] In another specific embodiment, an antibody or antigen-binding fragment thereof described herein, immunospecifically binds to the same B7-H4 (e.g., human B7-H4) epitope as that of an antibody comprising (i) a VH domain comprising a VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of the CDRs listed in Table 1 and (ii) a VL domain comprising a VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of the CDRs listed in Table 2.

[00225] In a specific aspect, an antigen-binding fragment as described herein, which immunospecifically binds to B7-H4 (e.g., human B7-H4), is selected from the group consisting of a Fab, Fab', F(ab')₂, and scFv, wherein the Fab, Fab', F(ab')₂, or scFv comprises a heavy chain variable region sequence and a light chain variable region sequence of an anti-B7-H4 antibody or antigen-binding fragment thereof as described herein. A Fab, Fab', F(ab')₂, or scFv can be produced by any technique known to those of skill in the art, including, but not limited to, those discussed in Section 5.3, *infra*. In certain embodiments, the Fab, Fab', F(ab')₂, or scFv further comprises a moiety that extends the half-life of the antibody *in vivo*. The moiety is also termed a "half-life extending moiety." Any moiety known to those of skill in the art for extending the half-life of a Fab, Fab', F(ab')₂, or scFv *in vivo* can be used. For example, the half-life extending moiety can include a Fc region, a polymer, an albumin, or an albumin binding protein or compound. The polymer can include a natural or synthetic, optionally substituted straight or branched chain polyalkylene, polyalkenylene, polyoxylalkylene, polysaccharide, polyethylene glycol, polypropylene glycol, polyvinyl alcohol, methoxypolyethylene glycol, lactose, amylose, dextran, glycogen, or derivative thereof. Substituents can include one or more hydroxy, methyl, or methoxy groups. In certain embodiments, the Fab, Fab', F(ab')₂, or scFv can be modified by the addition of one or more C-terminal amino acids for attachment of the half-life extending moiety. In certain embodiments the half-life extending moiety is polyethylene glycol or human serum albumin. In certain embodiments, the Fab, Fab', F(ab')₂, or scFv is fused to a Fc region.

[00226] An anti-B7-H4 antibody or antigen-binding fragment thereof can be fused or conjugated (e.g., covalently or noncovalently linked) to a detectable label or substance. Examples of detectable labels or substances include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (¹²⁵I, ¹²¹I), carbon (¹⁴C), sulfur (³⁵S), tritium (³H), indium (¹²¹In), and technetium (⁹⁹Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin. Such labeled antibodies or antigen-binding fragments thereof can be used to detect B7-H4 (e.g., human B7-H4) protein. See, e.g., Section 5.5.2, *infra*.

[00227] Antibody Production

[00228] Antibodies and antigen-binding fragments thereof that immunospecifically bind to B7-H4 (e.g., human B7-H4) can be produced by any method known in the art for the synthesis of antibodies and antigen-binding fragments thereof, for example, by chemical synthesis or by recombinant expression techniques. The methods described herein employ, unless otherwise indicated, conventional techniques in molecular biology, microbiology, genetic analysis, recombinant DNA, organic chemistry, biochemistry, PCR, oligonucleotide synthesis and modification, nucleic acid hybridization, and related fields within the skill of the art. These techniques are described, for example, in the references cited herein and are fully explained in the literature. See, e.g., Sambrook J et al., (2001) *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY; Ausubel FM et al., *Current Protocols in Molecular Biology*, John Wiley & Sons (1987 and annual updates); *Current Protocols in Immunology*, John Wiley & Sons (1987 and annual updates) Gait (ed.) (1984) *Oligonucleotide Synthesis: A Practical Approach*, IRL Press; Eckstein (ed.) (1991) *Oligonucleotides and Analogues: A Practical Approach*, IRL Press; Birren B et al., (eds.) (1999) *Genome Analysis: A Laboratory Manual*, Cold Spring Harbor Laboratory Press.

[00229] In a certain aspect, provided herein is a method of making an antibody or antigen-binding fragment which immunospecifically binds to B7-H4 (e.g., human B7-H4) comprising culturing a cell or host cell described herein. In a certain aspect, provided herein is a method of making an antibody or antigen-binding fragment thereof which immunospecifically binds to B7-H4 (e.g., human B7-H4) comprising expressing (e.g., recombinantly expressing) the antibody or antigen-binding fragment thereof using a cell or host cell described herein (e.g., a cell or a host cell comprising polynucleotides encoding an antibody or antigen-binding fragment thereof described herein). In a particular embodiment, the cell is an isolated cell. In a particular embodiment, the exogenous polynucleotides have been introduced into the cell. In a particular embodiment, the method further comprises the step of purifying the antibody or antigen-binding fragment obtained from the cell or host cell.

[00230] Methods for producing polyclonal antibodies are known in the art (see, for example, Chapter 11 in: *Short Protocols in Molecular Biology*, (2002) 5th Ed., Ausubel FM et al., eds., John Wiley and Sons, New York).

[00231] Monoclonal antibodies or antigen-binding fragments thereof can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, yeast-based presentation technologies, or a combination thereof. For example, monoclonal antibodies or antigen-binding fragments thereof can be produced using

hybridoma techniques including those known in the art and taught, for example, in Harlow E & Lane D, *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling GJ et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563 681 (Elsevier, N.Y., 1981), or as described in Kohler G & Milstein C (1975) *Nature* 256: 495. Examples of yeast-based presentation methods that can be employed to select and generate the antibodies described herein include those disclosed in, for example, WO2009/036379A2; WO2010/105256; and WO2012/009568, each of which is herein incorporated by reference in its entirety.

[00232] In specific embodiments, a monoclonal antibody or antigen-binding fragment is an antibody or antigen-binding fragment produced by a clonal cell (e.g., hybridoma or host cell producing a recombinant antibody or antigen-binding fragment), wherein the antibody or antigen-binding fragment immunospecifically binds to B7-H4 (e.g., human B7-H4) as determined, e.g., by ELISA or other antigen-binding assays known in the art or in the Examples provided herein. In particular embodiments, a monoclonal antibody or antigen-binding fragment thereof can be a chimeric or a humanized antibody or antigen-binding fragment thereof. In certain embodiments, a monoclonal antibody or antigen-binding fragment thereof can be a Fab fragment or a F(ab')₂ fragment. Monoclonal antibodies or antigen-binding fragments thereof described herein can, for example, be made by the hybridoma method as described in Kohler G & Milstein C (1975) *Nature* 256: 495 or can, e.g., be isolated from phage libraries using the techniques as described herein, for example. Other methods for the preparation of clonal cell lines and of monoclonal antibodies and antigen-binding fragments thereof expressed thereby are well known in the art (see, for example, Chapter 11 in: *Short Protocols in Molecular Biology*, (2002) 5th Ed., Ausubel FM et al., *supra*).

[00233] Antigen-binding fragments of antibodies described herein can be generated by any technique known to those of skill in the art. For example, Fab and F(ab')₂ fragments described herein can be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). A Fab fragment corresponds to one of the two identical arms of a tetrameric antibody molecule and contains the complete light chain paired with the VH and CH1 domains of the heavy chain. A F(ab')₂ fragment contains the two antigen-binding arms of a tetrameric antibody molecule linked by disulfide bonds in the hinge region.

[00234] Further, the antibodies or antigen-binding fragments thereof described herein can also be generated using various phage display and/or yeast-based presentation methods known in the

art. In phage display methods, proteins are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In particular, DNA sequences encoding VH and VL domains are amplified from animal cDNA libraries (e.g., human or murine cDNA libraries of affected tissues). The DNA encoding the VH and VL domains are recombined together with a scFv linker by PCR and cloned into a phagemid vector. The vector is electroporated in *E. coli* and the *E. coli* is infected with helper phage. Phage used in these methods are typically filamentous phage including fd and M13, and the VH and VL domains are usually recombinantly fused to either the phage gene III or gene VIII. Phage expressing an antibody or antigen-binding fragment thereof that binds to a particular antigen can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Examples of phage display methods that can be used to make the antibodies or fragments described herein include those disclosed in Brinkman U et al., (1995) *J Immunol Methods* 182: 41-50; Ames RS et al., (1995) *J Immunol Methods* 184: 177-186; Kettleborough CA et al., (1994) *Eur J Immunol* 24: 952-958; Persic L et al., (1997) *Gene* 187: 9-18; Burton DR & Barbas CF (1994) *Advan Immunol* 57: 191-280; PCT Application No. PCT/GB91/001134; International Publication Nos. WO 90/02809, WO 91/10737, WO 92/01047, WO 92/18619, WO 93/1 1236, WO 95/15982, WO 95/20401, and WO 97/13844; and U.S. Patent Nos. 5,698,426, 5,223,409, 5,403,484, 5,580,717, 5,427,908, 5,750,753, 5,821,047, 5,571,698, 5,427,908, 5,516,637, 5,780,225, 5,658,727, 5,733,743, and 5,969,108.

[00235] A humanized antibody or antigen-binding fragment thereof can be selected from any class of immunoglobulins, including IgM, IgG, IgD, IgA and IgE, and any isotype, including IgG1, IgG2, IgG3 and IgG4.

1.2.1 Polynucleotides

[00236] In certain aspects, provided herein are polynucleotides comprising a nucleotide sequence encoding an antibody or antigen-binding fragment thereof described herein or a domain thereof (e.g., a variable light chain region and/or variable heavy chain region) that immunospecifically binds to a B7-H4 (e.g., human B7-H4) antigen, and vectors, e.g., vectors comprising such polynucleotides for recombinant expression in host cells (e.g., *E. coli* and mammalian cells).

[00237] In particular aspects, provided herein are polynucleotides comprising nucleotide sequences encoding antibodies or antigen-binding fragments thereof, which immunospecifically bind to a B7-H4 polypeptide (e.g., human B7-H4) and comprise an amino acid sequence as

described herein, as well as antibodies or antigen-binding fragments that compete with such antibodies or antigen-binding fragments for binding to a B7-H4 polypeptide (e.g., in a dose-dependent manner), or which bind to the same epitope as that of such antibodies or antigen-binding fragments.

[00238] Also provided herein is a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs:11, 12, 21, 22, 31, 32, 41, 464, 42, 51, 52, 61, 62, 71, 72, 81, 82, 91, 92, 101, 102, 111, 112, 121, 122, 131, 132, 141, 142, 151, 152, 161, 162, 171, 172, 181, 182, 191, 192, 201, and 202. In some embodiments, an antibody or antigen-binding fragment thereof comprising the polypeptide immunospecifically binds to B7-H4.

[00239] Also provided herein is a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs:13, 14, 23, 24, 33, 34, 43, 469, 44, 53, 54, 63, 64, 73, 74, 83, 84, 93, 94, 103, 104, 113, 114, 123, 124, 133, 134, 143, 144, 153, 154, 163, 164, 173, 174, 183, 184, 193, 194, 203, and 204. In some embodiments, an antibody or antigen-binding fragment thereof comprising the polypeptide immunospecifically binds to B7-H4.

[00240] Also provided herein are polynucleotides comprising a variable heavy chain-encoding nucleotide sequence shown in Table 9, e.g., wherein an antibody or antigen-binding fragment thereof comprising the encoded variable heavy chain binds to B7-H4.

Table 9: Variable heavy chain-encoding polynucleotide sequences

Antibody	Variable Heavy Chain-Encoding Polynucleotide Sequence (SEQ ID NO)
15461	CAGCTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGTA GTTACTACTGGGGCTGGATCCGCCAGCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCCT CAAGAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAAGGATCTTACCCCAATTGGTTTGATCCATGGGGACAGGG TACATTGGTCACCGTCTCCTCA (SEQ ID NO:213)
20500	CAGCTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAAGAGTGGTA GTCACTACTGGGGCTGGATCCGCCAGCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCCT CAGGAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGGGAAGGATCTTACCCCAATTGGTTTGATCCATGGGGACAGGG TACATTGGTCACCGTCTCCTCA (SEQ ID NO:223)

20501	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAAGAGTGGTA GTCCTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCT CAAGAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAAGGATCTTACCCCAATTGGTTGGATCCATGGGGACAGGG TACATTGGTCACCGTCTCCTCA (SEQ ID NO:233)
20502	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAAAAGTGGTA GTTACTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCT CAGAAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAAGGATCTTACCCCAATCAGTTTGATCCATGGGGACAGGG TACATTGGTCACCGTCTCCTCA (SEQ ID NO:470)
20502.1	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAAGAGTGGTA GTTACTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCT CAAGAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAAGGATCTTACCCCAATCAGTTTGATCCATGGGGACAGGG TATATTGGTCACCGTCTCCTCA (SEQ ID NO:243)
22208	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAAGAGTGGTA GTCCTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCT CAAGAGTCGAGTCACCATGTCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAAGGATCTTACCCCAATTGGTTTGATCCATGGGGACAGGG TACATTGGTCACCGTCTCCTCA (SEQ ID NO:253)
15462	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGTA GTTACTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCT CAAGAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAAGGATCTTACACAACCGTGTTAAACGTATGGGGTCAGGG TACAATGGTCACCGTCTCCTCA (SEQ ID NO:263)
22213	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCGGGAGGGGGA GTTACTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGT GGATTGGGAACATCTATTATAGTGGGAGCACCTACTACAACCCGTCCT CAAGAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAAGGATCTTACACAACCGTGTTAAACGTATGGGGTCAGGG TACAATGGTCACCGTCTCCTCA (SEQ ID NO:273)

15465	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAG ACCCTGTCCCTCACCTGTACTGTCTCTGGTGGCTCCATCAGCAGTGGTG GTTACTACTGGAGCTGGATCCGCCAGCACCCAGGGAAGGGCCTGGAGT GGATTGGGAACATCTATTACAGTGGGAGCACCTACTACAACCCGTCCCT CAAGAGTCGAGTTACCATATCAGTAGACACGTCTAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAATCTAGCACCATATCTGCCGACTTCGACCTATGGGGGAG AGGTACCTTGGTCACCGTCTCCTCA (SEQ ID NO:283)
20506	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGTACTGCCTCTGGTGGCTCCATCAGCCATGGTG GGTACTACTGGAGCTGGATCCGCCAGCACCCAGGGAAGGGCCTGGAGT GGATTGGGAACATCTATTACAGTGGGAGCACCTACTACAATCCGTCCCT CAAGAGTCGAGTTACCATGTCAGTAGACACGTCTAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGAATCTAGCACCATATCTGCCGACTTCGACCTATGGGGGAG AGGTACCTTGGTCACCGTCTCCTCA (SEQ ID NO:293)
15483	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAG ACCCTGTCCCTCACCTGTACTGTCTCTGGTGGCTCCATCAGCAGTGGTG GTTACTACTGGAGCTGGATCCGCCAGCACCCAGGGAAGGGCCTGGAGT GGATTGGGAACATCTATTACAGTGGGAGCACCTACTACAACCCGTCCCT CAAGAGTCGAGTTACCATATCAGTAGACACGTCTAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGGGTTGAGCACCATAGACGAGGCATTTCGACCCATGGGGACA GGGTACATTGGTCACCGTCTCCTCA (SEQ ID NO:303)
20513	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCGATGGTA GTTACTACTGGAGCTGGATCCGCCAGCACCCAGGGAAGGGCCTGGAGT GGATTGGGAACATCTATTACAGTGGGAGCACCTACTACAACCCGTCCCT CAGGAGTCGAGTTACCATGTCAGTAGACACGTCTAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGGGTTGAGCACCATAGACGAGGCATTTCGACCCATGGGGACA GGGTACATTGGTCACCGTCTCCTCA (SEQ ID NO:313)
22216	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAG ACCCTGTCCCTCACCTGTACTGTCTCTGGTGGCTCCATCAGCGATGGTA GTTACTACTGGAGCTGGATCCGCCAGCACCCAGGGAAGGGCCTGGAGT GGATTGGGAACATCTATTACAGTGGGAGCACCTACTACAACCCGTCCCT CAGGAGTCGAGTTACCATGTCAGTAGACACGTCTAAGAACCAGTTCTC CCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTG CGCCAGAGGGTTGAGCACCATAGACGAGGCATTTCGACCCATGGGGACA GGGTACATTGGTCACCGTCTCCTCA (SEQ ID NO:323)
15489	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACT ACTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTG GGTATATCTATAGTAGTGGGAGCACCAACTACAACCCCTCCCTCAAGA GTCGAGTCACCATATCAGTAGACACGTCCAAGAACCAGTTCTCCCTGA AGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTGCGCCA GAGGCTCTGGACAGTATGCAGCTCCTGATTATGGAATGGACGTATGGG GCCAGGGAACAACCTGTCACCGTCTCCTCA (SEQ ID NO:333)

20516	CAGGTGCAGCTGCAGGAGTCGGGGCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCATTAGTTACTA CTGGGGGTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGG GTATATCTATTCTAGTGGGAGCACCTCGTACAACCCCTCCCTCAAGAGT CGAGTCACCATATCAGTAGACACGTCCAAGAACCAGTTCTCCCTGAAG CTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACTGCGCCAGA GGCTCTGGACTGTATGCAGCTCCTGATTATGGACTTGACGTATGGGGTC AGGGAACAACCTGTCACCGTCTCCTCA (SEQ ID NO:343)
15472	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGG TCCCTGAGACTCTCCTGTGCAGCCTCTGGATTACCTTTAGCAGCTATG CCATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCT CAACCATTAGTGGTAGTGGTGGTAGCACATACTACGCAGACTCCGTGA AGGGCCGGTTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATC TGCAAATGAACAGCCTGAGAGCCGAGGACACGGCGGTGTACTACTGCG CCAGAGGTGCCGGACACTACGACCTCGTCGGACGATACTGGGGACAGG GTACATTGGTACCGTCTCCTCA (SEQ ID NO:353)
15503	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGG TCCCTGAGACTCTCCTGTGCAGCCTCTGGATTACCTTTAGCAGCTATG CCATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCT CAGCTATTAGTGGTAGTGGTGGTAGCACATACTACGCAGACTCCGTGA AGGGCCGGTTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATC TGCAAATGAACAGCCTGAGAGCCGAGGACACGGCGGTGTACTACTGCG CCAGAGTGGGATTCAGAGCATTAACTACTGGGGACAGGGTACAACCTG TCACCGTCTCCTCA (SEQ ID NO:363)
15495	CAGGTGCAGCTGGTGCAGTCTGGGGGCTGAGGTGAAGAAGCCTGGGTCC TCGGTGAAGGTCTCCTGCAAGGCTTCTGGAGGCACCTTCAGCAGCTATG CTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGG GAGGGATCATCCCTATCTTTGGTACAGCAAGCTACGCACAGAAGTTCC AGGGCAGAGTCACGATTACCGCGGACGAATCCACGAGCACAGCCTACA TGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCGGTGTACTACTGCG CAAGACAGCAATACGACGGTAGACGATACTTCGGCCTATGGGGGAGAG GTACCTTGGTACCGTCTCCTCA (SEQ ID NO:373)
15478	CAGGTGCAGCTGGTGCAGTCTGGGGGCTGAGGTGAAGAAGCCTGGGTCC TCGGTGAAGGTCTCCTGCAAGGCTTCTGGAGGCACCTTCAGCAGCTATG CTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGG GAGGGATCATCCCTATCTTTGGTACAGCAAACTACGCACAGAAGTTCC AGGGCAGAGTCACGATTACCGCGGACGAATCCACGAGCACAGCCTACA TGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCGGTGTACTACTGCG CCAGAGGTGGGCCTTGGTTTGATCCATGGGGACAGGGTACATTGGTCA CCGTCTCCTCA (SEQ ID NO:383)
15441	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGG TCCCTGAGACTCTCCTGTGCAGCCTCTGGATTACCTTTAGCAGCTATG CCATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCT CAGCTATTAGTGGTAGTGGTGGTAGCACATCCTACGCAGACTCCGTGA AGGGCCGGTTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATC TGCAAATGAACAGCCTGAGAGCCGAGGACACGGCGGTGTACTACTGCG CCAAGCCTTCTTTGGCAACAATGTTAGCCTTCGATATCTGGGGTCAGGG TACAATGGTACCGTCTCCTCA (SEQ ID NO:393)

20496	CAGCTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAG ACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGTG TTTACTACTGGAGTTGGATCCGCCAGCCCCAGGGAAGGGGTGGAGT GGATTGGGAGTATCCTGGTGAAGTGGGAGCACCTACTACAACCCGTCCC TCAAGAGTCGAGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCT CCCTGAAGCTGAGTTCTGTGACCGCCGCAGACACGGCGGTGTACTACT GCGCCAGAGCTGTATCCTTCTTAGACGTATGGGGTCAGGGTACAATGGT CATCGTCTCCTCA (SEQ ID NO:403)

[00241] Also provided herein are polynucleotides comprising a variable light chain-encoding nucleotide sequence shown in Table 10, e.g., wherein an antibody or antigen-binding fragment thereof comprising the encoded variable light chain binds to B7-H4.

Table 10: Variable light chain-encoding polynucleotide sequences

Antibody	Variable Light Chain-Encoding Polynucleotide Sequence (SEQ ID NO)
15461	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAA CTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCAT CTATGGTGCATCCACCAGGGGCCACTGGTATCCCAGCCAGGTTCAAGTGG CAGTGGGTCTGGGACAGAGTTCCTCTCACCATCAGCAGCCTGCAGTC TGAAGATTTTGCAGTTTATTACTGTCAGCAGTACCACTCCTTCCCTTTC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:214)
20500	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAA CTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCAT CTATGGTGCATCCACCAGGGGCCACTGGTATCCCAGCCAGGTTCAAGTGG CAGTGGGTCTGGGACAGAGTTCCTCTCACCATCAGCAGCCTGCAGTC TGAAGATTTTGCAGTTTATTACTGTCAGCAGTACCACTCCTTCCCTTTC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:224)
20501	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAA CTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCAT CTATGGTGCATCCACCAGGGGCCACTGGTATCCCAGCCAGGTTCAAGTGG CAGTGGGTCTGGGACAGAGTTCCTCTCACCATCAGCAGCCTGCAGTC TGAAGATTTTGCAGTTTATTACTGTCAGCAGTACCACTCCTTCCCTTTC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:234)
20502 and 20502.1	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAA CTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCAT CTATGGTGCATCCACCAGGGGCCACTGGTATCCCAGCCAGGTTCAAGTGG CAGTGGGTCTGGGACAGAGTTCCTCTCACCATCAGCAGCCTGCAGTC TGAAGATTTTGCAGTTTATTACTGTCAGCAGTACCACTCCTTCCCTTTC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:244)
22208	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGTCCGTTAGCACCAAC TTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATC TATGACGCATCCGCCAGGGTCACTGGTATCCCAGCCAGGTTCAAGTGGC

	AGTGGGTCTGGGACAGAGTTCACTCTCACCATCAGCAGCCTGCAGTCT GAAGATTTTGCAGTTTATTACTGTCAGCAGTACCACTCCTTCCCTTTCA CTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:254)
15462	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAG CTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATGGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGGTTTCAG TGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGA GCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGGCCGCCAGTTACCC TCTCACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:264)
22213	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGCCAGCAGC CACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTC ATCTATGACGCAGTCAGCAGGGCCACTGGCATCCCAGACAGGTTTCAGT GGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAG CCTGAAGATTTTGCAGTGTATTACTGTCAGCAGGCCGCCAGTTACCC CTCACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:274)
15465	GACATCCAGATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGTCTGGGCGAGTCAGGGTATTAGCAGGTGG TTAGCCTGGTATCAGCAGAAACCAGGGGAAAGCCCCTAAGCTCCTGATC TATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCT GAAGATTTTGCAACTTATTACTGTCAGCAGGCACACACCTTCCCTTAC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:284)
20506	GACATCCAGATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGTCTGGGCGAGTCAGGGTATTAGCAGGTGG TTAGCCTGGTATCAGCAGAAACCAGGGGAAAGCCCCTAAGCTCCTGATC TATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCT GAAGATTTTGCAACTTATTACTGTCAGCAGGCACACACCTTCCCTTAC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:294)
15483	GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCCAGTCAGAGTATTAGTAGCTGG TTGGCCTGGTATCAGCAGAAACCAGGGGAAAGCCCCTAAGCTCCTGATC TATAAAGCCTCCAGTTTGGAAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGAATTCCTCTCACCATCAGCAGCCTGCAGCCT GATGATTTTGCAACTTATTACTGCCAGCAGGACAACAGTTACCCTTAC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:304)
20513	GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCCAGTCAGAGTATTAGTAGCTGG TTGGCCTGGTATCAGCAGAAACCAGGGGAAAGCCCCTAAGCTCCTGATC TATAAAGCCTCCAGTTTGGAAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGAATTCCTCTCACCATCAGCAGCCTGCAGCCT GATGATTTTGCAACTTATTACTGCCAGCAGGACAACAGTTACCCTTAC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:314)
22216	GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCCAGTAAAAGTATTAGTTCTGG TTGGCCTGGTATCAGCAGAAACCAGGGAAAAGCCCCTAAGCTCCTGATC

	TATGAAGCCTCCTCCTTGCACAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCT GATGATTTTGCAACTTATTACTGCCAGCAGGACAACAGTTACCCTTAC ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:324)
15489	GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCCAGTCAGAGTATTAGTAGCTGG TTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATAAAGCCTCCAGTTTGGAAAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCT GATGATTTTGCAACTTATTACTGCCAGCAGGACAATAGCTTCCCTTTCA CTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:334)
20516	GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCCAGTCAGAGTATTAGTAGCTGG TTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATAAAGCCTCCAGTTTGGAAAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCT GATGATTTTGCAACTTATTACTGCCAGCAGGACAATAGCTTCCCTTTCA CTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:344)
15472	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCAAGTCAGAGCATTAGCAGCTAT TTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTTCAGTGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCT GAAGATTTTGCAACTTACTACTGTCAGCAACTATACAGTCTCCCTCCTA CTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:354)
15503	GACATCCAGTTGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAG ACAGAGTCACCATCACTTGTCGGGCGAGTCAGGATATTAGCAGCTGGT TAGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCT ATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTTCAGCGGCA GTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTG AAGATTTTGCAACTTATTACTGTCAGCAGGCAACCAGTTACCCTCCTTG GACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:364)
15495	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGG GAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAA CTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCAT CTATAGCGCATCCACCAGGGCCACTGGTATCCCAGCCAGGTTTCAGTGG CAGTGGGTCTGGGACAGAGTTCACTCTCACCATCAGCAGCCTGCAGTC TGAAGATTTTGCAGTTTATTACTGTCAGCAGGTCAACGTCTGGCCTCCT ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:374)
15478	GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCCAGTCAGAGTATTAGTAGCTGG TTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATAAAGCCTCCAGTTTGGAAAGTGGGGTCCCATCAAGGTTTCAGCGGC AGTGGATCTGGGACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCT GATGATTTTGCAACTTATTACTGCCAGCAGTACAATAGCTACCCTCCTT TCACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:384)
15441	GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGGCCAGTCAGAGTATTAGTAGCTGG

	TTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATGATGCCTCCAGTTTGGAAAGTGGGGTCCCATCAAGGTTACAGCGGC AGTGGATCTGGGACAGAATTCCTCTCACCATCAGCAGCCTGCAGCCT GATGATTTTGCAACTTATTACTGCCAGCAGTCCAAAAGTTACCCTAGG ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:394)
20496	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGA GACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTAT TTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATC TATGGTGCATCCAGTTTGGCAAAGTGGGGTCCCATCAAGGTTACAGTGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCT GAAGATTTTGCAACTTACTACTGTCAGCAAAGCTACGACCCCCCTTGG ACTTTTGGCGGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO:404)

[00242] Also provided herein are polynucleotides comprising the nucleotide sequence of SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404. Also provided herein are polynucleotides comprising (i) the nucleotide sequence of SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404 and (ii) the nucleotide sequence of SEQ ID NO:408 or 406.

[00243] Also provided herein are polynucleotides comprising a nucleotide sequence that encodes SEQ ID NO:11, 12, 21, 22, 31, 32, 41, 464, 42, 51, 52, 61, 62, 71, 72, 81, 82, 91, 92, 101, 102, 111, 112, 121, 122, 131, 132, 141, 142, 151, 152, 161, 162, 171, 172, 181, 182, 191, 192, 201, or 202 and is at least about 80%, 85%, or 90% identical to SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404, respectively.

[00244] Also provided herein are polynucleotides comprising a nucleotide sequence that encodes SEQ ID NO:11, 12, 21, 22, 31, 32, 41, 464, 42, 51, 52, 61, 62, 71, 72, 81, 82, 91, 92, 101, 102, 111, 112, 121, 122, 131, 132, 141, 142, 151, 152, 161, 162, 171, 172, 181, 182, 191, 192, 201, or 202 and is at least about 95% identical to SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404, respectively.

[00245] Also provided herein are polynucleotides comprising a nucleotide sequence that encodes SEQ ID NO:11, 12, 21, 22, 31, 32, 41, 464, 42, 51, 52, 61, 62, 71, 72, 81, 82, 91, 92,

101, 102, 111, 112, 121, 122, 131, 132, 141, 142, 151, 152, 161, 162, 171, 172, 181, 182, 191, 192, 201, or 202 and is at least about 96% identical to SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404, respectively.

[00246] Also provided herein are polynucleotides comprising a nucleotide sequence that encodes SEQ ID NO:11, 12, 21, 22, 31, 32, 41, 464, 42, 51, 52, 61, 62, 71, 72, 81, 82, 91, 92, 101, 102, 111, 112, 121, 122, 131, 132, 141, 142, 151, 152, 161, 162, 171, 172, 181, 182, 191, 192, 201, or 202 and is at least about 97% identical to SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404, respectively.

[00247] Also provided herein are polynucleotides comprising a nucleotide sequence that encodes SEQ ID NO:11, 12, 21, 22, 31, 32, 41, 464, 42, 51, 52, 61, 62, 71, 72, 81, 82, 91, 92, 101, 102, 111, 112, 121, 122, 131, 132, 141, 142, 151, 152, 161, 162, 171, 172, 181, 182, 191, 192, 201, or 202 and is at least about 98% identical to SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404, respectively.

[00248] Also provided herein are polynucleotides comprising a nucleotide sequence that encodes SEQ ID NO:11, 12, 21, 22, 31, 32, 41, 464, 42, 51, 52, 61, 62, 71, 72, 81, 82, 91, 92, 101, 102, 111, 112, 121, 122, 131, 132, 141, 142, 151, 152, 161, 162, 171, 172, 181, 182, 191, 192, 201, or 202 and is at least about 99% identical to SEQ ID NO:213, 214, 223, 224, 233, 234, 243, 470, 244, 253, 254, 263, 264, 273, 274, 283, 284, 293, 294, 303, 304, 313, 314, 323, 324, 333, 334, 343, 344, 353, 354, 363, 364, 373, 374, 383, 384, 393, 394, 403, or 404, respectively.

[00249] In certain aspects, provided herein are polynucleotides comprising a nucleotide sequence encoding the light chain or heavy chain of an antibody or an antigen-binding fragment described herein. The polynucleotides can comprise nucleotide sequences encoding a heavy chain comprising the VH FRs and CDRs of antibodies described herein (*see, e.g.*, Tables 1 and 5). The polynucleotides can comprise nucleotide sequences encoding a light chain comprising the VL FRs and CDRs of antibodies described herein (*see, e.g.*, Tables 2 and 6).

[00250] In specific embodiments, a polynucleotide described herein encodes a VH domain comprising the amino acid sequence set forth in SEQ ID NO:464. In specific embodiments, a polynucleotide described herein encodes a VL domain comprising the amino acid sequence set forth in SEQ ID NO:42.

[00251] In specific embodiments, a polynucleotide described herein encodes a VH domain

comprising the amino acid sequence set forth in SEQ ID NO:41. In specific embodiments, a polynucleotide described herein encodes a VL domain comprising the amino acid sequence set forth in SEQ ID NO:42.

[00252] In specific embodiments, a polynucleotide described herein encodes a VH domain comprising the amino acid sequence set forth in SEQ ID NO:71. In specific embodiments, a polynucleotide described herein encodes a VL domain comprising the amino acid sequence set forth in SEQ ID NO:72.

[00253] In particular embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding an anti-B7-H4 antibody comprising three VH chain CDRs, e.g., containing VH CDR1, VH CDR2, VH VL CDR3 of any one of antibodies described herein (e.g., see Table 1). In specific embodiments, provided herein are polynucleotides comprising three VL chain CDRs, e.g., containing VL CDR1, VL CDR2, and VL CDR3 of any one of antibodies described herein (e.g., see Table 2). In specific embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding an anti-B7-H4 antibody comprising three VH chain CDRs, e.g., containing VH CDR1, VH CDR2, and VH CDR3 of any one of antibodies described herein (e.g., see Table 1) and three VL chain CDRs, e.g., containing VL CDR1, VL CDR2, and VL CDR3 of any one of antibodies described herein (e.g., see Table 2).

[00254] In particular embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding an anti-B7-H4 antibody or an antigen-binding fragment thereof or a fragment thereof comprising a VH domain, e.g., containing FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4, comprising an amino acid sequence described herein (e.g., see Tables 1 and 5, e.g., the VH CDRs and VH FRs of a particular antibody identified by name in the tables). In specific embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding an anti-B7-H4 antibody or antigen-binding fragment thereof or a fragment thereof comprising a VL domain, e.g., containing FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4, comprising an amino acid sequence described herein (e.g., see Tables 2 and 6, e.g., the VL CDRs and VL FRs of a particular antibody identified by name in the Tables).

[00255] In certain embodiments, a polynucleotide described herein comprises a nucleotide sequence encoding a heavy chain variable region comprising an amino acid sequence described herein (e.g., SEQ ID NO:464, 41, or 71), wherein an antibody containing the heavy chain variable region immunospecifically binds to B7-H4 (e.g., human B7-H4). In a certain embodiment, a polynucleotide described herein comprises a heavy chain variable region-encoding sequence provided herein (e.g., the variable region-encoding portion of SEQ ID

NO:470, 243, or 273), wherein an antibody containing the heavy chain variable region immunospecifically binds to B7-H4 (e.g., human B7-H4).

[00256] In certain embodiments, a polynucleotide described herein comprises a nucleotide sequence encoding a light chain variable region comprising an amino acid sequence described herein (e.g., SEQ ID NO:42 or 72), wherein an antibody containing the light chain variable region immunospecifically binds to B7-H4 (e.g., human B7-H4). In a certain embodiment, a polynucleotide described herein comprises a light chain variable region-encoding sequence provided herein (e.g., the variable region-encoding portion of SEQ ID NO:244 or 274), wherein an antibody containing the heavy chain variable region immunospecifically binds to B7-H4 (e.g., human B7-H4).

[00257] In a particular embodiment, a polynucleotide or combination of polynucleotides provided herein comprises a nucleotide sequence or combination of nucleotide sequences encoding an antibody or antigen-binding fragment thereof that immunospecifically binds to B7-H4 (e.g., human B7-H4), wherein the antibody or antigen-binding fragment thereof comprises a heavy chain, wherein the heavy chain comprises a heavy chain variable domain comprising an amino acid sequence set forth in Table 3 (e.g., SEQ ID NO:464, 41, or 71) and a constant region comprising the amino acid sequence of a human gamma (γ) heavy chain constant region.

[00258] In a particular embodiment, a polynucleotide or combination of polynucleotides provided herein comprises a nucleotide sequence or combination of nucleotide sequences encoding an antibody or antigen-binding fragment thereof that immunospecifically binds to B7-H4 (e.g., human B7-H4), wherein the antibody or antigen-binding fragment thereof comprises a light chain, wherein the light chain comprises a light chain variable domain comprising an amino acid sequence set forth in Table 4 (e.g., SEQ ID NO:42 or 72) and a constant region comprising the amino acid sequence of a human lambda light chain constant region.

[00259] In a particular embodiment, a polynucleotide or combination of polynucleotides provided herein comprises a nucleotide sequence or combination of nucleotide sequences encoding an antibody or antigen-binding fragment thereof that immunospecifically binds to B7-H4 (e.g., human B7-H4), wherein the antibody or antigen-binding fragment thereof comprises (i) a heavy chain, wherein heavy chain comprises a heavy chain variable domain comprising an amino acid sequence set forth in Table 3 (e.g., SEQ ID NO:464, 41, or 71) and a constant region comprising the amino acid sequence of a human gamma (γ) heavy chain constant region and (ii) a light chain, wherein light chain comprises a light chain variable domain comprising an amino acid sequence set forth in Table 4 (e.g., SEQ ID NO:42 or 72) and a constant region comprising

the amino acid sequence of a human lambda light chain constant region.

[00260] In one embodiment, a combination of polynucleotides provided herein comprises a polynucleotide comprising the nucleotide sequence of SEQ ID NO:470 and a polynucleotide comprising the nucleotide sequence of SEQ ID NO:244.

[00261] In one embodiment, a combination of polynucleotides provided herein comprises a polynucleotide comprising the nucleotide sequence of SEQ ID NO:243 and a polynucleotide comprising the nucleotide sequence of SEQ ID NO:244.

[00262] In one embodiment, a combination of polynucleotides provided herein comprises a polynucleotide comprising the nucleotide sequence of SEQ ID NO:273 and a polynucleotide comprising the nucleotide sequence of SEQ ID NO:274.

[00263] In a specific embodiment, provided herein are polynucleotides comprising a nucleotide sequence encoding an anti-B7-H4 antibody or antigen-binding fragment thereof or a domain thereof, designated herein, see, e.g., Tables 1-8.

[00264] Also provided herein are polynucleotides encoding an anti-B7-H4 antibody or antigen-binding fragment thereof described herein or a domain thereof that are optimized, e.g., by codon/RNA optimization, replacement with heterologous signal sequences, and elimination of mRNA instability elements. Methods to generate optimized nucleic acids encoding an anti-B7-H4 antibody or antigen-binding fragment thereof or a domain thereof (e.g., heavy chain, light chain, VH domain, or VL domain) for recombinant expression by introducing codon changes (e.g., a codon change that encodes the same amino acid due to the degeneracy of the genetic code) and/or eliminating inhibitory regions in the mRNA can be carried out by adapting the optimization methods described in, e.g., U.S. Patent Nos. 5,965,726; 6,174,666; 6,291,664; 6,414,132; and 6,794,498, accordingly.

[00265] A polynucleotide encoding an antibody or antigen-binding fragment thereof described herein or a domain thereof can be generated from nucleic acid from a suitable source (e.g., a hybridoma) using methods well known in the art (e.g., PCR and other molecular cloning methods). For example, PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of a known sequence can be performed using genomic DNA obtained from hybridoma cells producing the antibody of interest. Such PCR amplification methods can be used to obtain nucleic acids comprising the sequence encoding the light chain and/or heavy chain of an antibody or antigen-binding fragment thereof. Such PCR amplification methods can be used to obtain nucleic acids comprising the sequence encoding the variable light chain region and/or the variable heavy chain region of an antibody or antigen-binding fragment thereof. The amplified

nucleic acids can be cloned into vectors for expression in host cells and for further cloning, for example, to generate chimeric and humanized antibodies or antigen-binding fragments thereof.

[00266] Polynucleotides provided herein can be, e.g., in the form of RNA or in the form of DNA. DNA includes cDNA, genomic DNA, and synthetic DNA, and DNA can be double-stranded or single-stranded. If single stranded, DNA can be the coding strand or non-coding (anti-sense) strand. In certain embodiments, the polynucleotide is a cDNA or a DNA lacking one or more endogenous introns. In certain embodiments, a polynucleotide is a non-naturally occurring polynucleotide. In certain embodiments, a polynucleotide is recombinantly produced. In certain embodiments, the polynucleotides are isolated. In certain embodiments, the polynucleotides are substantially pure. In certain embodiments, a polynucleotide is purified from natural components.

1.2.2 Cells and Vectors

[00267] In certain aspects, provided herein are vectors (*e.g.*, expression vectors) comprising polynucleotides comprising nucleotide sequences encoding anti-B7-H4 antibodies and antigen-binding fragments thereof or a domain thereof for recombinant expression in host cells, preferably in mammalian cells. Also provided herein are cells, *e.g.* host cells, comprising such vectors for recombinantly expressing anti-B7-H4 antibodies or antigen-binding fragments thereof described herein (*e.g.*, human or humanized antibodies or antigen-binding fragments thereof). In a particular aspect, provided herein are methods for producing an antibody or antigen-binding fragments thereof described herein, comprising expressing such antibody or antigen-binding fragment thereof in a host cell.

[00268] In certain embodiments, recombinant expression of an antibody or antigen-binding fragment thereof or domain thereof described herein (*e.g.*, a heavy or light chain described herein) that specifically binds to B7-H4 (*e.g.*, human B7-H4) involves construction of an expression vector containing a polynucleotide that encodes the antibody or antigen-binding fragment thereof or domain thereof. Once a polynucleotide encoding an antibody or antigen-binding fragment thereof or domain thereof (*e.g.*, heavy or light chain variable domain) described herein has been obtained, the vector for the production of the antibody or antigen-binding fragment thereof can be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody or antigen-binding fragment thereof or domain thereof (*e.g.*, light chain or heavy chain)

encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody or antigen-binding fragment thereof or domain thereof (e.g., light chain or heavy chain) coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. Also provided are replicable vectors comprising a nucleotide sequence encoding an antibody or antigen-binding fragment thereof described herein, a heavy or light chain, a heavy or light chain variable domain, or a heavy or light chain CDR, operably linked to a promoter. Such vectors can, for example, include the nucleotide sequence encoding the constant region of the antibody or antigen-binding fragment thereof (see, e.g., International Publication Nos. WO 86/05807 and WO 89/01036; and U.S. Patent No. 5,122,464), and variable domains of the antibody or antigen-binding fragment thereof can be cloned into such a vector for expression of the entire heavy, the entire light chain, or both the entire heavy and light chains.

[00269] An expression vector can be transferred to a cell (e.g., host cell) by conventional techniques and the resulting cells can then be cultured by conventional techniques to produce an antibody or antigen-binding fragment thereof described herein (e.g., an antibody or antigen-binding fragment thereof comprising the six CDRs, the VH, the VL, the VH and the VL, the heavy chain, the light chain, or the heavy and the light chain of 20502, 20502.1, or 22213) or a domain thereof (e.g., the VH, the VL, the VH and the VL, the heavy chain, or the light chain of 20502, 20502.1, or 22213). Thus, provided herein are host cells containing a polynucleotide encoding an antibody or antigen-binding fragment thereof described herein (e.g., an antibody or antigen-binding fragment thereof comprising the six CDRs, the VH, the VL, the VH and the VL, the heavy chain, the light chain, or the heavy and the light chain of 20502, 20502.1, or 22213) or a domain thereof (e.g., the VH, the VL, the VH and the VL, the heavy chain, or the light chain of 20502, 20502.1, or 22213), operably linked to a promoter for expression of such sequences in the host cell. In certain embodiments, for the expression of double-chained antibodies or antigen-binding fragments thereof, vectors encoding both the heavy and light chains, individually, can be co-expressed in the host cell for expression of the entire immunoglobulin, as detailed below. In certain embodiments, a host cell contains a vector comprising a polynucleotide encoding both the heavy chain and light chain of an antibody described herein (e.g., the heavy and the light chain of 20502, 20502.1, or 22213), or a domain thereof (e.g., the VH and the VL of 20502, 20502.1, or 22213). In specific embodiments, a host cell contains two different vectors, a first vector comprising a polynucleotide encoding a heavy chain or a heavy chain variable region of an

antibody or antigen-binding fragment thereof described herein, and a second vector comprising a polynucleotide encoding a light chain or a light chain variable region of an antibody described herein (*e.g.*, an antibody comprising the six CDRs of 20502, 20502.1, or 22213), or a domain thereof. In other embodiments, a first host cell comprises a first vector comprising a polynucleotide encoding a heavy chain or a heavy chain variable region of an antibody or antigen-binding fragment thereof described herein, and a second host cell comprises a second vector comprising a polynucleotide encoding a light chain or a light chain variable region of an antibody or antigen-binding fragment thereof described herein (*e.g.*, an antibody or antigen-binding fragment thereof comprising the six CDRs of 20502, 20502.1, or 22213). In specific embodiments, a heavy chain/heavy chain variable region expressed by a first cell associated with a light chain/light chain variable region of a second cell to form an anti-B7-H4 antibody or antigen-binding fragment thereof described herein (*e.g.*, antibody or antigen-binding fragment thereof comprising the six CDRs of 20502, 20502.1, or 22213). In certain embodiments, provided herein is a population of host cells comprising such first host cell and such second host cell.

[00270] In a particular embodiment, provided herein is a population of vectors comprising a first vector comprising a polynucleotide encoding a light chain/light chain variable region of an anti-B7-H4 antibody or antigen-binding fragment thereof described herein, and a second vector comprising a polynucleotide encoding a heavy chain/heavy chain variable region of an anti-B7-H4 antibody or antigen-binding fragment thereof described herein (*e.g.*, antibody or antigen-binding fragment thereof comprising the CDRs of 20502, 20502.1, or 22213). Alternatively, a single vector can be used which encodes, and is capable of expressing, both heavy and light chain polypeptides.

[00271] A variety of host-expression vector systems can be utilized to express antibodies and antigen-binding fragments thereof described herein (*e.g.*, an antibody or antigen-binding fragment thereof comprising the CDRs of 20502, 20502.1, or 22213) (see, *e.g.*, U.S. Patent No. 5,807,715). Such host-expression systems represent vehicles by which the coding sequences of interest can be produced and subsequently purified, but also represent cells which can, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody or antigen-binding fragment thereof described herein *in situ*. These include but are not limited to microorganisms such as bacteria (*e.g.*, *E. coli* and *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (*e.g.*, *Saccharomyces Pichia*) transformed with recombinant yeast

expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems (e.g., green algae such as *Chlamydomonas reinhardtii*) infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS (e.g., COS1 or COS), CHO, BHK, MDCK, HEK 293, NS0, PER.C6, VERO, CRL703O, HsS78Bst, HeLa, and NIH 3T3, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20 and BMT10 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). In a specific embodiment, cells for expressing antibodies and antigen-binding fragments thereof described herein (e.g., an antibody or antigen-binding fragment thereof comprising the CDRs of 20502, 20502.1, or 22213) are CHO cells, for example CHO cells from the CHO GS System™ (Lonza). In a particular embodiment, cells for expressing antibodies described herein are human cells, e.g., human cell lines. In a specific embodiment, a mammalian expression vector is pOptiVEC™ or pcDNA3.3. In a particular embodiment, bacterial cells such as *Escherichia coli*, or eukaryotic cells (e.g., mammalian cells), especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary (CHO) cells in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking MK & Hofstetter H (1986) *Gene* 45: 101-105; and Cockett MI et al., (1990) *Biotechnology* 8: 662-667). In certain embodiments, antibodies or antigen-binding fragments thereof described herein are produced by CHO cells or NS0 cells.

[00272] In addition, a host cell strain can be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products can contribute to the function of the protein. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product can be used. Such mammalian host cells include but are not limited to CHO, VERO, BHK, HeLa, MDCK, HEK 293, NIH 3T3, W138, BT483, Hs578T, HTB2, BT20 and T47D, NS0 (a murine myeloma cell line that does not endogenously produce any immunoglobulin chains), CRL703O, COS (e.g., COS1 or COS), PER.C6, VERO,

HsS78Bst, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20, BMT10 and HsS78Bst cells. In certain embodiments, anti-B7-H4 antibodies described herein (e.g., an antibody or antigen-binding fragment thereof comprising the CDRs of 20502, 20502.1, or 22213) are produced in mammalian cells, such as CHO cells.

[00273] In certain embodiments, anti-B7-H4 antibodies described herein (e.g., an antibody or antigen-binding fragment thereof comprising the CDRs of 20502, 20502.1, or 22213) are produced in Potelligent® CHOK1SV cells.

[00274] In some embodiments, host cells are provided that comprise nucleic acid encoding a B7-H4 antibody or antigen-binding fragment thereof described herein, wherein the host cell lacks a functional alpha-1,6-fucosyltransferase gene (FUT8) gene. In some embodiments, the host cell is a CHO cell.

[00275] Once an antibody or antigen-binding fragment thereof described herein has been produced by recombinant expression, it can be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. Further, the antibodies or antigen-binding fragments thereof described herein can be fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification.

[00276] In specific embodiments, an antibody or antigen-binding fragment thereof described herein is isolated or purified. Generally, an isolated antibody or antigen-binding fragment thereof is one that is substantially free of other antibodies or antigen-binding fragments thereof with different antigenic specificities than the isolated antibody or antigen-binding fragment thereof. For example, in a particular embodiment, a preparation of an antibody or antigen-binding fragment thereof described herein is substantially free of cellular material and/or chemical precursors.

1.3 Pharmaceutical Compositions

[00277] Provided herein are compositions comprising an antibody or antigen-binding fragment thereof described herein having the desired degree of purity in a physiologically acceptable carrier, excipient or stabilizer (Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA). Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed.

[00278] In various embodiments, compositions comprising an anti-B7-H4 antibody or antigen-binding fragment thereof are provided in formulations with a pharmaceutically acceptable carrier (see, e.g., Gennaro, Remington: The Science and Practice of Pharmacy with Facts and Comparisons: Drugfacts Plus, 20th ed. (2003); Ansel et al., Pharmaceutical Dosage Forms and Drug Delivery Systems, 7th ed., Lippencott Williams and Wilkins (2004); Kibbe et al., Handbook of Pharmaceutical Excipients, 3rd ed., Pharmaceutical Press (2000)).

[00279] Pharmaceutical compositions described herein can be useful in blocking the inhibitory activity of B7-H4 against T cells and/or in ADCC-dependent depletion of B7-H4 expressing cells. Pharmaceutical compositions described herein can be useful in treating a condition such as cancer. Examples of cancer that can be treated in accordance with the methods described herein include, but are not limited to, breast cancer (e.g., triple negative breast cancer, ductal carcinoma), endometrial carcinoma, ovarian cancer, and non-small cell lung cancer (e.g., squamous cell carcinoma), pancreatic cancer, thyroid cancer, kidney cancer (e.g., renal cell carcinoma), and bladder cancer (e.g., urothelial cell carcinoma). A non-small cell lung cancer can be, e.g., an adenocarcinoma. Additional examples of cancer that can be treated in accordance with the methods described herein include, but are not limited to, head and neck cancer, small cell lung cancer, gastric cancer, melanoma, and cholangiocarcinoma. In one embodiment, the ovarian cancer is a serous adenocarcinoma. In one embodiment, the breast cancer is a ductal adenocarcinoma.

[00280] The pharmaceutical compositions described herein are in one embodiment for use as a medicament. The pharmaceutical compositions described herein are in one embodiment for use as a diagnostic, e.g., to detect the presence of B7-H4 in a sample obtained from a patient (e.g., a human patient).

[00281] The compositions to be used for in vivo administration can be sterile. This is readily accomplished by filtration through, e.g., sterile filtration membranes.

[00282] In some embodiments, pharmaceutical compositions are provided, wherein the pharmaceutical composition comprises anti-B7-H4 antibodies or antigen-binding fragments thereof described herein and a pharmaceutically acceptable carrier. In some embodiments, pharmaceutical compositions are provided, wherein the pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments thereof described herein and a pharmaceutically acceptable carrier. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 80% of the antibodies in the composition are afucosylated. In specific embodiments, such

pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 85% of the antibodies in the composition are afucosylated. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 90% of the antibodies in the composition are afucosylated. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 95% of the antibodies in the composition are afucosylated. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 96% of the antibodies in the composition are afucosylated. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 97% of the antibodies in the composition are afucosylated. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 98% of the antibodies in the composition are afucosylated. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments e.g., wherein at least 99% of the antibodies in the composition are afucosylated. In specific embodiments, such pharmaceutical composition comprises afucosylated anti-B7-H4 antibodies or antigen-binding fragments wherein fucose is undetectable in the composition.

[00283] In some embodiments, a pharmaceutical composition comprises (i) an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising (a) the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:458-463, respectively, (b) a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:464 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42, or (c) a heavy chain comprising the amino acid sequence of SEQ ID NO:469 and a light chain comprising the amino acid sequence of SEQ ID NO:44, and (ii) a pharmaceutically acceptable excipient.

[00284] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:458-463, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% , or at least 99% of the

antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:464 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:469 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[00285] In some embodiments, a pharmaceutical composition comprises (i) an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising (a) the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:35-40, respectively, (b) a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:41 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42, or (c) a heavy chain comprising the amino acid sequence of SEQ ID NO:43 and a light chain comprising the amino acid sequence of SEQ ID NO:44, and (ii) a pharmaceutically acceptable excipient.

[00286] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:35-40, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% , or at least 99% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:41 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:42 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:43 and a light chain comprising the amino acid sequence of SEQ ID NO:44.

[00287] In some embodiments, a pharmaceutical composition comprises (i) an isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising (a) the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:65-70, respectively, (b) a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:71 and a variable light chain region comprising the amino acid

sequence of SEQ ID NO:72, or (c) a heavy chain comprising the amino acid sequence of SEQ ID NO:73 and a light chain comprising the amino acid sequence of SEQ ID NO:74, and (ii) a pharmaceutically acceptable excipient.

[00288] Also provided herein is a pharmaceutical composition comprising (i) antibodies or antigen-binding fragments thereof that specifically bind to human B7-H4 and comprise the heavy chain variable region (VH) complementarity determining region (CDR) 1, VH CDR2, VH CDR3 and light chain variable region (VL) CDR1, CDR2, and CDR3 sequences of SEQ ID NOs:65-70, respectively and (ii) a pharmaceutically acceptable excipient, wherein at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% , or at least 99% of the antibodies or antigen-binding fragments thereof in the composition are afucosylated. In one embodiment, (i) the antibody or antigen-binding fragment thereof comprises a variable heavy chain region comprising the amino acid sequence of SEQ ID NO:71 and a variable light chain region comprising the amino acid sequence of SEQ ID NO:72 or (ii) the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:73 and a light chain comprising the amino acid sequence of SEQ ID NO:74.

1.4 Uses and Methods

1.4.1 Therapeutic Uses and Methods

[00289] In one aspect, presented herein are methods for modulating one or more immune functions in a subject, comprising administering to a subject in need thereof an anti-B7-H4 antibody or antigen-binding fragment thereof described herein, or a pharmaceutical composition thereof as described above and herein.

[00290] In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) to increase the proliferation of T cells, CD4⁺ T cells, or CD8⁺ T cells in the patient. In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) to increase interferon-gamma (IFN γ) production in the patient. In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) to block the inhibitory activity of B7-H4 against T cells in the patient. In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) to deplete B7-H4 expressing cancer cells in the

patient. In another embodiment, the anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to achieve two or more of the above effects.

[00291] In a certain embodiment, provided herein are methods of treating a cancer, e.g., a B7-H4 expressing cancer. The method of treating cancer can comprise administering an anti-B7-H4 antibody or antigen-binding fragment thereof provided herein or a pharmaceutical composition comprising an anti-B7-H4 antibody or antigen-binding fragment thereof provided herein to a patient (e.g., a human patient) in need thereof.

[00292] In a certain embodiment, provided herein are methods of treating a cancer selected from the group consisting of: breast cancer (e.g., triple negative breast cancer, ductal carcinoma), endometrial carcinoma, ovarian cancer, non-small cell lung cancer (e.g., squamous cell carcinoma), pancreatic cancer, thyroid cancer, kidney cancer (e.g., renal cell carcinoma), and bladder cancer (e.g., urothelial cell carcinoma). In a certain embodiment, provided herein are methods of treating a non-small cell lung cancer that is an adenocarcinoma. In a certain embodiment, provided herein are methods of treating a cancer selected from the group consisting of: head and neck cancer, small cell lung cancer, gastric cancer, melanoma, and cholangiocarcinoma. In one embodiment, the ovarian cancer is a serous adenocarcinoma. In one embodiment, the breast cancer is a ductal adenocarcinoma. In some embodiments, such methods comprise administering an anti-B7-H4 antibody or antigen-binding fragment thereof provided herein or a pharmaceutical composition comprising an anti-B7-H4 antibody or antigen-binding fragment thereof provided herein to a patient (e.g., a human patient) in need thereof. In some embodiments, the cancer is a B7-H4 expressing cancer.

[00293] In a certain embodiment, provided herein is a method of treating a cancer that is a PD-1/PD-L1 inhibitor inadequate responder. A cancer that is a PD-1/PD-L1 inhibitor inadequate responder, may have previously responded to a PD-1/PD-L1 inhibitor, but may have become less responsive to the PD-1/PD-L1 inhibitor, or the cancer may have never responded to the PD-1/PD-L1 inhibitor. Inadequate response to a PD-1/PD-L1 inhibitor means that aspects of the cancer that would be expected to improve following a standard dose of the PD-1/PD-L1 inhibitor do not improve, and/or improvement only occurs if greater than a standard dose is administered. In some embodiments, a subject with a cancer that is a PD-1/PD-L1 inhibitor inadequate responder has experienced, or is experiencing, an inadequate response to the PD-1/PD-L1 inhibitor after receiving a standard dose for at least two weeks, at least three weeks, at least four weeks, at least six weeks, or at least twelve weeks. A “standard” dose is determined by a medical professional, and may depend on the subject’s age, weight, healthy history, severity of

disease, the frequency of dosing, etc. In some embodiments, subject with a cancer that is a PD-1/PD-L1 inhibitor inadequate responder has experienced, or is experiencing, an inadequate response to an anti-PD-1 antibody and/or an anti-PD-L1 antibody. In some embodiments, a subject with cancer that is a PD-1/PD-L1 inhibitor inadequate responder has experienced, or is experiencing, an inadequate response to AMP-224. In some embodiments, a subject with cancer that is a PD-1/PD-L1 inhibitor inadequate responder has experienced, or is experiencing, an inadequate response to a PD-1/PD-L1 inhibitor selected from nivolumab, pembrolizumab, and atezolizumab.

[00294] In a certain embodiment, provided herein is a method of treating a cancer that expresses a low level of PD-L1. In some embodiments, a cancer that expresses a "low level of PD-L1," or expresses "PD-L1 at a low level," denotes that the level of PD-L1 is under the level of expression for a cancer that is indicated for treatment with a PD-1 or PD-L1 antagonist in which patients are selected for treatment based on PD-L1 expression levels. In some embodiments, a "low level of PD-L1" is one in which less than 1% of the cells in the tumor have membrane staining. In some embodiments, a "low level" in regard to PD-L1 is less than 1% staining, for example, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, 0.1% or 0% of the cells of the tumor are stained. In some embodiments, PD-L1 expression levels can be measured by chromogenic IHC or immunofluorescence IHC (Aqua scoring). In certain embodiments, PD-L1 staining of 5% or less (including tumor and/or immune cells) can indicate that a sample expresses a "low level of PD-L1." In certain embodiments, PD-L1 staining of 10% or less (including tumor and/or immune cells) can indicate that a sample expresses a "low level of PD-L1." Unless indicated otherwise herein, a 5% threshold is used herein (i.e., 5% or less indicates a "low level of PD-L1").

[00295] In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) diagnosed with cancer to increase the proliferation of T cells, CD4⁺ T cells, or CD8⁺ T cells in the patient. In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) diagnosed with cancer to increase interferon-gamma (IFN γ) production in the patient. In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) diagnosed with cancer to block the inhibitory activity of B7-H4 against T cells in the patient. In another embodiment, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient (e.g., a human patient) diagnosed with cancer to deplete B7-H4 expressing cancer cells in the

patient.

[00296] In further embodiments, an anti-B7-H4 antibody or antigen-binding fragment thereof, or pharmaceutical composition, is administered to a patient as provided above, and further in combination with an additional therapeutic agent, e.g., a chemotherapeutic agent or an immune stimulating agent, such as a T cell checkpoint inhibitor.

[00297] In an exemplary embodiment, the additional therapeutic agent is a PD-1 antagonist, such as an antagonistic PD-1 antibody. Suitable PD-1 antibodies include, for example, OPDIVO (nivolumab), KEYTRUDA (pembrolizumab), or MEDI-0680 (AMP-514; WO2012/145493). Suitable PD-1 antibodies also include, for example, camrelizumab (SHR-1210), tislelizumab (BGB-A317), or spartalizumab (NPVPDR001, NVS240118, PDR001). The additional therapeutic agent may also include pidilizumab (CT-011). A recombinant protein composed of the extracellular domain of PD-L2 (B7-DC) fused to the Fc portion of IgG1, called AMP-224, can also be used to antagonize the PD-1 receptor.

[00298] In another exemplary embodiment, the additional therapeutic agent is a PD-L1 antagonist, such as an antagonistic PD-L1 antibody. Suitable PD-L1 antibodies include, for example, TECENTRIQ (atezolizumab), durvalumab (MEDI4736), BMS-936559 (WO2007/005874), MSB0010718C (WO2013/79174) or rHigM12B7.

[00299] In yet another exemplary embodiment, the additional therapeutic agent is a GITR agonist, such as an agonistic GITR antibody. Suitable GITR antibodies include, for example, TRX-518 (WO06/105021, WO09/009116), MK-4166 (WO11/028683), or a GITR antibody disclosed in WO2015/031667. In another embodiment, the additional therapeutic agent is a GITR antibody disclosed in WO2017/015623. In a particular embodiment, the GITR antibody is selected from: a) an antibody comprising a GITR binding domain (GITR-BD) comprising a CDR1 comprising the sequence of SEQ ID NO:411, a CDR2 comprising the sequence of SEQ ID NO:412, and a CDR3 comprising the sequence of SEQ ID NO:413; b) an antibody comprising a GITR-BD comprising the sequence of SEQ ID NO:414; c) a tetravalent molecule comprising two copies of a polypeptide having the structure (GITR-BD)-Linker-(GITR-BD)-Linker-Hinge-Fc, wherein (i) the GITR-BD comprises a CDR1 comprising the sequence of SEQ ID NO:411, a CDR2 comprising the sequence of SEQ ID NO:412, and a CDR3 comprising the sequence of SEQ ID NO:413, (ii) the Linker is a polypeptide, (iii) the Hinge is a polypeptide derived from an immunoglobulin hinge region, and (iv) the Fc is an immunoglobulin Fc polypeptide; d) a tetravalent molecule comprising two copies of a polypeptide having the structure (GITR-BD)-Linker-(GITR-BD)-Linker-Hinge-Fc, wherein (i) the GITR-BD comprises the amino acid

sequence of SEQ ID NO:414, (ii) the Linker is a polypeptide, (iii) the Hinge is a polypeptide derived from an immunoglobulin hinge region, and (iv) the Fc is an immunoglobulin Fc polypeptide; and e) a tetravalent molecule comprising two copies of a polypeptide comprising the sequence of SEQ ID NO: 415. In any of the above embodiments of a tetravalent molecule, a Hinge may comprise the sequence of SEQ ID NO:416, 417 or 418. In any of the above embodiments of a tetravalent molecule, a Linker may comprise an amino acid sequence selected from GG, GGG, and SEQ ID NOs:419-425. In certain embodiments, the Hinge comprises SEQ ID NO:417 and the Linker comprises any one of SEQ ID NOs:419-423.

[00300] In yet another exemplary embodiment, the additional therapeutic agent is a CD80 extracellular domain (CD80 ECD), e.g., SEQ ID NO:426; or a CD80 ECD fusion molecule comprising CD80 ECD and a fusion partner, as disclosed in WO2017/079117. In certain embodiments, the CD80 ECD fusion molecule is a CD80 ECD-Fc fusion protein. In a specific embodiment, the CD80 ECD-Fc fusion protein comprises the sequence of SEQ ID NO:427 or 428.

[00301] In yet another exemplary embodiment, the additional therapeutic agent is an anti-CSF1R antibody disclosed in US8,182,813, US8,206,715, US8,263,079, US8,513,199 or US9,221,910. In a particular embodiment, the anti-CSF1R antibody is selected from: a) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO:429 and a light chain comprising the sequence of SEQ ID NO:430; b) an antibody comprising a heavy chain comprising a heavy chain (HC) complementarity determining region 1 (CDR1) comprising the sequence of SEQ ID NO:431, an HC CDR2 comprising the sequence of SEQ ID NO:432, and an HC CDR3 comprising the sequence of SEQ ID NO:433, and a light chain comprising a light chain (LC) CDR1 comprising the sequence of SEQ ID NO:434, a LC CDR2 comprising the sequence of SEQ ID NO:435, and a LC CDR3 comprising the sequence of SEQ ID NO:436; and c) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO:437 and a light chain comprising the sequence of SEQ ID NO:438.

[00302] Usually, the patient is a human but non-human mammals including transgenic mammals can also be treated.

[00303] In some embodiments, the present invention relates to an antibody or antigen-binding fragment thereof or pharmaceutical composition provided herein for use as a medicament. In some aspects, the present invention relates to an antibody or antigen-binding fragment thereof or pharmaceutical composition provided herein, for use in a method for the treatment of cancer. In some aspects, the present invention relates to an antibody or antigen-binding fragment thereof or

pharmaceutical composition provided herein, for use in a method for the treatment of cancer in a subject, comprising administering to the subject an effective amount of an antibody or antigen-binding fragment thereof or pharmaceutical composition provided herein.

1.4.1.1 Routes of Administration & Dosage

[00304] An antibody or antigen-binding fragment thereof or composition described herein can be delivered to a subject by a variety of routes, such as parenteral, subcutaneous, intravenous, intradermal, transdermal, intranasal, intratumoral, and administration to a tumor draining lymph node. In one embodiment, the antibody or antigen-binding fragment thereof or composition is administered by an intravenous route.

[00305] The amount of an antibody or antigen-binding fragment thereof or composition which will be effective in the treatment of a condition will depend on the nature of the disease. The precise dose to be employed in a composition will also depend on the route of administration, and the seriousness of the disease.

1.4.2 Detection & Diagnostic Uses

[00306] An anti-B7-H4 antibody or antigen-binding fragment thereof described herein (see, e.g., Section 5.2) can be used to assay B7-H4 protein levels in a biological sample using classical methods known to those of skill in the art, including immunoassays, such as the enzyme linked immunosorbent assay (ELISA), immunoprecipitation, or Western blotting. Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (¹²⁵I, ¹²¹I), carbon (¹⁴C), sulfur (³⁵S), tritium (³H), indium (¹²¹In), and technetium (⁹⁹Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin. Such labels can be used to label an antibody or antigen-binding fragment thereof described herein. Alternatively, a second antibody or antigen-binding fragment thereof that recognizes an anti-B7-H4 antibody or antigen-binding fragment thereof described herein can be labeled and used in combination with an anti-B7-H4 antibody or antigen-binding fragment thereof to detect B7-H4 protein levels.

[00307] Assaying for the expression level of B7-H4 protein is intended to include qualitatively or quantitatively measuring or estimating the level of a B7-H4 protein in a first biological sample either directly (e.g., by determining or estimating absolute protein level) or relatively (e.g., by comparing to the disease associated protein level in a second biological sample). B7-H4 polypeptide expression level in the first biological sample can be measured or estimated and compared to a standard B7-H4 protein level, the standard being taken from a second biological

sample obtained from an individual not having the disorder or being determined by averaging levels from a population of individuals not having the disorder. As will be appreciated in the art, once the “standard” B7-H4 polypeptide level is known, it can be used repeatedly as a standard for comparison.

[00308] As used herein, the term “biological sample” refers to any biological sample obtained from a subject, cell line, tissue, or other source of cells potentially expressing B7-H4. Methods for obtaining tissue biopsies and body fluids from animals (e.g., humans) are well known in the art. Biological samples include peripheral mononuclear blood cells. A biological sample may also be a blood sample, in which circulating tumor cells (or “CTCs”) may express B7-H4 and be detected.

[00309] An anti-B7-H4 antibody described herein can be used for prognostic, diagnostic, monitoring and screening applications, including in vitro and in vivo applications well known and standard to the skilled artisan and based on the present description. Prognostic, diagnostic, monitoring and screening assays and kits for in vitro assessment and evaluation of immune system status and/or immune response may be utilized to predict, diagnose and monitor to evaluate patient samples including those known to have or suspected of having an immune system-dysfunction or cancer. This type of prognostic and diagnostic monitoring and assessment is already in practice utilizing antibodies against the HER2 protein in breast cancer (HercepTest™, Dako) where the assay is also used to evaluate patients for antibody therapy using Herceptin®. In vivo applications include directed cell therapy and immune system modulation and radio imaging of immune responses.

[00310] Anti-B7-H4 antibodies and antigen-binding fragments thereof described herein can carry a detectable or functional label. When fluorescence labels are used, currently available microscopy and fluorescence-activated cell sorter analysis (FACS) or combination of both methods procedures known in the art may be utilized to identify and to quantitate the specific binding members. Anti-B7-H4 antibodies or antigen-binding fragments thereof described herein can carry a fluorescence label. Exemplary fluorescence labels include, for example, reactive and conjugated probes, e.g., Aminocoumarin, Fluorescein and Texas red, Alexa Fluor dyes, Cy dyes and DyLight dyes. An anti-B7-H4 antibody can carry a radioactive label, such as the isotopes ³H, ¹⁴C, ³²P, ³⁵S, ³⁶Cl, ⁵¹Cr, ⁵⁷Co, ⁵⁸Co, ⁵⁹Fe, ⁶⁷Cu, ⁹⁰Y, ⁹⁹Tc, ¹¹¹In, ¹¹⁷Lu, ¹²¹I, ¹²⁴I, ¹²⁵I, ¹³¹I, ¹⁹⁸Au, ²¹¹At, ²¹³Bi, ²²⁵Ac and ¹⁸⁶Re. When radioactive labels are used, currently available counting procedures known in the art may be utilized to identify and quantitate the specific binding of anti-B7-H4 antibody or antigen-binding fragment to B7-H4

(e.g., human B7-H4). In the instance where the label is an enzyme, detection may be accomplished by any of the presently utilized colorimetric, spectrophotometric, fluorospectrophotometric, amperometric or gasometric techniques as known in the art. This can be achieved by contacting a sample or a control sample with an anti-B7-H4 antibody or antigen-binding fragment thereof under conditions that allow for the formation of a complex between the antibody or antigen-binding fragment thereof and B7-H4. Any complexes formed between the antibody or antigen-binding fragment thereof and B7-H4 are detected and compared in the sample and the control. In light of the specific binding of the antibodies or antigen-binding fragments thereof described herein for B7-H4, the antibodies or antigen-binding fragments thereof can be used to specifically detect B7-H4 expression on the surface of cells. The antibodies or antigen-binding fragments thereof described herein can also be used to purify B7-H4 via immunoaffinity purification.

[00311] Also included herein is an assay system which may be prepared in the form of a test kit for the quantitative analysis of the extent of the presence of, for instance, B7-H4. The system or test kit may comprise a labeled component, e.g., a labeled antibody or antigen-binding fragment, and one or more additional immunochemical reagents. See, e.g., Section 5.6 below for more on kits.

[00312] In some aspects, methods for in vitro detecting B7-H4 in a sample, comprising contacting said sample with an antibody or antigen-binding fragment thereof, are provided herein. In some aspects, provided herein is the use of an antibody or antigen-binding fragment thereof provided herein, for in vitro detecting B7-H4 in a sample. In one aspect, provided herein is an antibody or antigen-binding fragment thereof or pharmaceutical composition provided herein for use in the detection of B7-H4 in a subject or a sample obtained from a subject. In one aspect, provided herein is an antibody or antigen-binding fragment thereof or pharmaceutical composition provided herein for use as a diagnostic. In one preferred embodiment, the antibody comprises a detectable label. In one preferred embodiment, B7-H4 is human B7-H4. In one preferred embodiment, the subject is a human.

1.5 Kits

[00313] Provided herein are kits comprising one or more antibodies or antigen-binding fragments thereof described herein or conjugates thereof. In a specific embodiment, provided herein is a pharmaceutical pack or kit comprising one or more containers filled with one or more

of the ingredients of the pharmaceutical compositions described herein, such as one or more antibodies or antigen-binding fragments thereof provided herein. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use, or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

[00314] Also provided herein are kits that can be used in diagnostic methods. In one embodiment, a kit comprises an antibody or antigen-binding fragment thereof described herein, preferably a purified antibody or antigen-binding fragment thereof, in one or more containers. In a specific embodiment, kits described herein contain a substantially isolated B7-H4 antigen (e.g., human B7-H4) that can be used as a control. In another specific embodiment, the kits described herein further comprise a control antibody or antigen-binding fragment thereof which does not react with a B7-H4 antigen. In another specific embodiment, kits described herein contain one or more elements for detecting the binding of an antibody or antigen-binding fragment thereof to a B7-H4 antigen (e.g., the antibody or antigen-binding fragment thereof can be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody or antigen-binding fragment thereof which recognizes the first antibody or antigen-binding fragment thereof can be conjugated to a detectable substrate). In specific embodiments, a kit provided herein can include a recombinantly produced or chemically synthesized B7-H4 antigen. The B7-H4 antigen provided in the kit can also be attached to a solid support. In a more specific embodiment, the detecting means of the above described kit includes a solid support to which a B7-H4 antigen is attached. Such a kit can also include a non-attached reporter-labeled anti-human antibody or antigen-binding fragment thereof or anti-mouse/rat antibody or antigen-binding fragment thereof. In this embodiment, binding of the antibody or antigen-binding fragment thereof to the B7-H4 antigen can be detected by binding of the said reporter-labeled antibody or antigen-binding fragment thereof.

[00315] The following examples are offered by way of illustration and not by way of limitation.

EXAMPLES

[00316] The examples in this Section (*i.e.*, Section 6) are offered by way of illustration, and not by way of limitation.

Example 1: Assessment of prevalence of B7-H4 expression in multiple indications

[00317] The B7-H4 mouse monoclonal antibody A57.1 (ATCC Catalog No. PTA-5180) was used to detect the presence of B7-H4 on archival samples, a mixture of whole sections, and tumor microarrays. The samples were treated with the primary antibody and detected using a polymer detection system attached to DAB (Ventana Medical Systems).

[00318] B7-H4 was readily detected in the membrane and the cytosol in tumor tissues harvested from a variety of cancer patients, including invasive ductal carcinoma, triple negative breast cancer, ovarian cancer, non-small cell lung cancer and endometrial cancer. (Fig. 1). Moreover, frequency of expression was also high in the indications listed in Table 11.

Table 11: B7-H4 detection in tumors

Tumor Type	#Total	#Positive	Percent Positive
Triple Negative Breast Cancer	74	58	78%
Invasive Ductal Carcinoma	51	38	74.50%
Endometrial Carcinoma	77	54	70%
Ovarian Cancer	141	85	60%
Non-Small Cell Lung Cancer (Squamous)	47	19	40%

[00319] B7-H4 is expressed in other cancers, such as kidney cancer (e.g., renal cell carcinoma), bladder cancer (e.g., urothelial cell carcinoma), pancreatic cancer, and thyroid cancer. See e.g., Zhu, J., et al., Asian Pacific J. Cancer Prev. 14: 3011-3015 (2011), Krambeck A, et al., PNAS 103: 10391-10396 (2006), Fan, M. et al., Int. J. Clin. Exp. Pathol. 7: 6768-6775 (2014), Xu, H., et al., Oncology Letters 11: 1841-1846 (2016), and Liu, W., et al., Oncology Letters 8: 2527-2534 (2014).

[00320] In a subsequent experiment, B7-H4 prevalence in various tumor types was assessed by immunohistochemistry (IHC) (Fig. 1B). The following tumor types and stages of disease were tested: endometrial, breast invasive ductal carcinoma (IDC), breast triple negative (TN), breast triple negative (late stage), ovarian cancer, bladder cancer (early stage), non-small cell lung cancer (sq (squamous), early stage), non-small cell lung cancer (sq, late stage), head and neck cancer, bladder (late stage), small cell lung cancer, cholangiocarcinoma, non-small cell lung cancer (ad (adenocarcinoma)), thyroid cancer, pancreatic cancer, gastric cancer, melanoma, glioblastoma or glioblastoma multiforme (GBM), and merkel cell carcinoma. B7-H4 surface protein expression on tumor cells was evaluated on procured tumor samples from various tumor types and stages of disease where available (early stage (I/II), late stage (III/IV)). IHC intensity with the antibody A57.1 was scored by category 0 to 3, and samples were attributed a single IHC score by the highest intensity observed in a minimum of 10% of all tumor cells per whole

section. A total of 50 to 100 samples per tumor type were evaluated.

Example 2: Generation of novel antibodies against human B7-H4

[00321] B7-H4-specific antibodies were isolated from full-length human IgG1 naïve antibody libraries using an in vitro yeast presentation system. The libraries are designed to mimic the immune system; they do not contain pre-defined heavy and light chain pairs. Libraries were subjected to multiple rounds of positive and negative selection strategies using B7-H4 protein to enrich for IgG that were cross-reactive to human, cynomolgus, and murine B7-H4 target. After four rounds of selection, the resulting IgG were sequenced, and unique antibodies were produced and evaluated for both avid and monomeric binding affinity to recombinant B7-H4 ectodomain, for epitope binning, and for target-specific cell binding.

[00322] A more detailed description of the selection, affinity maturation, and analytical methods that were used to generate and characterize the B7-H4 antibodies is provided below.

Materials and methods

[00323] Antigens were biotinylated using the EZ-Link Sulfo-NHS-Biotinylation Kit from Pierce. Goat F(ab')₂ anti-human kappa-FITC (LC-FITC), ExtrAvidin-PE (EA-PE) and Streptavidin-AF633 (SA-633) were obtained from Southern Biotech, Sigma, and Molecular Probes, respectively. Streptavidin MicroBeads and MACS LC separation columns were purchased from Miltenyi Biotec. Goat anti-human IgG-PE (Human-PE) was obtained from Southern Biotech.

Naïve Discovery

[00324] Eight naïve human synthetic yeast libraries each of ~10⁹ diversity were propagated as previously described (see Y. Xu et al, Addressing polyspecificity of antibodies selected from an in vitro yeast presentation system: a FACS-based, high-throughput selection and analytical tool. PEDS 26.10, 663-70 (2013); WO2009036379; WO2010105256; and WO2012009568.) For the first two rounds of selection, a magnetic bead sorting technique utilizing the Miltenyi MACS system was performed, as previously described (see Siegel et al, High efficiency recovery and epitope-specific sorting of an scFv yeast display library." J Immunol Methods 286(1-2), 141-153 (2004).) Briefly, yeast cells (~10¹⁰ cells/library) were incubated with 10 ml of 10 nM biotinylated Fc fusion antigen for 30 min at 30°C in wash buffer (phosphate-buffered saline (PBS)/0.1% bovine serum albumin (BSA)). After washing once with 40 ml ice-cold wash buffer, the cell pellet was resuspended in 20 mL wash buffer, and Streptavidin MicroBeads (500 µl)

were added to the yeast and incubated for 15 min at 4°C. Next, the yeast were pelleted, resuspended in 20 mL wash buffer, and loaded onto a Miltenyi LS column. After the 20 mL were loaded, the column was washed 3 times with 3 mL 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 selection were performed using flow cytometry. Approximately 2×10^7 yeast were pelleted, washed three times with wash buffer, and incubated at 30°C with either decreasing concentrations of biotinylated Fc fusion antigen (10 to 1 nM) under equilibrium conditions, 10 nM biotinylated Fc fusion antigens of different species in order to obtain species cross-reactivity, or with a poly-specificity depletion reagent (PSR) to remove non-specific antibodies from the selection. For the PSR depletion the libraries were incubated with a 1:10 dilution of biotinylated PSR reagent as previously described (see Y. Xu et al., addressing polyspecificity of antibodies selected from an in vitro yeast presentation system: a FACS-based, high-throughput selection and analytical tool. *PNAS* 110, 663-70 (2013).) Yeast were then washed twice with wash buffer and stained with LC-FITC (diluted 1:100) and either SA-633 (diluted 1:500) or EAPE (diluted 1:50) secondary reagents for 15 min at 4°C. After washing twice with wash buffer, the cell pellets were resuspended in 0.3 mL wash buffer and transferred to strainer-capped sort tubes. Sorting was performed using a FACS ARIA sorter (BD Biosciences) and sort gates were determined to select for antibodies with desired characteristics. Selection rounds were repeated until a population with all of the desired characteristics was obtained. After the final round of sorting, yeast were plated and individual colonies were picked for characterization.

Antibody Optimization

[00325] Optimization of antibodies was performed via a light chain batch shuffle method, and then by introducing diversities into the heavy chain and light chain variable regions as described below. A combination of some of these approaches was used for each antibody.

[00326] Light chain batch shuffle: Heavy chain plasmids from a naïve selection output were extracted from the yeast via smash and grab, propagated in and subsequently purified from *E. coli*, and transformed into a light chain library with a diversity of 5×10^6 . Selections were performed with one round of MACS and four rounds of FACS employing the same conditions as the naïve discovery.

[00327] CDRH1 and CDRH2 selection: The CDRH3 of a single antibody was recombined into a premade library with CDRH1 and CDRH2 variants of a diversity of 1×10^8 and selections were performed with one round of MACS and four rounds of FACS as described in the naïve

discovery. For each FACS round the libraries were looked at for PSR binding, species cross-reactivity, and affinity pressure, and sorting was performed in order to obtain a population with the desired characteristics. For these selections affinity pressures were applied by using decreasing concentrations of biotinylated HIS-B7-H4 antigen (100 to 1 nM) under equilibrium conditions at 30°C.

[00328] VH Mut selection: The heavy chain variable region (VH) was mutagenized via error prone PCR. The library was then created by transforming this mutagenized VH and the heavy chain expression vector into yeast already containing the light chain plasmid of the parent. Selections were performed similar to previous cycles using FACS sorting for two rounds. For each FACS round the libraries were looked at for PSR binding and affinity pressure, and sorting was performed in order to obtain a population with the desired characteristics. Affinity pressures for these selections were performed as described above in the CDRH1 and CDRH2 selection.

[00329] CDRL1 and CDRL2 selection: The CDRL3 of a single antibody was recombined into a premade library with CDRL1 and CDRL2 variants of a diversity of $\sim 5 \times 10^5$ and selections were performed similar to previous cycles using FACS sorting for three rounds. For each FACS round the libraries were looked at for PSR binding and affinity pressure, and sorting was performed in order to obtain a population with the desired characteristics. Affinity pressures for these selections were performed as described above in the CDRH1 and CDRH2 selection.

Antibody production and purification

[00330] 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).

ForteBio K_D measurements

[00331] ForteBio affinity measurements were performed on an Octet RED384 generally as previously described (see Estep et al, High throughput solution-based measurement of antibody-antigen affinity and epitope binning. *Mabs* 5(2), 270-278 (2013)). Briefly, ForteBio affinity measurements were performed by loading IgGs on-line onto 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 100 nM antigen for 3 minutes, and afterwards were transferred to assay buffer for 3 min for off-rate measurement. For monovalent affinity assessment Fabs were used instead of IgGs. For this assessment the

unbiotinylated Fc fusion antigen was loaded on-line onto the 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 antigen were exposed to 100 nM Fab for 3 minutes, and afterwards they were transferred to assay buffer for 3 min for off-rate measurement. All kinetics were analyzed using the 1:1 binding model.

ForteBio Epitope Binning/Ligand Blocking

[00332] Epitope binning/ligand blocking was performed using a standard sandwich format cross-blocking assay. Control anti-target IgG was loaded onto AHQ sensors and unoccupied Fc-binding sites on the sensor were blocked with an irrelevant human IgG1 antibody. The sensors were then exposed to 100 nM target antigen followed by a second anti-target antibody or ligand. Additional binding by the second antibody or ligand after antigen association indicates an unoccupied epitope (non-competitor), while no binding indicates epitope blocking (competitor or ligand blocking).

[00333] Four non-competing antibodies (“binning antibodies” 1, 2, 3, and 4) were used to identify four distinct portions of the B7-H4 ectodomain by SPR. All of the antibodies generated during this campaign were then assessed for competitive binding with these four binning antibodies to the B7-H4 ectodomain. If a B7-H4 antibody competed with one of the four binning antibodies (e.g., binning antibody 1), the B7-H4 antibody was determined to be in that BIN (e.g., BIN 1). If a B7-H4 antibody competed with two of the four binning antibodies (e.g., binning antibodies 2 and 3), the B7-H4 antibody was determined to be in both of those BINS (e.g., BIN2/3).

[00334] The IgG antibodies fell into at least four binding bins, with >90% of the antibodies binding to human/cyno or mouse B7-H4 with an affinity response ranging between >0.1 nM and <100 nM. Of the recombinant protein binders, approximately 75% also bind to B7-H4 on cells.

Cell Binding Analysis

[00335] 100,000 cells overexpressing the antigen were washed with wash buffer and incubated with 100 ul 100 nM IgG for 5 minutes at room temperature. Cells were then washed twice with wash buffer and incubated with 100ul of 1:100 anti-human IgGPE for 15 minutes on ice. Cells were then washed twice with wash buffer and analyzed on a FACS Canto II analyzer (BD Biosciences.)

PSR Binding Assay

[00336] The PSR assay was done as previously described (see Xu Y, et al. (2013) Addressing polyspecificity of antibodies selected from an in vitro yeast presentation system: A FACS-based,

high-throughput selection and analytical tool. *Protein Eng Des Sel* **26(10)**:663–670). In short, soluble membrane proteins were prepared from CHO cells. The enriched membrane fraction was biotinylated using NHS-LCBiotin (Pierce, Thermo Fisher). This polyspecificity reagent was incubated with IgG-presenting yeast, followed by washing. Then secondary labeling mix (Extravidin-R-PE, anti-human LC-FITC, and propidium iodide) was added to the mixture. Samples were analyzed on a FACSCanto II analyzer (BD Biosciences) using an HTS sample injector. Flow cytometry data were analyzed for mean fluorescence intensity (MFI) in the R-PE channel to assess nonspecific binding. MFI values were normalized from 0 to 1 based on three reference antibodies exhibiting low, medium, and high PSR MFI values.

Dynamic Scanning Fluorimetry

[00337] 10 uL of 20x Sypro Orange is added to 20 uL of 0.2-1mg/mL mAb or Fab solution. A RT-PCR instrument (BioRad CFX96 RT PCR) is used to ramp the sample plate temperature from 40 to 95 C at 0.5C increment, with 2min equilibrate at each temperature. The negative of first derivative for the raw data is used to extract T_m.

AC-SINS

[00338] The AC-SINS assay was performed as described previously (see Liu Y, et al. (2014) High-throughput screening for developability during early-stage antibody discovery using self-interaction nanoparticle spectroscopy. *MAbs* **6(2)**:483–492). In short, gold nanoparticles (Ted Pella Inc.) were coated with 80% capturing anti-human goat IgG Fc (Jackson ImmunoResearch) and 20% with polyclonal goat nonspecific antibody (Jackson ImmunoResearch). The antibodies of interest were then incubated with the particles for 2 h and the wavelength shift was measured using Molecular Devices SpectraMax M2 with SoftMax Pro6 software. The self-interacting clones show a higher wavelength shift away from the PBS sample.

Example 3: Structural characterization of human monoclonal antibodies against B7-H4

[00339] The B7-H4 antibodies are human IgG1/kappa isotype. The variable heavy (VH) regions are comprised of alleles from the germline genes VH1, VH3, and VH4, and the variable light (VL) of alleles from germline genes that include Vk1 and Vk3. Some subsets of the antibodies share high identity within the respective CDR regions of the VH and VL that can

range from 72-100%. Antibodies that share the same germline allele have high identity in their VH and VL framework (FR) regions that ranges from 88-100%. Sequences of the B7-H4 antibodies are provided in Tables 1-10.

Example 4: Characterization of monoclonal antibody binding to B7-H4 protein

[00340] Binding affinities of anti-B7-H4 antibodies to B7-H4-extracellular domain (ECD) were determined by biolayer interferometry (BLI). ForteBio affinity assays are described in more detail above in Example 2. Briefly, the recombinant human B7-H4-huIgG1 (SEQ ID NO:409) protein was immobilized on Protein A tips, followed by an isotype control hIgG1 in order to saturate any remaining binding sites on the capturing tip. Anti-B7-H4 antibodies were then evaluated for binding. In addition, antibody binding to cynomolgus monkey (SEQ ID NO: 2) and mouse B7-H4 (SEQ ID NO: 3) was also assessed using the same protocol. The results are summarized in Table 12.

B7-H4-huIgG1:

MASLGQILFWSIISIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDIKLSDI
VIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASRLKKNVQLTDA
GTYKCYIITSKGKGNANLEYKTGAFSMPEVNVNDYNASSETLRCEAPRWFPQPTVVWAS
QVDQGANFSEVSNTSFELNSENVTMKVVSVLNVNTINNTYSCMIENDIAKATGDIKVTES
EIKRRSHLQLLSKASGSEPKSSDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEV
TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH
YTQKSLSLSPGK (SEQ ID NO:409)

Table 12: B7-H4 Antibody Binding to Extracellular Domain by Biolayer Interferometry

Anti-body	BIN	Human B7-H4			Cynomolgus B7-H4			Mouse B7-H4		
		K _D (M)	k _{on} (1/Ms)	k _{off} (1/s)	K _D (M)	k _{on} (1/Ms)	k _{off} (1/s)	K _D (M)	k _{on} (1/Ms)	k _{off} (1/s)
15441	2	7.15E-09	1.22E+06	8.72E-03	5.46E-08	1.33E+06	7.27E-02	NB	-	-

15461	2/3	6.29E-08	3.81E+05	2.40E-02	6.21E-08	4.34E+05	2.70E-02	5.57E-08	3.05E+05	1.70E-02
15462	2/3	PF	-	-	6.65E-08	6.72E+05	4.47E-02	8.31E-08	4.59E+05	3.81E-02
15465	2/3	5.13E-08	4.84E+05	2.48E-02	5.11E-08	5.44E+05	2.78E-02	8.96E-08	2.96E+05	2.65E-02
15472	4	7.11E-09	7.00E+05	4.97E-03	7.80E-09	7.46E+05	5.82E-03	3.80E-08	4.22E+05	1.60E-02
15478	4	3.25E-08	4.77E+05	1.55E-02	3.11E-08	5.44E+05	1.69E-02	NB	-	-
15483	2/3	PF	-	-	1.08E-07	3.80E+05	4.09E-02	2.63E-07	2.65E+05	6.95E-02
15489	2/3	6.37E-08	3.66E+05	2.33E-02	7.21E-08	3.98E+05	2.87E-02	2.01E-07	2.93E+05	5.90E-02
15495	2	9.44E-09	2.89E+06	2.72E-02	5.17E-09	3.25E+06	1.68E-02	NB	-	-
15503	2	1.04E-08	1.96E+06	2.05E-02	6.32E-09	1.82E+06	1.15E-02	NB	-	-
20496	othe r	8.05E-10	6.89E+05	5.55E-04	7.21E-10	7.90E+05	5.69E-04	2.46E-08	6.92E+05	1.71E-02
20500	3	5.97E-09	3.91E+05	2.33E-03	5.47E-09	4.18E+05	2.29E-03	8.25E-09	4.08E+05	3.36E-03
20501	3	2.56E-09	9.80E+05	2.51E-03	2.42E-09	1.02E+06	2.46E-03	3.35E-09	1.12E+06	3.75E-03
20502	3	1.20E-09	9.36E+05	1.15E-03	1.20E-09	9.62E+05	1.12E-03	3.40E-09	6.32E+05	2.13E-03
20502.1	3	3.07E-09	4.87E+05	1.50E-03	2.64E-09	5.28E+05	1.39E-03	3.99E-09	5.20E+05	2.07E-03
20506	3	1.69E-09	4.41E+05	7.46E-04	1.48E-09	4.58E+05	6.78E-04	3.53E-09	4.66E+05	1.64E-03
20513	3	3.98E-09	4.53E+05	1.80E-03	3.67E-09	4.91E+05	1.80E-03	4.57E-09	5.17E+05	2.36E-03
20516	3	1.80E-08	4.10E+05	7.38E-03	1.76E-08	4.45E+05	7.83E-03	4.14E-08	3.98E+05	1.65E-02

22208	3	5.67E-09	1.84E+05	1.04E-03	5.44E-09	1.99E+05	1.08E-03	1.67E-08	9.95E+04	1.67E-03
22213	3	1.44E-08	4.96E+04	7.13E-04	7.48E-09	6.44E+04	4.82E-04	1.37E-08	4.03E+04	5.52E-04
22216	3	1.47E-09	2.45E+05	3.59E-04	1.47E-09	2.45E+05	3.59E-04	1.47E-09	2.45E+05	3.59E-04

[00341] In addition, the binding affinities of selected anti-B7-H4 antibodies to the N-terminal domain of human B7-H4 (B7-H4 IgV-huIgG1; SEQ ID NO:410) were determined by surface plasmon resonance (SPR). Briefly, anti-human Fab antibody was immobilized on a carboxyl-derivatized SPR chip surface, and anti-B7-H4 antibodies were captured on the resulting surface at 5 ug/ml for 30 seconds. B7-H4 IgV-huIgG1 at various concentrations (0 nM, 3.7 nM, 11.1 nM, 33.3 nM, 100 nM, and 300 nM) was then flowed over the surface and allowed to bind to the anti-B7-H4 antibodies during the association phase, followed by a buffer wash during the dissociation phase. Data was fitted using a 1:1 binding model, and the results are summarized in Table 13.

B7-H4 IgV-huIgG1:

MASLGQILFWSIISIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDIKLSDI
VIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASRLKKNVQLTDA
GTYKCYIITSKGKGNANLEYKTGA FSGSEPKSSDKTHTCPPCPAPPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:410)

Table 13: B7-H4 Antibody Binding to N-terminal Domain by Surface Plasmon Resonance

Antibody	BIN	Human B7-H4		
		K _D (M)	k _{on} (1/Ms)	k _{off} (1/s)
15461	2/3	3.04E-08	1.71E+05	5.19E-03
15462	2/3	1.69E-08	2.95E+05	4.98E-03
15465	2/3	1.73E-08	2.41E+05	4.17E-03

15483	2/3	1.84E-08	2.41E+05	4.43E-03
15489	2/3	2.37E-08	1.64E+05	3.89E-03
20502	3	2.03E-09	1.78E+05	3.61E-04

[00342] Thus, multiple assays demonstrate that the antibodies bind to B7-H4.

Example 5: Epitope Mapping

[00343] Anti-B7-H4 antibody binding bins were determined by biolayer interferometry (BLI). Epitope mapping assays are described in more detail above in Example 2. Briefly, a first anti-B7-H4 antibody was captured on Protein A tips, followed by a control huIgG1 antibody to saturate additional binding sites on the tips. Next, the sensor tips were exposed to the antigen (B7-H4-huIgG1) (SEQ ID NO:409) followed by the second anti-B7-H4 antibody, which was then evaluated for binding. Epitope bins were determined by comparison to binding after a non-B7-H4 antibody was used as the first antibody. Results are summarized in Table 12.

Example 6: Characterization of monoclonal antibody binding to B7-H4 expressed on the surface of cells

[00344] HEK293T cell lines were transfected to express full-length human, cynomolgus monkey, mouse, or rat B7-H4. In addition, the endogenous human B7-H4 expressing SK-BR-3 breast cancer cell line was used to assess the ability of the antibodies to bind B7-H4 expressed on the cell surface. 1×10^5 parental HEK293T or transfected HEK293T cell lines were incubated with 100nM of the B7-H4 antibodies. Following incubation, cells were pelleted, washed, and incubated with a secondary labeling antibody, and samples were acquired on a flow cytometer. Fold binding over the parental cell line (FOP) was calculated as follows: MFI transfected HEK293T cells/MFI parental HEK293T cells. A FOP value greater than 10 was considered to demonstrate specific binding.

[00345] To assess the cell binding potency of the B7-H4 antibodies, 1×10^5 SK-BR-3 cells or 293 cells transfected to express cynomolgus monkey, mouse or rat B7-H4 were incubated with titrating doses of the B7-H4 antibodies. Following incubation, cells were pelleted, washed and incubated with a secondary labeling antibody and samples were acquired on a flow cytometer. Data was analyzed using the FlowJo software and MFI was plotted vs. antibody concentration. The EC50 cell binding potency was calculated using nonlinear regression curve fit (GraphPad

Prism).

[00346] All B7-H4 antibodies demonstrated binding to HEK293T cells that expressed human B7-H4, cynomolgus monkey B7-H4, or mouse B7-H4. Antibodies also demonstrated potent dose-dependent binding to SK-BR-3 cells endogenously expressing human B7-H4 on the cell surface or HEK293T cell lines transfected to express cynomolgus monkey, mouse, or rat B7-H4 on the cell surface. These data demonstrate that the majority of B7-H4 antibodies are fully cross-reactive to cynomolgus monkey, mouse, and rat B7-H4 (Figs. 2A and 2B, Table 14).

[00347]

Table 14: B7-H4 Antibody Binding to Cell-Surface B7-H4

Antibody	BIN	293- huB7- H4 (FOP)	293- cynoB7- H4 (FOP)	293- moB7- H4 (FOP)	SK-BR- 3 (EC50; nM)	293- cynoB7- H4 (EC50; nM)	293- mouseB7- H4 (EC50; nM)	293- ratB7- H4 (EC50; nM)
15441	2	67	9	3	34.29	ND	ND	ND
15461	2/3	333	610	887	5.66	6.77	6.37	1.67
15462	2/3	530	416	456	4.55	5.29	5.40	1.13
15465	2/3	626	1324	690	2.13	4.90	5.34	1.47
15472	4	580	1279	685	8.86	-	-	-
15478	4	518	1130	125	PF	-	-	-
15483	2/3	805	1012	1402	14.81	17.4	8.82	1.87
15489	2/3	612	1118	674	31.73	13.7	17.5	4.55
15495	2	619	524	6	61.2	-	-	-
15503	2	289	877	5	PF	-	-	-
20496	other	179	758	604	7.60	7.91	6.70	ND
20500	3	182	630	478	1.54	3.38	4.00	1.14
20501	3	205	728	546	1.90	3.89	4.67	1.15
20502.1	3	200	683	559	2.50	4.94	5.57	1.26

Example 7: Characterization of monoclonal antibody T cell checkpoint blockade activity

[00348] In order to characterize the T cell checkpoint blockade activity of the B7-H4 antibodies, primary human T cells were enriched from peripheral blood mononuclear cells (PBMCs) using the EasySep™ Human T Cell Enrichment Kit based on manufacturer's instructions. Enriched T cells were incubated at 2×10^5 cell/mL with anti-CD3/anti-CD28 Dynabeads, at a one bead per cell ratio, at 37°C. Six days later, the beads were magnetically removed, and the T cells were washed and incubated at 1×10^6 cell/mL with 10 U/mL IL-2 at 37°C. Four days later, T cells were washed and incubated at a 1×10^6 cells/mL along with artificial antigen presenting cells (aAPCs) at 2×10^6 cells/mL at 37°C in the presence of 10 ug/mL of antibody or an antibody dose titration. aAPCs are a HEK293T cell line that has been transfected to co-express a scFv format of anti-human CD3 clone OKT3 and full-length human B7-H4 on the cell surface. aAPCs were treated with Mitomycin C for one hour at 37°C and then thoroughly washed prior to adding to the T cell co-culture. 72 hours after co-culture of T cells, aAPCs and B7-H4 antibodies, plates were centrifuged, supernatants harvested and assessed for IFN γ production by ELISA, and cells were harvested and stained to assess proliferation by FACS (specifically, the cells in each well were incubated with antibodies against CD4 and CD8). Cells were then washed, fixed, permeabilized, and incubated with the Edu-Click reagent according the manufacturer's instructions. Cells were washed, and the number of proliferating CD4 $^{+}$, CD8 $^{+}$ or total T cells was measured using flow cytometry. Data was analyzed using the FlowJo software. For samples only treated with a single concentration of antibody, the data was calculated and reported as a fold increase over control-huIgG treated samples. For samples treated with a dose titration of antibody, IFN γ production was plotted vs. antibody concentration and the EC50 potency was calculated using nonlinear regression curve fit (GraphPad Prism).

[00349] All BIN2/3 and BIN3 antibodies reproducibly resulted in T cell checkpoint blockade activity as measured by an increase in IFN γ production and/or CD4 $^{+}$, CD8 $^{+}$ or total T cell proliferation. Figure 3A shows that antibody 15441 increases T cell proliferation by at least 3% and increases CD4 $^{+}$ and CD8 $^{+}$ T cell proliferation by at least 2%. Figure 3A also shows that antibody 15461 increases T cell proliferation by at least 21%, increases CD4 $^{+}$ T cell proliferation by at least 9%, and increases CD8 $^{+}$ T cell proliferation by at least 11%. Figures 3B-3D show other dose-dependent T cell checkpoint blockade activities.

Table 15: B7-H4 Antibody – T Cell Checkpoint Blockade Activity

Antibody	BIN	aAPC Assay (EC50 +/-STD; nM)	Donor 1 (Max IFN γ , pg/mL)	Donor 2 (Max IFN γ , pg/mL)	Donor 3 (Max IFN γ , pg/mL)	Donor 4 (Max IFN γ , pg/mL)
15461	2/3	531.18 +/- 403.66	311.64	164.66	1957.34	986.73
15462	2/3	1312.01 +/- 1112.5	205.72	176.33	1661.59	484.8
15465	2/3	4310.72 +/- 7642.6	230.45	133.64	1523.82	865.22
15483	2/3	728.84 +/- 711.1	93.2	87.84	1382.03	939.04
15489	2/3	291.31 +/- 327.82	82.47	96.63	1133.02	799.9

Table 16: B7-H4 Antibody Binding to Cell-Surface B7-H4

Antibody	BIN	aAPC Assay (EC50 +/- STD; nM)	Donor 1 (Max IFN γ , pg/mL)	Donor 2 (Max IFN γ , pg/mL)	Donor 3 (Max IFN γ , pg/mL)	Donor 4 (Max IFN γ , pg/mL)	
20496	other	PF	185.88	ND	ND	ND	
20500	3	0.84 +/- 0.35	821	273.83	117.9	4027.1	
20501	3	0.79 +/- 0.18	849.6	310	135.6	4493.1	
20502.1	3	0.79 +/- 0.03	937	303.9	174.02	4269.7	
20506	3	1.25 +/- 0.26	980.8	258.8	86.1	2301.8	
20513	3	1.16 +/- 0.16	658.8	240.3	91.1	1634.5	
20516	3	PF	ND	441.1	ND	ND	
22213	3	1.79 +/- 1.83	ND	ND	ND	ND	

Example 8: Generation of afucosylated and fucosylated monoclonal antibodies

[00350] Antibodies with Fc regions having reduced fucose content in glycan moieties may exhibit higher ADCC activity compared to a fully fucosylated antibody (Niwa R et al., *Clinical Cancer Research* 11(6):2327-36 (2005)). B7-H4 antibodies were generated in CHO-x cells (Yamane-Ohnuki N, et al. *Biotechnology and Bioengineering* 87(5): 614-22 (2004)) to produce normally fucosylated antibodies and in a CHO cell line engineered to produce afucosylated antibodies (CHO-y cells) (*id.*).

Example 9: Characterization of binding of afucosylated and fucosylated monoclonal antibodies

[00351] The fucosylated and afucosylated anti B7-H4 antibodies were characterized by SPR following protocol as described in Example 4. The antibodies showed similar binding to human B7-H4 protein and thus there is no impact of the glycosylation on binding (Table 17).

Table 17: Binding of afucosylated and fucosylated antibodies

Antibody	BIN		Human B7-H4			SK-BR-3 (EC50; nM)	293-cynoB7-H4 (EC50; nM)	293-mouseB7-H4 (EC50; nM)	293-ratB7-H4 (EC50; nM)
			K _D (M)	k _{on} (1/Ms)	k _{off} (1/s)				
20502	3	Fucosylated	2.58E-09	4.28E+05	1.10E-03	0.571	3.291	4.371	2.486
20502	3	Afucosylated	2.74E-09	4.19E+05	1.15E-03	0.483	2.923	1.655	2.446
20506	3	Fucosylated	1.93E-09	3.65E+05	7.03E-04	0.739	1.770	1.77	3.249
20506	3	Afucosylated	2.01E-09	3.60E+05	7.25E-04	0.767	1.769	1.769	PF
22213	3	Fucosylated	5.81E-09	1.53E+05	8.88E-04	0.651	5.199	2.445	4.401
22213	3	Afucosylated	5.11E-09	1.69E+05	8.62E-04	0.667	3.878	2.453	3.545

[00352] The fucosylated and afucosylated anti B7-H4 antibodies were also characterized by flow cytometry. In these experiments, HEK293T cell lines were transfected to express full-length cynomolgus monkey, mouse, or rat B7-H4. In addition, the endogenous human B7-H4 expressing SK-BR-3 breast cancer cell lines were used to assess the cell binding potency of B7-H4 antibodies. 1x10⁵ SK-BR-3 cells or 293 cells transfected to express full-length human, cynomolgus monkey, mouse, or rat B7-H4 were incubated with titrating doses of the B7-H4 antibodies. Following incubation, cells were pelleted, washed, incubated with a secondary labeling antibody, and run on a flow cytometer. Data were analyzed using the FlowJo software. MFI was plotted vs. antibody concentration, and the EC₅₀ cell binding potency was calculated using nonlinear regression curve fit (GraphPad Prism).

[00353] The B7-H4 antibodies demonstrated potent dose-dependent binding to SK-BR-3 cells endogenously expressing B7-H4 on the cell surface or 293 cell lines transfected to express cynomolgus monkey, mouse, or rat B7-H4 on the cell surface. Binding potency and species cross-reactivity was not impacted by whether an antibody was fucosylated or afucosylated (Figs. 4A-4D and Table 17).

Example 10: Binding of afucosylated and fucosylated monoclonal antibodies to human Fcγ receptor IIIa (FcγRIIIa) V158 allele

[00354] Antibody 20502 was produced as both fucosylated (Ab-F) and afucosylated (Ab-A) and tested for the binding affinity of the Fc region to FcγRIIIa (V158) by surface plasmon resonance (SPR). Briefly, Protein A was covalently attached to a dextran chip using the amine coupling kit with 100 mM ethylenediamine in 100 mM Sodium Borate buffer, pH 8.0 as the blocking reagent. Ab-A or Ab-F was captured at 2 densities on separate flow cells, and a Protein A derivatized flow served as a reference control. Fc gamma RIIIA (V158) was diluted in HBS-P+ running buffer and injected at 6 concentrations (0 nM, 1.37 nM, 12.3 nM, 37 nM, 111 nM, 333 nM, and 1000 nM) in duplicate. The association constant, dissociation constant, and affinity for Ab-A binding were calculated using the Biacore T200 Evaluation Software 1:1 binding model. The affinity constant for Ab-A and Ab-F binding were determined using the Biacore T200 Evaluation Software steady state affinity model. The afucosylated B7-H4 antibody (Ab-A) has a 140-fold higher affinity for Fc gamma receptor IIIA (V158) than the same antibody with a fucosylated Fc (Ab-F) (Figs. 5A and 5B, Table 18).

Table 18: Fcγ receptor IIIa (FcγRIIIa) V158 allele binding

	ka (1/Ms)	kd (1/s)	K _D (nM)
Ab-A	6.46E+05	9.54E-10	15
Ab-F	N/A	N/A	210

Example 11: Afucosylated and fucosylated monoclonal antibodies T cell checkpoint blockade activity

[00355] Primary human T cells were enriched from PBMCs using the EasySep™ Human T Cell Enrichment Kit based on the manufacturer's instructions. Enriched T cells were incubated at 2×10^5 cell/mL with anti-CD3/anti-CD28 Dynabeads, at a one bead per cell ratio, at 37°C. Six days later, the beads were magnetically removed, and T cells were washed and incubated at 1×10^6 cell/mL with 10 U/mL IL-2 at 37°C. Four days later, T cells were washed and incubated at 1×10^6 cells/mL along with artificial antigen presenting cells (aAPCs) at a 2×10^6 cells/mL concentration at 37°C in the presence of B7-H4 antibody dose titration. aAPCs were treated with Mitomycin C for one hour at 37°C and then thoroughly washed prior to adding to the T cell co-culture. 72 hours after co-culture of T cells, aAPCs, and B7-H4 antibodies, plates were centrifuged and supernatants were harvested and assessed for IFN γ production by ELISA. IFN γ production was plotted vs. antibody concentration and the EC50 potency was calculated using nonlinear regression curve fit (GraphPad Prism).

[00356] The B7-H4 antibodies demonstrated potent T cell checkpoint blockade activity as measured by an increase in IFN γ production. Moreover, there was no demonstrable difference in potency between afucosylated and fucosylated antibodies (Fig. 6A and Table 19.)

Table 19: T Cell Checkpoint blockade potency

Antibody	BIN	aAPC Assay (EC50 +/- STD; nM)	
		Afucosylated	Fucosylated
20502	3	0.89 +/-0.44	0.74 +/-0.39
20506	3	1.05 +/-0.28	0.95 +/-0.46
22213	3	0.16 +/-0.05	0.17 +/-0.08

[00357] Next, primary human T cells were enriched from HLA-A2+ donor PBMCs using the Human Pan T Cell Isolation Kit following the manufacturer's instructions. MART-I TCR

expressing T cells were generated by first activating 5×10^6 enriched Pan T cells with 1.5×10^7 anti-CD3/anti-CD28 Dynabeads, 100ng/mL IL-2 and 15ng/mL IL-7 for 48 hours. 5×10^6 activated T cells were then transduced with MART-I TCR lentiviral particles in the presence of 200ng/mL IL-2, 30ng/mL IL-7 and 10ug/mL polybrene. 24 hours post transduction, MART-I TCR+ Pan T cells were expanded over a 15-day period in the presence of 33.3ng/mL IL-2 and 5ng/mL IL-7. To generate HLA-A2 expressing target cell lines, the endogenous B7-H4 expressing human breast cancer cell lines MDA-MB-468 and SK-BR-3 were transduced with HLA-A2 lentiviral particles for 48 hours. Furthermore, B7-H4 was knocked-out of the HLA-A2+ SK-BR-3 cell line. MART-I TCR+ Pan T cells were co-cultured in the presence of the various target cell lines at a 1:1 E:T ratio, 500 μ g/mL of MART-I peptide and 67nM of the B7-H4 antibody 20502 (afucosylated) or a human isotype control. 24 hours post co-incubation, plates were centrifuged and supernatants were harvested and assessed for IL-2 production by AlphaLisa, according to the manufacturer's instructions.

[00358] As shown in Fig. 6B, B7-H4 demonstrated T cell checkpoint ligand activity in this assay when endogenously expressed at physiologic levels as IL-2 production was reduced in wells containing SK-BR-3 B7-H4+ cells relative to SK-BR-3 KO cells. Moreover, the B7-H4 antibody also demonstrated T cell checkpoint blockade activity as measured by an increase in IL-2 production relative to isotype control treated cells (Fig. 6B). Thus, this data confirm the T cell checkpoint blockade activity of B7-H4 antibody 20502 (afucosylated) and show that the B7-H4 antibody 20502 provides T cell checkpoint blockade activity in cells that endogenously express B7-H4.

Example 12: Afucosylated and fucosylated monoclonal antibodies ADCC activity

[00359] B7-H4 antibodies were assessed for ADCC activity against a B7-H4-expressing target cell line. Specifically, primary human PBMCs cells were cytokine activated at 1×10^6 cells/mL with 200 IU/mL IL-2 at 37°C. The next day, cells were washed and incubated at a 40:1 Effector:Target ratio with SK-BR-3 target cells that were labeled with Calcein-AM. 4 hours after incubation, target cell lysis was quantified using a fluorimeter. A Triton/X treated sample served as the max lysis control sample, whereas a media alone treated sample served as the background lysis control sample. The percent (%) specific lysis was calculated as follows: $[1 - ((\text{sample} - \text{media control}) / (\text{max lysis} - \text{media control}))] \times 100$. The percent (%) specific lysis was plotted vs. antibody concentration and the EC50 potency was calculated using nonlinear regression curve fit

(GraphPad Prism).

[00360] The B7-H4 antibodies demonstrated potent dose-dependent ADCC activity against the endogenous B7-H4 expressing breast cell line SK-BR-3. Moreover, the afucosylated antibodies demonstrated significantly more potent ADCC activity in comparison to the fucosylated antibodies (Fig. 7 and Table 20).

Table 20: ADCC activity

Antibody	BIN	ADCC Assay (EC50 +/- STD; nM)	
		Afucosylated	Fucosylated
20502	3	0.0007 +/-1.1x10E-3	0.0370 +/-6.2E-2
20506	3	0.0015 +/-2.5x10E-3	0.0135 +/-2.1E-2
22213	3	0.0015	0.014

Example 13: Correlation of ADCC activity with receptor density

[00361] B7-H4 density was quantified on the surface of SK-BR-3, HCC1569, ZR-75-1, MDA-MB-48, and HCC1964 cells by FACS according to the manufacturer's specifications. Specifically, 1×10^5 cells were incubated with 15 ug/mL B7-H4 antibody on ice for 25 minutes. In parallel, one drop of Quantum™ Simply Cellular (QSC) microspheres (pre-coated with increasing concentrations of anti-mouse IgG capture antibody) was also incubated with 15 ug/mL B7-H4 antibody on ice for 25 minutes. Following incubation, cells and QSC microspheres were pelleted and washed, and samples were acquired on a flow cytometer. Data was analyzed using the FlowJo software. Mean fluorescence intensity (MFI) was calculated and entered into the QuickCal® spreadsheet. A regression associating each bead's fluorescence channel value to its pre-assigned Antibody Binding Capacity (ABC) value will be calculated automatically. An ABC value was assigned once the MFI values for the labeled cells are also added into the template).

[00362] B7-H4 antibodies were assessed for ADCC activity against B7-H4 expressing target cell lines with different levels of B7-H4 cell surface density. Specifically, 1×10^4 SK-BR-3, HCC1569, ZR-75-1, MDA-MB-468, or HCC1964 target cells were co-incubated with dose-titrations of B7-H4 antibody at 4oC. 25 minutes later, a single use vial of Jurkat-huCD16 reporter cells from Promega was thawed, and 7.5×10^4 cells were added to the target cell/B7-H4 antibody mixture and incubated at 37oC. 24 hours later, the samples were brought to room temperature (RT) and incubated with Bio-Glo buffer. The substrate and luminescence were

quantified on an EnVision multi-label reader. The data was plotted as luminescence vs. antibody concentration and the EC50 potency was calculated using nonlinear regression curve fit (GraphPad Prism).

[00363] B7-H4 antibody ADCC activity was dependent on B7-H4 cell surface density: as the numbers of cell surface molecules decreased, the amount of maximal ADCC activity also decreased. Moreover, afucosylated antibodies demonstrated improved ADCC activity in comparison to the fucosylated antibodies, especially against target cells with lower levels of B7-H4 cell surface density (Fig. 8).

Example 14: *In vivo* anti-tumor efficacy

[00364] Seven week old female BALB/c mice were purchased from Charles River Laboratories (Hollister, CA) and were acclimated for up to three weeks before the start of the studies. The murine colorectal carcinoma cell line CT26 was engineered to express a chimeric protein consisting of the extracellular domain of murine B7-H4 with the transmembrane domain of murine B7H3. These tumor cells were implanted subcutaneously over the right flank of the mice at 1.0×10^6 cells/200 μ l/mouse. Prior to inoculation, the cells were cultured for no more than three passages in RPMI 1640 medium supplemented with 10% heat-inactivated Fetal Bovine Serum (FBS), 2mM L-Glutamine. Cells were grown at 37°C in a humidified atmosphere with 5% CO₂. Upon reaching 80-85% confluence, cells were harvested and resuspended in a 1:1 mixture of serum-free RPMI 1640 and Matrigel at 5×10^6 cells per milliliter).

[00365] Mice were monitored twice weekly following cell implantation for tumor growth. For tumor measurements, the length and width of each tumor was measured using calipers and volume was calculated according to the formula: tumor volume (mm³) = (width (mm) x length (mm)²)/2. On the day of treatment initiation, all tumors were measured, outliers were excluded, and mice were randomly assigned to treatment groups. For anti-B7-H4 treatment, antibodies used include 20502 (Fig. 9A) and 22213 (Fig. 9B). As controls, mice were administered polyclonal human IgG (Bio X Cell, BE0092) or mouse IgG2a (Bio X Cell, BE0085). The antibodies were administered four times via intravenous (i.v.) injection twice weekly beginning on Day 4 or 5 after inoculation.

[00366] Tumors continued to be measured at least twice per week until tumor volume exceeded 10% of animal weight, or approximately 2000 mm³. The change in tumor size is shown by graphing individual tumors relative to the day upon which animals were inoculated

with CT26 cells. P-values were calculated using unpaired, two-tailed t-test analyses of the calculated tumor volumes on each day of the study. Treatment with 20502 or 22213 significantly reduced tumor growth compared to human IgG control ($p < 0.05$) when administered between doses of 10-20 mg/kg (Figs. 9A and 9B).

[00367] Similar experiments were performed using mice with implanted 4T1 cells (a murine breast carcinoma cell line) or B16 (a murine melanoma cell line). These mice were treated with 20 mg/kg of a mouse surrogate of 20502 called 20502-msIgG2a-F, which contains the 20502 variable region fused to fucosylated mouse IgG2a, or with murine IgG control antibody. Treatment with 20502-msIgG2a-F significantly reduced tumor growth compared to the murine IgG control in both the 4T1 breast carcinoma and B16 melanoma models (Fig. 10).

[00368] Additional experiments were also performed using afucosylated 20502 in a MX-1 human breast cancer xenograft model. Female NSG (NOD-scid, IL2R gammanull) mice were purchased from the Jackson Laboratory (Bar Harbor, ME) and were acclimated for one week before the start of the studies. The human breast cancer cell line MX-1 had previously been shown to endogenously express cell-surface B7H4 protein. These tumor cells were implanted subcutaneously over the right flank of the mice at 1.0×10^6 cells/100 μ l/mouse in a 1:1 mixture of serum-free RPMI 1640 and Matrigel at 5×10^6 cells per milliliter.

[00369] Mice were monitored twice weekly following cell implantation for tumor growth. For tumor measurements, the length and width of each tumor was measured using calipers, and volume was calculated according to the formula: Tumor volume (mm^3) = (width (mm) $\times$ length (mm)²)/2. On Day 7 after inoculation, all tumors were measured, outliers were excluded, and mice were randomly assigned to treatment groups. All animals were administered a DNA construct that induced constitutive human IL-15 expression in the circulation for the remainder of the study. On Day 9, half of the mice received an intravenous (i.v.) injection of 20×10^6 human peripheral blood monocyctic cells (PBMCs), acquired from StemCell Technologies (Tukwila, WA). Beginning on Day 11, mice were administered afucosylated 20502 (20 mg/kg) or saline as a negative control. Therapeutics were administered four times via intravenous (i.v.) injection twice weekly.

[00370] Tumors continued to be measured at least twice per week until tumor volume exceeded 10% of animal weight or until the animals demonstrated a 15% or greater loss of initial body weight. P-values were calculated using One-Way ANOVA comparing the mean tumor volumes across all treatment groups on Day 28. As shown in Figure 11, treatment with afucosylated 20502 significantly reduced tumor growth compared to saline control ($p < 0.05$) only

when administered to mice previously injected with human PBMCs.

Example 15: *In vivo* anti-tumor efficacy in combination with anti-PD-1 antibody

Methods

[00371] Eight week old female BALB/c mice were purchased from Charles River Laboratories (Hollister, CA) and were acclimated for up to two weeks before the start of the study. The murine breast carcinoma cell line 4T1 was engineered to express a chimeric protein containing the extracellular domain of murine B7-H4 and the transmembrane domain of murine B7H3. Tumor cells were implanted orthotopically in the mammary fat pad of the mice at 0.5×10^5 cells/50 μ l/mouse. Prior to inoculation, the cells were cultured for no more than three passages in RPMI 1640 medium supplemented with 10% heat-inactivated Fetal Bovine Serum (FBS). Cells were grown at 37°C in a humidified atmosphere with 5% CO₂. Upon reaching 80-85% confluence, cells were harvested and resuspended in serum-free RPMI 1640 on the ventral flank of each mouse into the mammary fat pad.

[00372] Mice were monitored twice weekly following cell implantation for tumor growth. The length and width of each tumor was measured using calipers, and the volume was calculated according to the formula: Tumor volume (mm³) = (width (mm) x length (mm)²)/2. On the day of treatment initiation, all tumors were measured, outliers were excluded, and mice were randomly assigned to treatment groups. For the anti-B7-H4 treatment, a mouse surrogate of 20502 called 20502-msIgG2a-F, which contains the 20502 variable region fused to fucosylated mouse IgG2a, was utilized. As a control, mice were administered msIgG2a (anti-HEL). 20502-msIgG2a-F or msIgG2a were administered four times via intravenous (i.v.) injection twice weekly beginning on Day 11 after inoculation. Anti-PD-1 (a modified version of RMP1-14 (Bio X Cell) containing a Fc silent msIgG2a domain) was administered three times via intraperitoneal (i.p.) injection twice weekly beginning on Day 11 after inoculation. Tumors continued to be measured at least twice per week until tumor volume exceeded 10% of animal weight, or approximately 2000 mm³.

Results

[00373] The change in tumor size, the change in mean tumor volume, and the percent survival are shown in Figs. 12A, 12B and 12C, respectively. Treatment with either 20502-msIgG2a-F or anti-PD-1 significantly reduced tumor growth compared to msIgG2a control ($p < 0.05$). The co-administration of 20502-msIgG2a-F and anti-PD-1 significantly enhanced tumor growth

inhibition compared to either monotherapy ($p < 0.05$). Moreover, combination therapy resulted in complete tumor regression in 5 of 12 mice. P-values were calculated using One-Way ANOVA analyses of the calculated tumor volumes on each day of the study with multiple comparisons between each group.

Example 16: Anti-B7-H4 antibody increases NK-cell and T-cell infiltration and up-regulates PD-L1

[00374] Eight week old female BALB/c mice were purchased from Charles River Laboratories (Hollister, CA) and implanted orthotopically in the mammary fat pad of the mice with 4T1+moB7-H4/H3 cells at 0.5×10^5 cells/50 μ l/mouse. On the day of treatment initiation, all tumors were measured, outliers were excluded, and mice were randomly assigned to treatment groups. Mice were administered huIgG1 (anti-HEL) or afucosylated 20502 at 20 mg/kg via intravenous (i.v.) injection twice (Day 11 and Day 14 post-inoculation).

[00375] At 24 hours after the second dose administration, mice were euthanized and perfused with phosphate-buffered saline (PBS). Tumors were then extracted, fixed in 10% formalin for five hours, rinsed in PBS, and placed in a 30% sucrose solution for at least 24 hours. Tumors were embedded in Tissue-Tek® O.C.T. Compound and sectioned at 20 μ m in a -15°C chamber (cryostat). Tissue-mounted slides were rinsed in 0.3% Triton in PBS, blocked with 5% normal goat serum, and stained with primary antibody (anti-NKp46, anti-CD3, or anti-PD-L1; 1:500) overnight. Two serial sections from each tumor were stained.

[00376] Following overnight incubation, slides were rinsed in 0.3% Triton then incubated with secondary antibody (1:400) for three hours in a dark humid chamber and rinsed. The tissue was then fixed in 1% paraformaldehyde and rinsed in PBS. Coverslips were mounted using Vectashield® with DAPI, sealed with Cytoseal™, and left to dry in a dark chamber. Images were acquired manually with a fluorescence microscope and camera. As shown in Figure 13, treatment with afucosylated 20502 resulted in increased natural killer (NK) cells (as measured by the anti-NKp46 antibody) and increased CD3+ T cells at tumor edges with a moderate increase of CD3+ T cells in the tumor core. Increased PD-L1 expression was also observed.

Example 17: Anti-B7-H4 antibody significantly reduces tumor growth *in vivo* in

4T1- and B16-moB7-H4/H3 models in a dose dependent manner

[00377] Six- to eight-week old female BALB/c or C57Bl/6 mice were purchased from Charles River Laboratories (Hollister, CA) and were acclimated for up to three weeks before the start of the studies. The murine breast carcinoma cell line 4T1 and melanoma cell line B16-F10 were engineered to express murine a chimeric protein consisting of the extracellular domain of murine B7-H4 with the transmembrane domain of murine B7-H3. These tumor cells were implanted orthotopically in the mammary fat pad at 0.05×10^6 cells/50 μ l/mouse for 4T1+moB7-H4/H3 or subcutaneously over the right flank of the mice at 0.5×10^6 cells/100 μ l/mouse for B16+moB7-H4/H3. Prior to inoculation, the cells were cultured for no more than three passages in RPMI-1640 or DMEM medium supplemented with 10% heat-inactivated Fetal Bovine Serum (FBS) and 2mM L-Glutamine. Cells were grown at 37°C in a humidified atmosphere with 5% CO₂.

[00378] Mice were monitored twice weekly following cell implantation for tumor growth. For tumor measurements, the length and width of each tumor was measured using calipers, and volume was calculated according to the formula: Tumor volume (mm³) = (width (mm) x length (mm)²)/2. On the day of treatment initiation, all tumors were measured, outliers were excluded, and mice were randomly assigned to treatment groups. Mice were administered 20502-msIgG2a-F antibody (anti-B7-H4, msIgG2a, fucosylated (also called “cmFPA150-F”) or a mouse IgG2a control antibody four times via intravenous (i.v.) injection twice weekly beginning on Day 11 (4T1+moB7-H4/H3) or Day 6 (B16+moB7-H4/H3) after inoculation, except for the 20 mg/kg group, which was administered continuously twice weekly until the end of study.

[00379] Tumors continued to be measured at least twice per week until tumor volume exceeded 10% of animal weight, or approximately 2000 mm³. The change in tumor size is shown by graphing mean tumor volume relative to the day upon which animals were inoculated. Treatment with 20502-msIgG2a-F significantly reduced tumor growth compared to mouse IgG2a control ($p < 0.05$) when administered at doses of 1 mg/kg or greater in the 4T1+moB7-H4/H3 model (see Figs. 14A and 14B) and at doses of 3 mg/kg or greater in the B16+moB7-H4/H3 model (Figs. 15A and 15B). Statistical significance was calculated using OneWay ANOVA comparing all treatment groups to msIgG2a.

[00380] Figs. 14A and 14B show that 20502-msIgG2a-F antibody significantly reduces growth of 4T1 expressing B7-H4/H3. BALB/c mice were inoculated orthotopically with 4T1 breast carcinoma cells engineered to express murine B7-H4 ECD fused to B7-H3 TM. Mice were administered 20502-msIgG2a-F antibody (anti-B7-H4, msIgG2a, fucosylated) twice weekly

beginning on Day 11 after inoculation. 20502-msIgG2a-F antibody demonstrated a dose-dependent reduction in tumor growth, with significant tumor growth inhibition at 30 mg/kg ($p = 0.0003$), 20 mg/kg ($p = 0.0103$), 10 mg/kg ($p = 0.0419$), 3 mg/kg ($p = 0.0277$), and 1 mg/kg ($p = 0.0333$) as assessed by OneWay ANOVA on Day 30.

[00381] Figs. 15A and 15B show that 20502-msIgG2a-F antibody significantly reduces growth of B16 expressing B7-H4/H3. C57Bl/6 mice were inoculated subcutaneously with B16-F10 melanoma cells engineered to express murine B7-H4 ECD fused to B7-H3 TM. Mice were administered 20502-msIgG2a-F antibody (anti-B7-H4, msIgG2a, fucosylated) twice weekly beginning on Day 6 after inoculation. 20502-msIgG2a-F antibody demonstrated a dose-dependent reduction in tumor growth (Fig. 15A), with significant tumor growth inhibition at 30 mg/kg ($p = 0.0085$), 20 mg/kg ($p = 0.0041$), 10 mg/kg ($p = 0.0017$), and 3 mg/kg ($p = 0.0420$) as assessed by OneWay ANOVA on Day 23 (Fig. 15B).

[00382] Thus, the 20502-msIgG2a-F antibody significantly reduced tumor size in a dose-dependent manner in two different cancer models. This data in breast carcinoma and melanoma cell lines indicate that the 20502-msIgG2a-F antibody can be used to treat patients with cancer.

Sequence Tables

GITR Antibody Sequences

SEQ ID NO	Sequence
411	SGSVFSIDAM
412	LSGISSAK
413	YADVSTGWGRDAHGYW
414	EVQLLES GGGEVQPGGSLRLSCAASGSVFSIDAMGWYRQAPGKQRELVA VLSGISSAKYAASAPGRFTISRDNKNTVYLMSSSLRAEDTAVYYCYADV STGWGRDAHGYWGQGTLVTV
415	EVQLLES GGGEVQPGGSLRLSCAASGSVFSIDAMGWYRQAPGKQRELVA VLSGISSAKYAASAPGRFTISRDNKNTVYLMSSSLRAEDTAVYYCYADV STGWGRDAHGYWGQGTLVTVKPGGSGGSEVQLLES GGGEVQPGGSLRLS CAASGSVFSIDAMGWYRQAPGKQRELVAVLSGISSAKYAASAPGRFTISR DNKNTVYLMSSSLRAEDTAVYYCYADVSTGWGRDAHGYWGQGTLVT VKPGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVTV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD

	WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
416	EPKSSDKTHTCPPC
417	DKTHTCPPC
418	ESKYGPPCPPC
419	GGSGGS
420	GGSGGSGGS
421	GGSGGSGGSGGS
422	GGSGGSGGSGGSGGS
423	GGGG
424	GGGGG
425	GGGGGG

CD80 Sequences

SEQ ID NO	Sequence
426	VIHVTKEVKEVATLSCGHNVSVEELAQTIRYWQKEKKMVLTMMSGD MNIWPEYKNRTIFDITNNLSIVILALRPSDEGTYECVVLKYEKDAFKREH LAEVTLVKADFPTPSISDFEIPSTNIRRIICSTSGGFPEPHLSWLENGEEL NAINTTVSQDPETELYAVSSKLDFNMTTNHSMCLIKYGHRLRVNQTFN WNTTKQEHFPDN
427	VIHVTKEVKEVATLSCGHNVSVEELAQTIRYWQKEKKMVLTMMSGD MNIWPEYKNRTIFDITNNLSIVILALRPSDEGTYECVVLKYEKDAFKREH LAEVTLVKADFPTPSISDFEIPSTNIRRIICSTSGGFPEPHLSWLENGEEL NAINTTVSQDPETELYAVSSKLDFNMTTNHSMCLIKYGHRLRVNQTFN WNTTKQEHFPDNEPKSSDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMI <u>SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY</u> <u>RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV</u> <u>YTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV</u> <u>LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP</u> <u>GK</u>

428	VIHVTKEVKEVATLSCGHNVSV EELAQTRIYWQKEKKMVLTMMSGD MNIWPEYKNRTIFDITNNLSIVILALRPSDEGTYECVVLKYEKDAFKREH LAEVTLSVKADFPTPSISDFEIPTSNIRRIICSTSGGFPEPHLSWLENGEEL NAINTTVSQDPETELYAVSSKLDFNMTTNHSFMCLIKYGHLRVNQTFN WNTTKQEHFPDNEPKSSDKTHTCPPCPAPEFEGGPSVFLFPPKPKDTLMI <u>SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY</u> <u>RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQV</u> <u>YTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV</u> <u>LDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSP</u> <u>GK</u>

CSFR1 Sequences

SEQ ID NO	Sequence
429	QVQLVQSGAE VKKPGSSVKV SCKASGYTFT DNYMIWVRQA PGQGLEWMGD INPYNGGTTF NQKFKGRVTI TADKSTSTAY MELSSLRSED TAVYYCARES PYFSNLYVMD YWGQGTLLTV SS
430	EIVLTQSPAT LSLSPGERAT LSCASQSVD YDGDNYMNWY QKPGQAPRL LIYAASNLES GIPARFSGSG SGTDFLTITIS SLEPEDFAVY YCHLSNEDLS TFGGGTKVEI K
431	GYTFTDNYMI
432	DINPYNGGTT FNQKFKG
433	ESPYFSNLYV MDY
434	KASQSVDYDG DNYMN
435	AASNLES
436	HLSNEDLST
437	QVQLVQSGAE VKKPGSSVKV SCKASGYTFT DNYMIWVRQA PGQGLEWMGD INPYNGGTTF NQKFKGRVTI TADKSTSTAY MELSSLRSED TAVYYCARES PYFSNLYVMD YWGQGTLLTV

	SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTPVSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP SVFLFPPKPK DTLMISRTPE VTCVVVDVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTTPVL DSDGSFFLYS RLTVDKSRWQ EGNVFSCSVM HEALHNHYTQ KSLSLSLGK
438	EIVLTQSPAT LSLSPGERAT LSCKASQSVD YDGDNYMNWY QQKPGQAPRL LIYAASNLES GIPARFSGSG SGTDFLTIS SLEPEDFAVY YCHLSNEDLS TFGGGTKVEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV QWKVDNALQS GNSQESVTEQ DSKDSTYSLs STLTLKADY EKHKVYACEV THQGLSSPVT KSFNRGEC

PD-1 (nivolumab) Antibody Sequences

SEQ ID NO:	Descrip -tion	Sequence
440	heavy chain variable region	QVQLVESGGGVVQPGSRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWDGSKRYYA DSVKGRFTISRDN SKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGT LVTVSS
441	heavy chain constant region	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGT KTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSC SVMHEALHNHYTQKSLSLSLGK
442	light chain variable region	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPAR FSGSGSGTDFLTISLLEPEDFAVYYCQQSSNWPRTFGQGTKEIK
443	light chain constant	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSSTLTLSKADYEKHKVYACEVTHQGLSSPVT KSFNRGEC

	region	
444	heavy FR1	QVQLVESGGGVVQPGRSLRLDCKASGITFS
445	heavy CDR1	NSGMH
446	heavy FR2	WVRQAPGKGLEWVA
447	heavy CDR2	VIWYDGSKRYYADSVKG
448	heavy FR3	RFTISRDN SKNTLFLQMNSLRAEDTAVYYCAT
449	heavy CDR3	NDDY
450	heavy FR4	WGQGTLLTVSS
451	light FR1	EIVLTQSPATLSLSPGERATLSC
452	light CDR1	RASQSVSSYLA
453	light FR2	WYQQKPGQAPRLLIY
454	light CDR2	DASNRAT
455	light FR3	GIPARFSGSGSGTDFTLTISSELPEDFAVYYC
456	light CDR3	QQSSNWPRT
457	light FR4	FGQGTKVEIK

* * *

[00383] The invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

[00384] All references (e.g., publications or patents or patent applications) cited herein are incorporated herein by reference in their entirety and for all purposes to the same extent as if each individual reference (e.g., publication or patent or patent application) was specifically and individually indicated to be incorporated by reference in its entirety for all purposes.

[00385] Other embodiments are within the following claims.

WHAT IS CLAIMED:

1. An isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising:
 - (a) a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 41 and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 42; or
 - (b) a VH comprising the amino acid sequence of SEQ ID NO: 464 and a VL comprising the amino acid sequence of SEQ ID NO: 42.
2. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment further comprises a heavy chain constant region.
3. The antibody or antigen-binding fragment thereof of claim 2, wherein the heavy chain constant region is selected from the group consisting of human immunoglobulins IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2 heavy chain constant regions.
4. The antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein the antibody or antigen-binding fragment further comprises a light chain constant region.
5. The antibody or antigen-binding fragment thereof of claim 4, wherein the light chain constant region is selected from the group consisting of human immunoglobulins IgG κ and IgG λ light chain constant regions.
6. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain and light chain comprising the amino acid sequences of:
 - (a) SEQ ID NOs: 469 and 44, respectively; or
 - (b) SEQ ID NOs: 43 and 44, respectively.
7. An isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, wherein the antibody or antigen-binding fragment thereof comprises the VH and the VL of an antibody selected from the group consisting of 20502 and 20502.1.
8. The antibody or antigen-binding fragment thereof of any one of claims 1 or 7, wherein the antibody or antigen-binding fragment thereof is a human, murine, humanized, or chimeric antibody or antigen-binding fragment thereof.

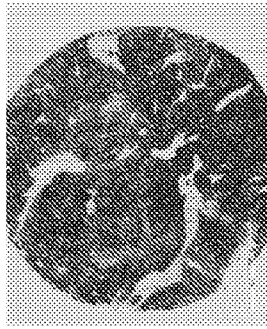
9. The antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof induces T cell proliferation.
10. The antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody or antigen-binding fragment thereof induces CD4⁺ T cell proliferation; induces CD8⁺ T cell proliferation; or induces interferon-gamma (IFN γ) production.
11. The antibody or antigen-binding fragment thereof of any one of claims 1-10, wherein the antibody or antigen-binding fragment thereof is capable of inducing antibody dependent cell mediated cytotoxicity (ADCC) in a B7-H4-expressing cell.
12. The antibody or antigen-binding fragment thereof of any one of claims 1-11, wherein the antibody or antigen-binding fragment thereof inhibits tumor growth in a murine CT26 colorectal carcinoma model, a murine breast carcinoma 4T1 model, or a melanoma cell line B16-moB7-H4/H3 model.
13. The antibody or antigen-binding fragment thereof of any one of claims 1-12, wherein the antibody or antigen-binding fragment thereof binds to the IgV domain of human B7-H4.
14. The antibody or antigen-binding fragment thereof of any one of claims 1-13, wherein the antibody or antigen-binding fragment thereof is afucosylated.
15. The antibody or antigen-binding fragment thereof of any one of claims 1-14, further comprising a detectable label.
16. The antibody or antigen-binding fragment thereof of any one of claims 1-14, wherein the antibody or antigen-binding fragment thereof is conjugated to a toxin.
17. The antibody or antigen-binding fragment thereof of claim 16, wherein the toxin is cytostatic or cytotoxic.
18. The antibody or antigen-binding fragment thereof of claim 16 or claim 17, wherein the toxin is cytotoxic.
19. An isolated polynucleotide comprising a nucleic acid molecule encoding the heavy chain variable region or heavy chain of the antibody or antigen-binding fragment thereof of any one of claims 1-15, and wherein the nucleic acid molecule encodes the VH of SEQ ID NO: 41 or 464 or the heavy chain of SEQ ID NO: 43.
20. An isolated polynucleotide comprising a nucleic acid molecule encoding the light chain variable region or light chain of the antibody or antigen-binding fragment thereof of any one

of claims 1-15, and wherein the nucleic acid molecule encodes the VL of SEQ ID NO: 42 or the light chain of SEQ ID NO: 44.

21. An isolated vector comprising the polynucleotide of claim 19 or claim 20.
22. A host cell comprising the polynucleotide of claim 19 or claim 20, the vector of claim 21, or a first vector comprising the polynucleotide of claim 19 and a second vector comprising the polynucleotide of claim 20.
23. The host cell of claim 22, which is selected from the group consisting of *E. coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, yeast, CHO, YB/20, NS0, PER-C6, HEK-293T, NIH-3T3, HeLa, BHK, Hep G2, SP2/0, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, BMT10 cell, plant cell, insect cell, and human cell in tissue culture.
24. The host cell of claim 22 or 23, wherein the host cell lacks a functional alpha-1,6-fucosyltransferase gene (FUT8) gene.
25. A method of producing an antibody or antigen-binding fragment thereof that binds to human B7-H4 comprising culturing the host cell of any one of claims 22-24 so that the nucleic acid molecule is expressed and the antibody or antigen-binding fragment thereof is produced.
26. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-18 and a pharmaceutically acceptable excipient.
27. The pharmaceutical composition of claim 26, wherein fucosylation is undetectable in the composition.
28. The pharmaceutical composition of claim 26 or claim 27 further comprising an anti-PD-1 antibody or antigen-binding fragment thereof.
29. The pharmaceutical composition of claim 28, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is nivolumab, pembrolizumab, AMP-514, camrelizumab, tislelizumab, or spartalizumab.
30. The pharmaceutical composition of claim 26 or claim 27 further comprising an anti-PD-L1 antibody or antigen-binding fragment thereof.
31. A method for inducing T cell proliferation comprising contacting a T cell with the antibody or antigen-binding fragment thereof of any one of claims 1-18 or the pharmaceutical composition of any one of claims 26-30.

32. A method for inducing CD4⁺ T cell proliferation, CD8⁺ T cell proliferation, and/or interferon gamma production comprising contacting a CD4⁺ T cell or a CD8⁺ T cell with the antibody or antigen-binding fragment thereof of any one of claims 1-18 or the pharmaceutical composition of any one of claims 26-30.
33. A method for killing a cell expressing B7-H4 comprising contacting the cell with the antibody or antigen-binding fragment thereof of any one of claims 1-18 or the pharmaceutical composition of any one of claims 26-30.
34. The method of any one of claims 31-33, further comprising contacting the T cell, the CD4⁺ T cell, the CD8⁺ T cell, or the cell with an anti-PD-1 or anti-PD-L1 antibody or antigen-binding fragment thereof.
35. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-18 or the pharmaceutical composition of any one of claims 26-30 in the preparation of a medicament for the treatment of a B7-H4 expressing cancer.
36. A method of treating a B7-H4 expressing cancer in a subject, the method comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof of any one of claims 1-18 or the pharmaceutical composition of any one of claims 26-30.
37. The use of claim 35 or the method of claim 36, wherein the cancer is selected from the group consisting of breast cancer, ductal carcinoma, endometrial carcinoma, ovarian cancer, non-small cell lung cancer, pancreatic cancer, thyroid cancer, kidney cancer, head and neck cancer, small cell lung cancer, gastric cancer, melanoma, and bladder cancer.
38. The use of claim 35 or claim 37 or the method of claim 36 or claim 37, wherein the cancer is a PD-1 or PD-L1 inhibitor inadequate responder.
39. The use of any one of claims 35, 37, and 38, wherein the treatment further comprises administration of an anti-PD-1 antibody or antigen-binding fragment thereof to the subject, or the method of any one of claims 36-38, further comprising administering to the subject an anti-PD-1 antibody or antigen-binding fragment thereof.
40. The method of claim 39 or the use of claim 39, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is AMP-514, camrelizumab, tislelizumab, spartalizumab, nivolumab, or pembrolizumab.

41. A method for detecting B7-H4 in a sample comprising contacting said sample with the antibody or antigen-binding fragment thereof of any one of claims 1-18.
42. A kit comprising the antibody or antigen-binding fragment thereof of any one of claims 1-18 or the pharmaceutical composition of any one of claims 26-30 and a) a detection reagent, b) a B7-H4 antigen, c) a notice that reflects approval for use or sale for human administration, or d) a combination thereof.
43. An isolated antibody or antigen-binding fragment thereof of any one of claims 1-18, wherein the antibody or antigen-binding fragment thereof inhibits T cell checkpoint blockade activity of B7-H4.



Ovarian Cancer



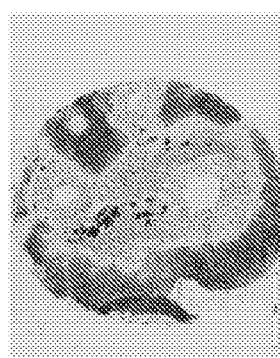
Triple Negative Breast Cancer



Endometrial Cancer



Invasive Ductal Carcinoma



Non-Small Cell Lung Cancer

FIG. 1A

B7-H4 prevalence in various tumor types by IHC

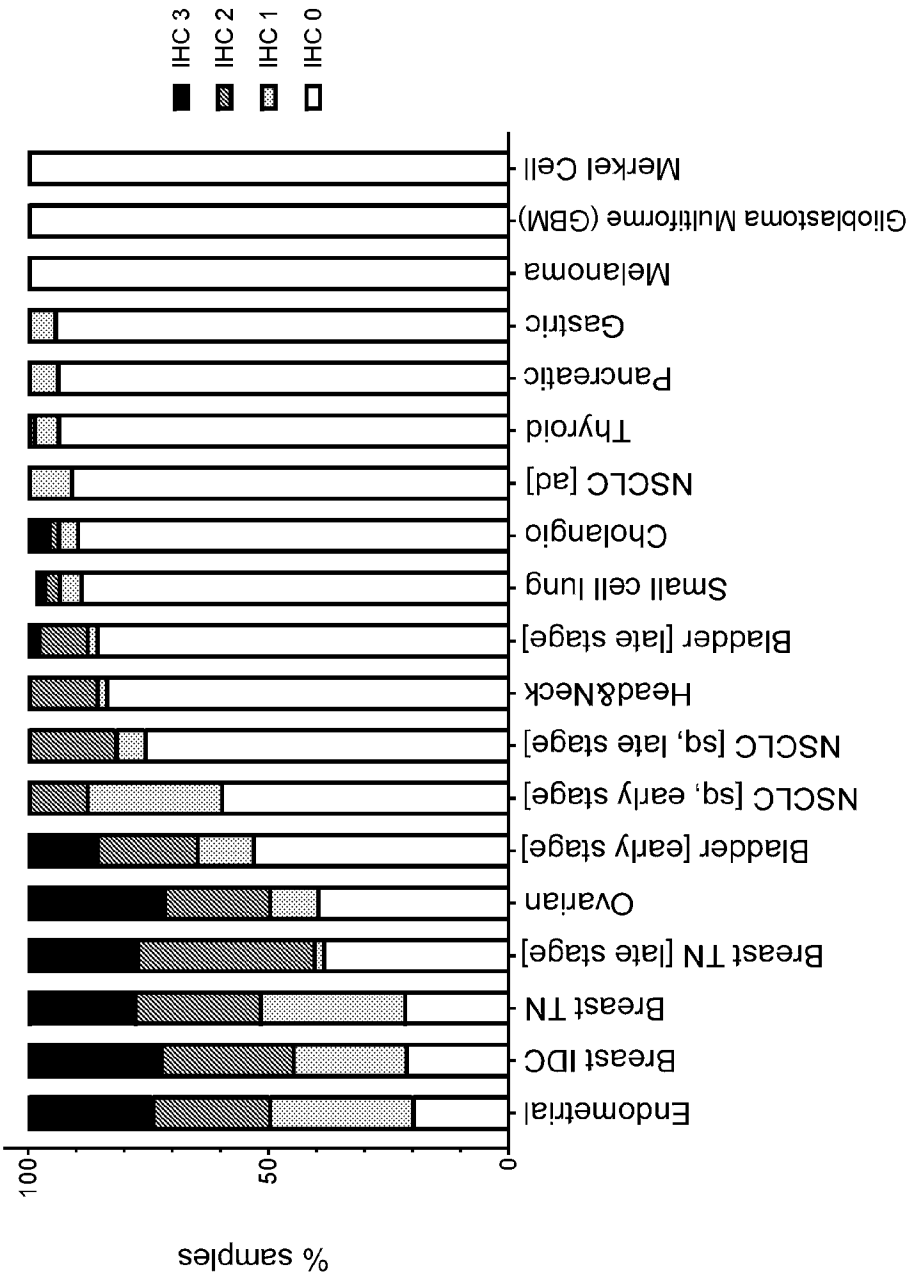


FIG. 1B

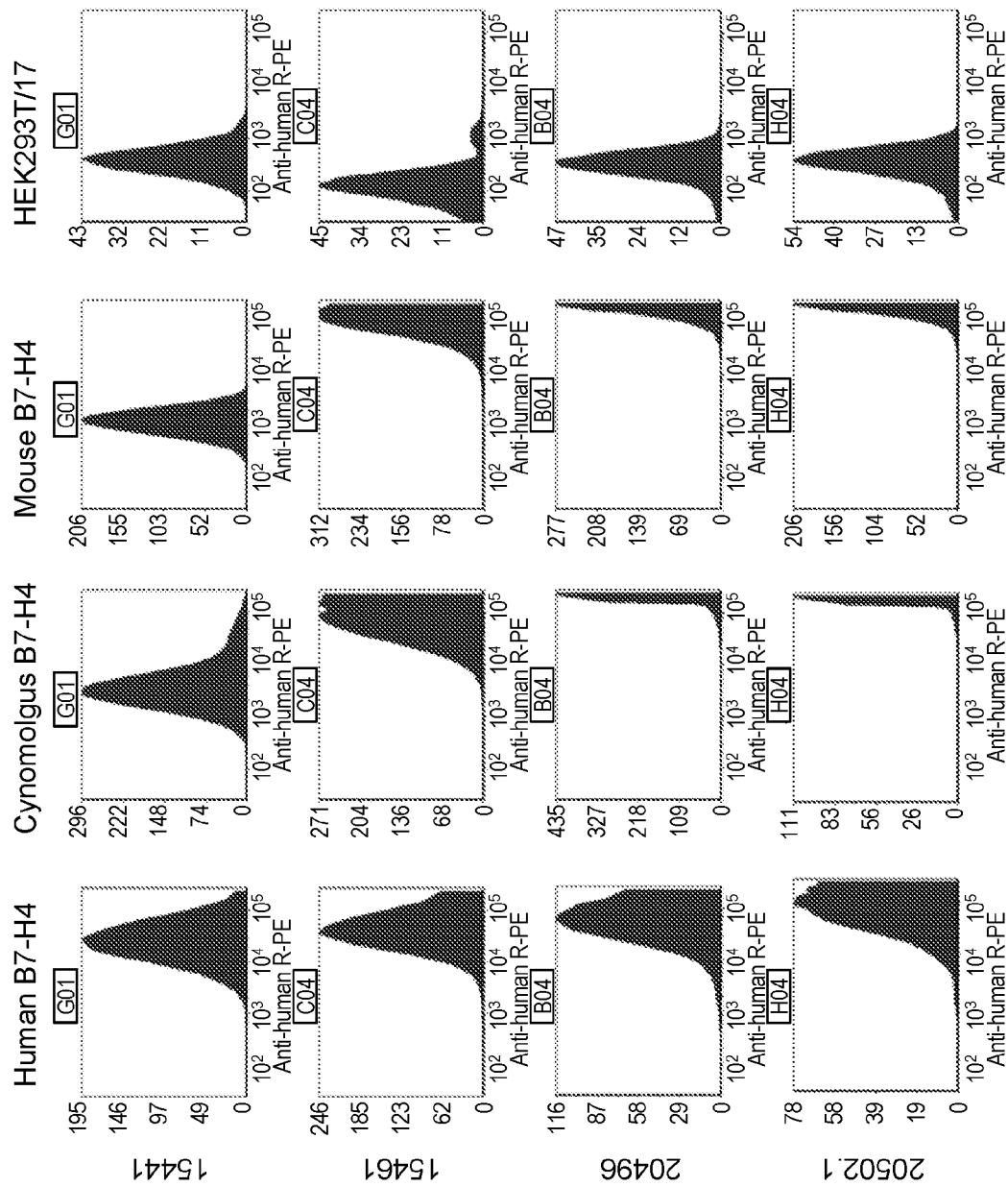


FIG. 2A

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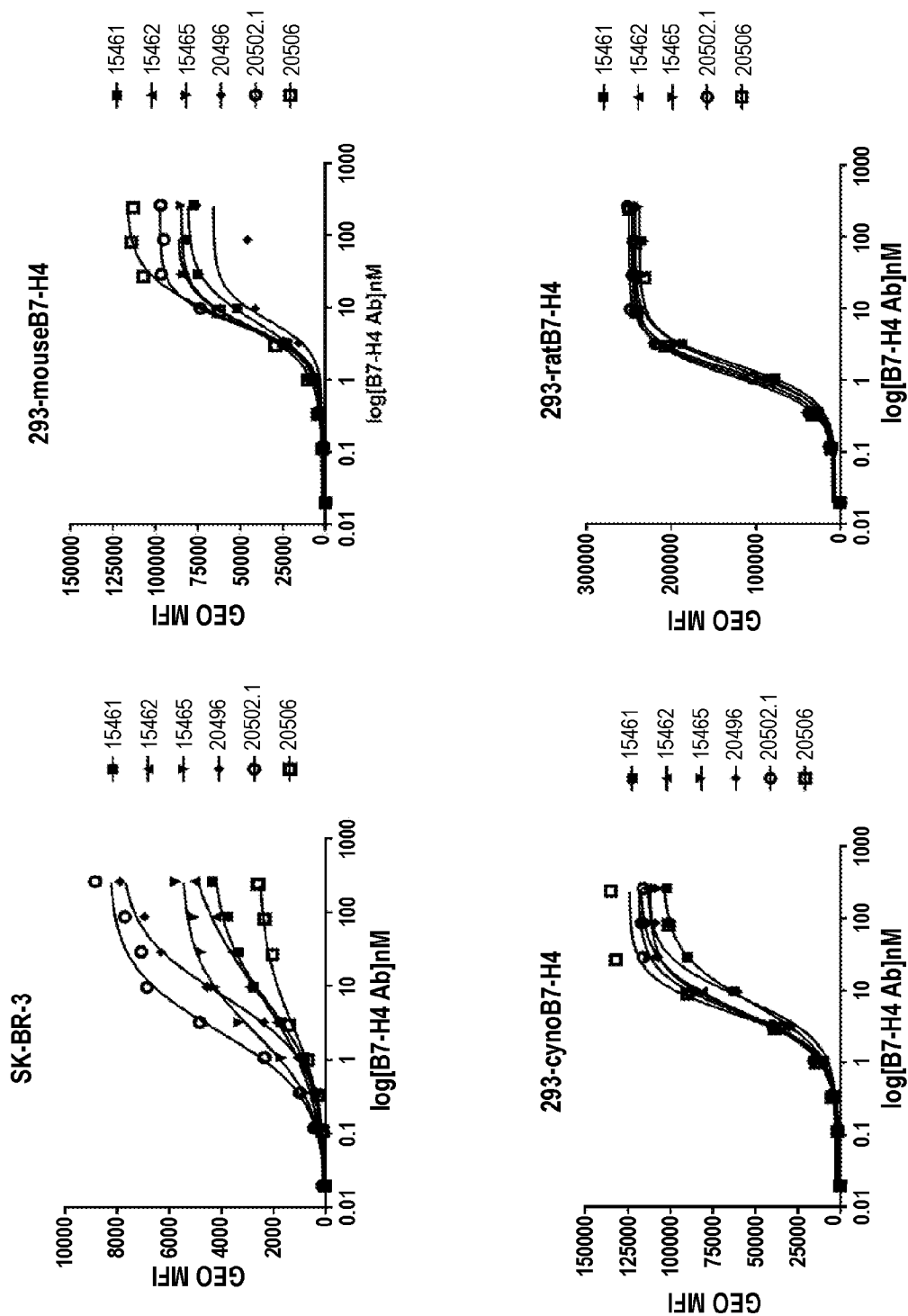


FIG. 2B

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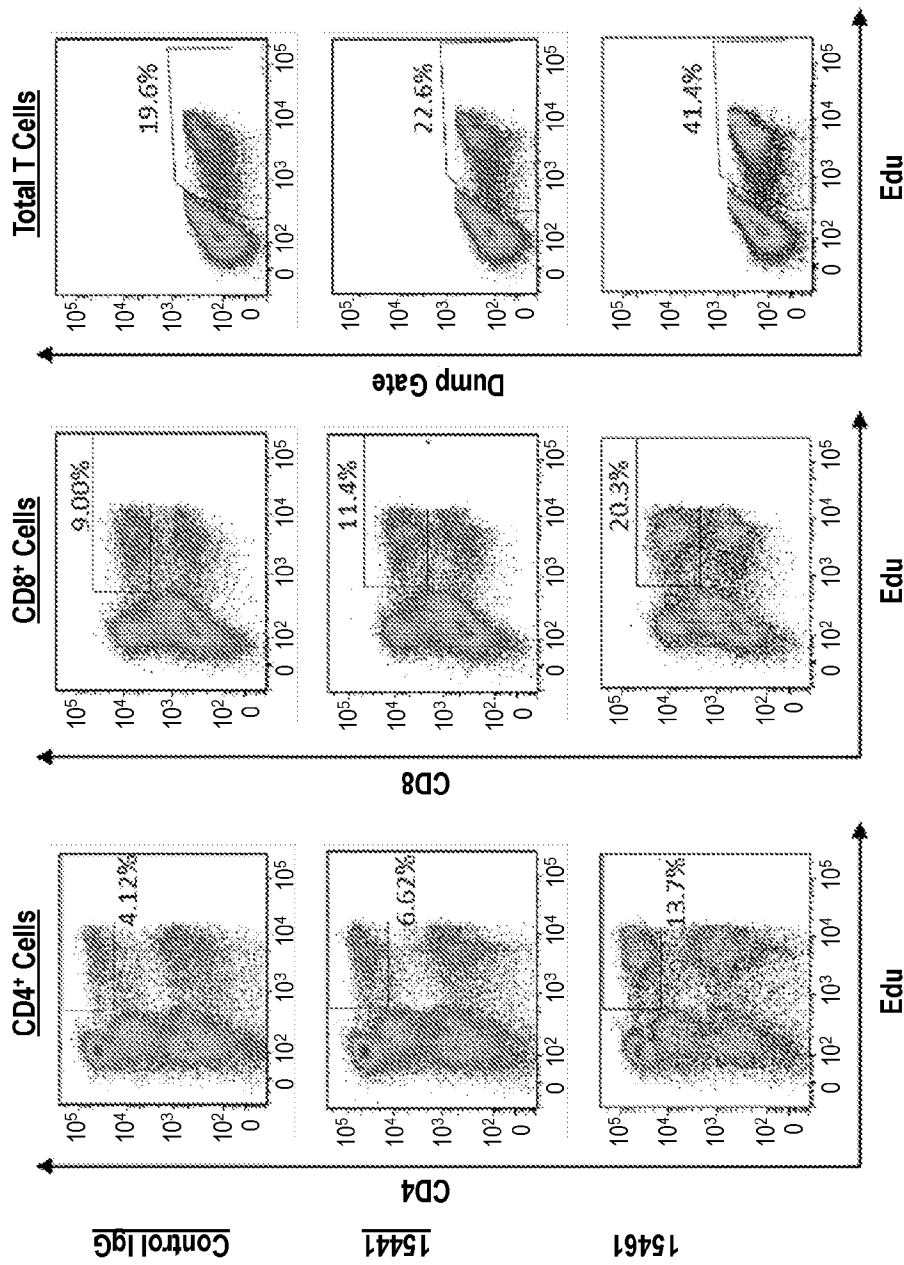


FIG. 3A

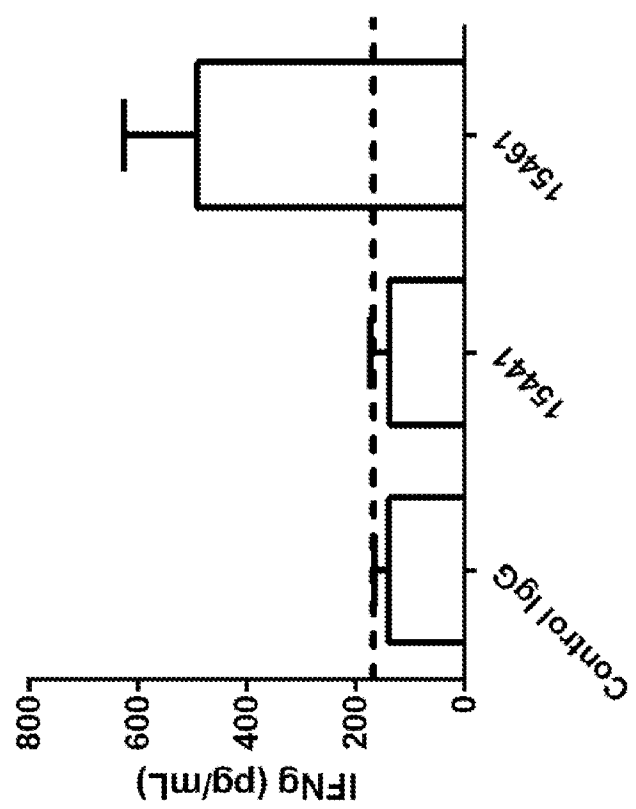
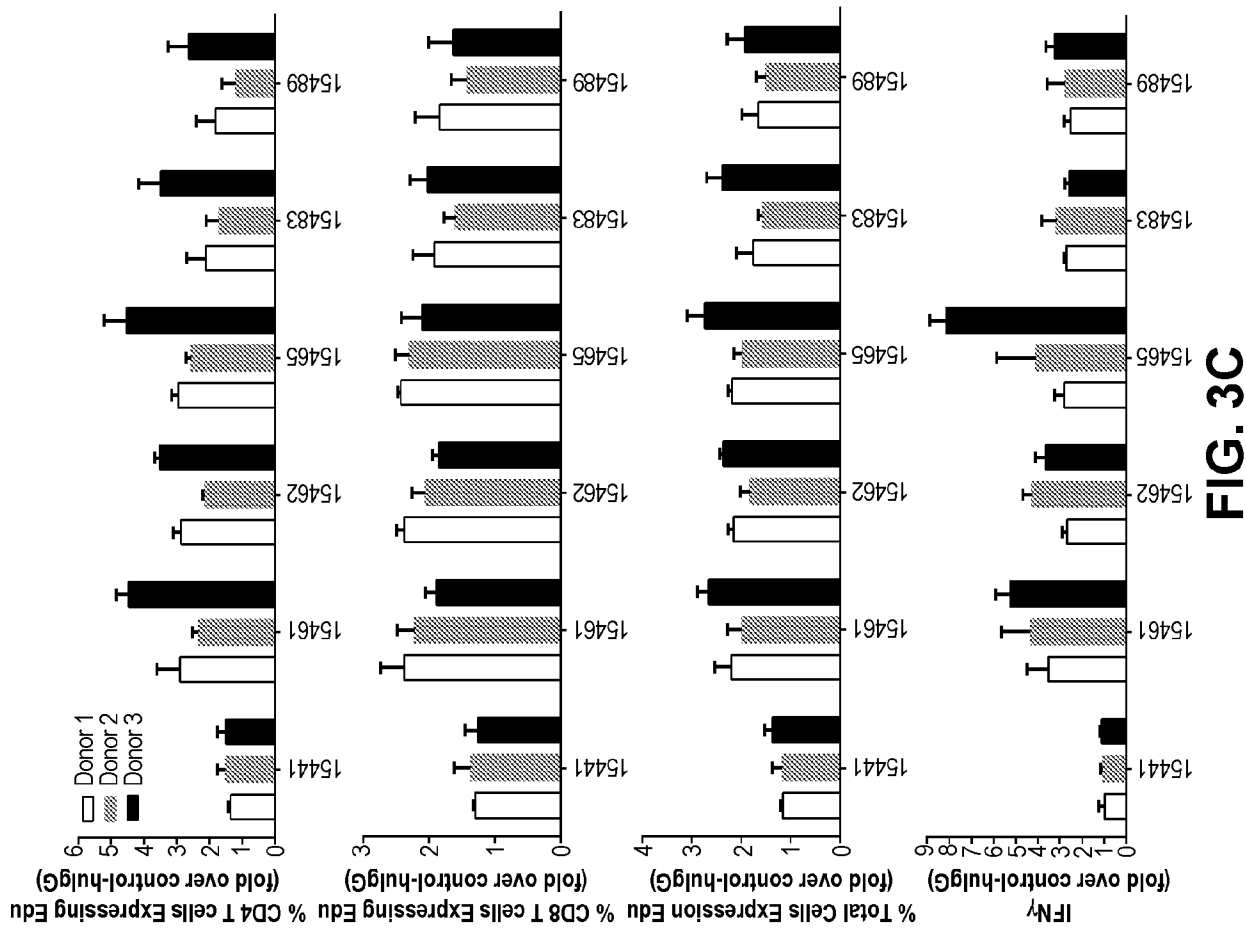


FIG. 3B



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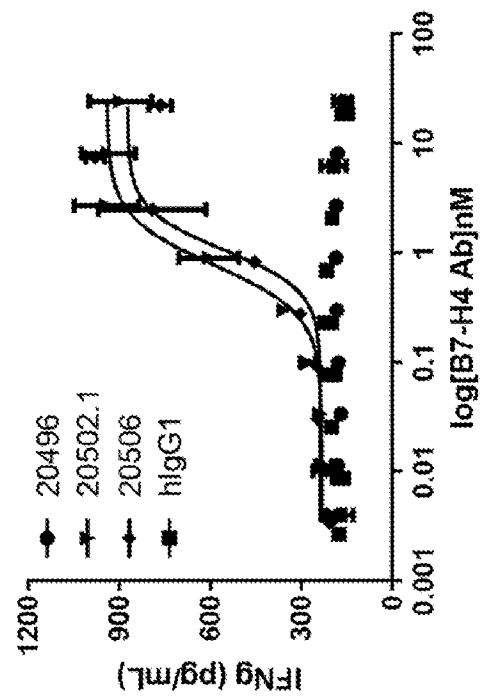


FIG. 3D

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FIG. 4B

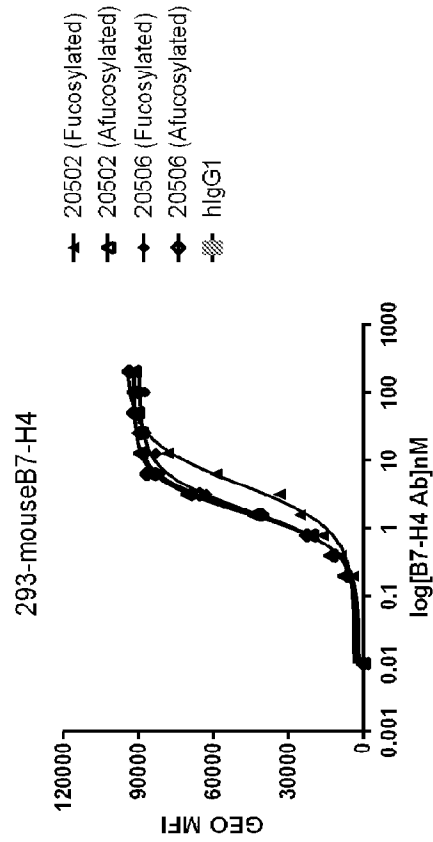


FIG. 4D

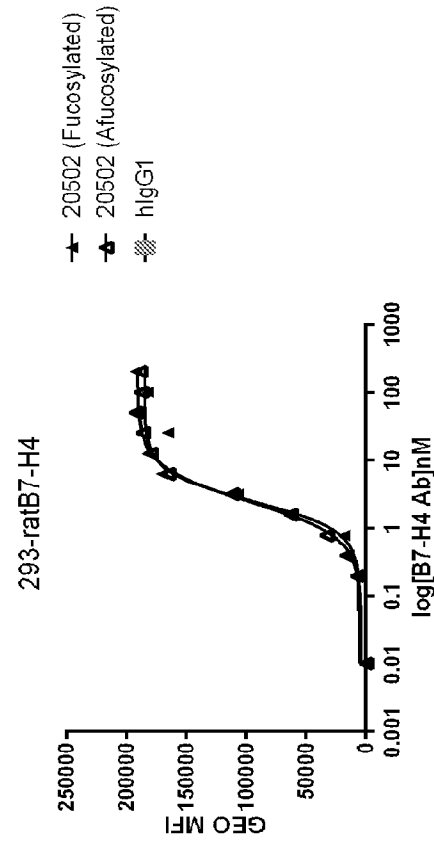


FIG. 4A

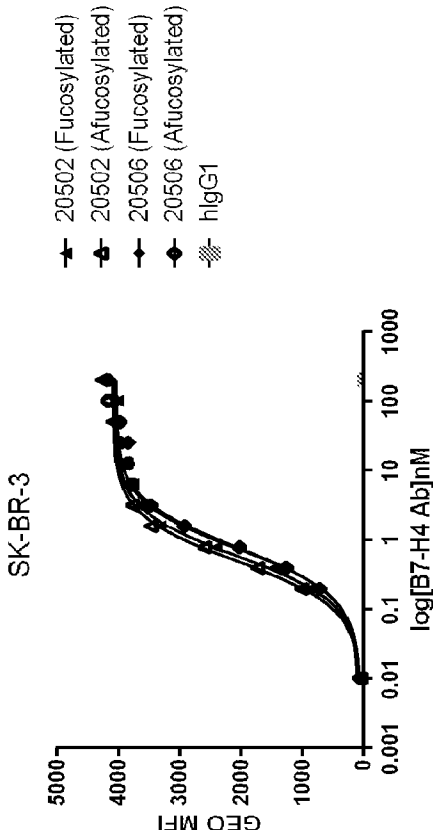
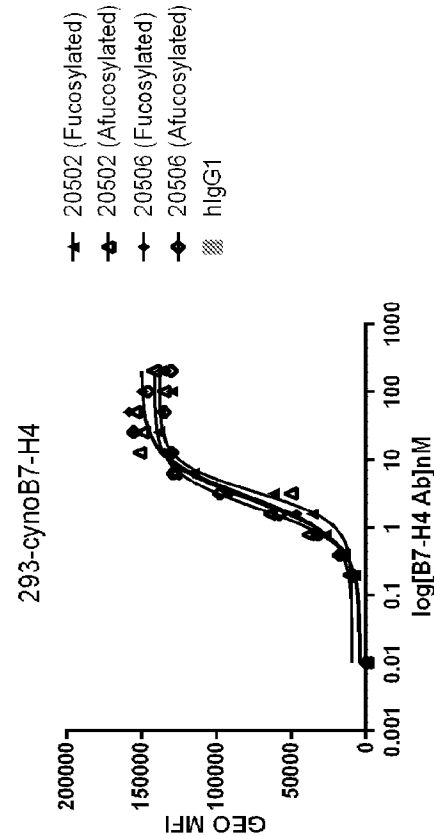


FIG. 4C



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FIG. 5A Sensorgram of FcγRIIIa (v158) binding to Ab-A

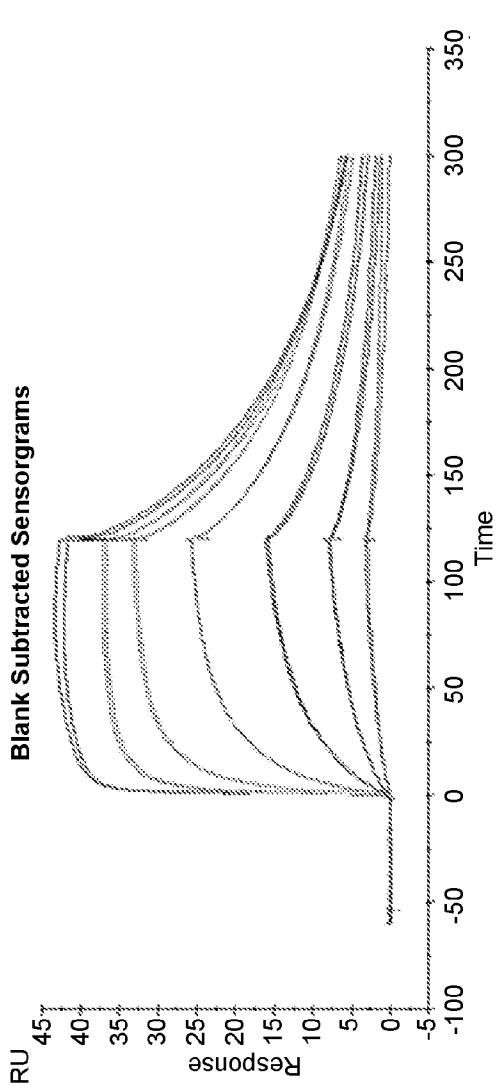
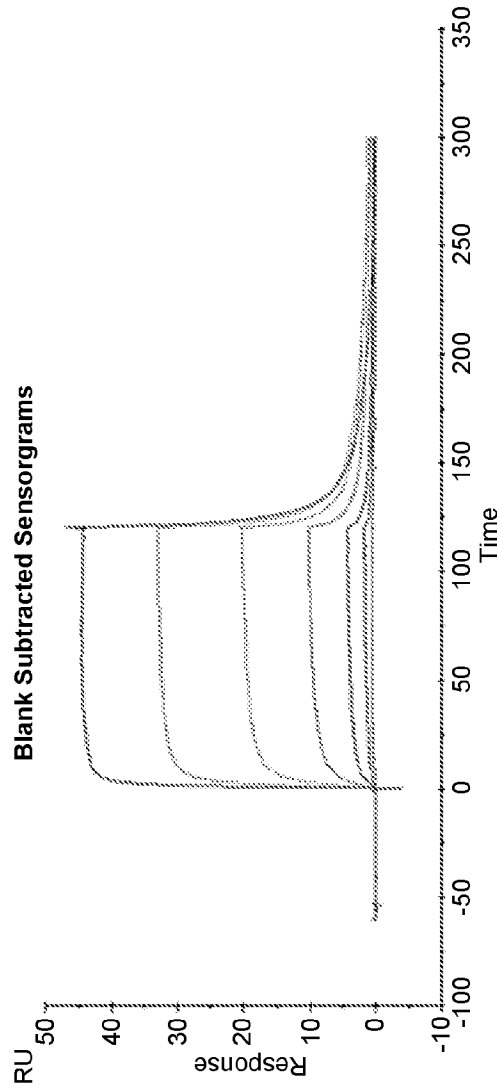


FIG. 5B Sensorgram of FcγRIIIa (v158) binding to Ab-F



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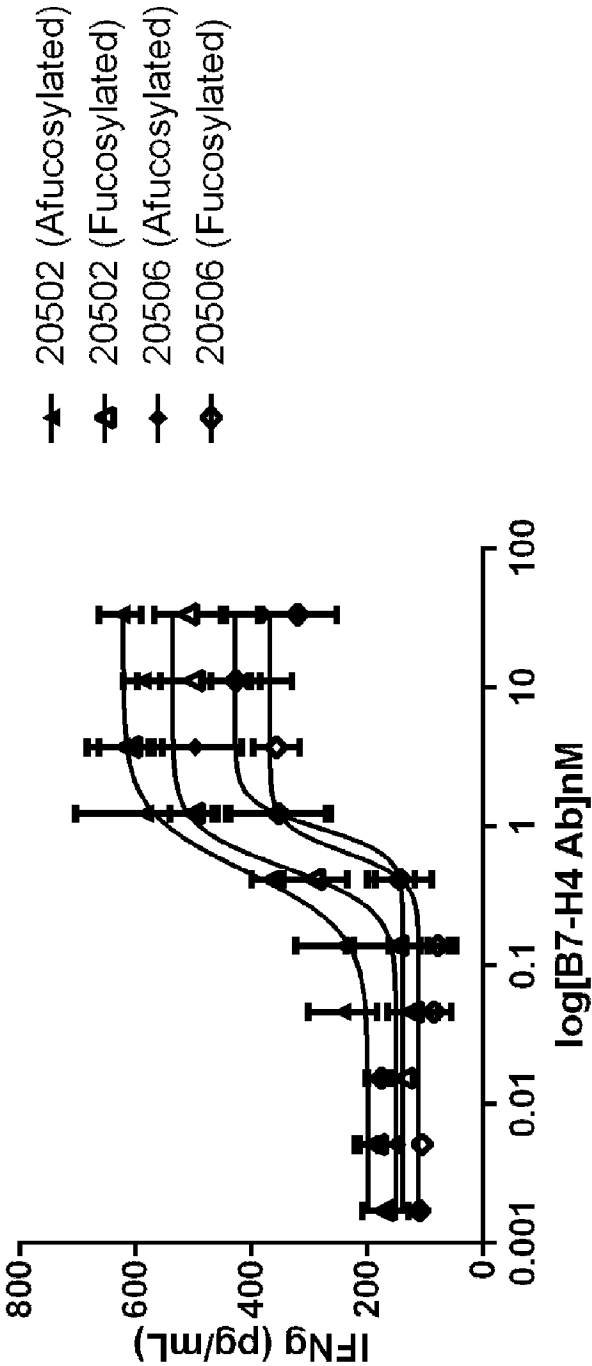


FIG. 6A

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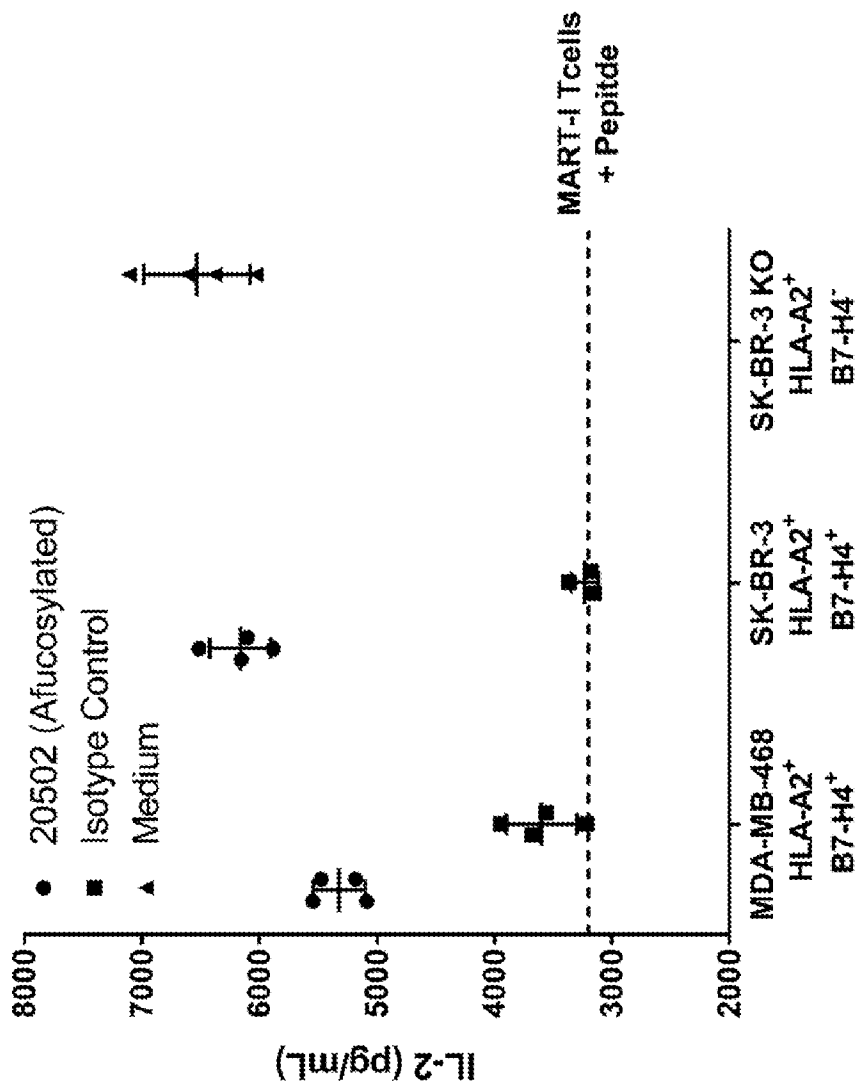


FIG. 6B

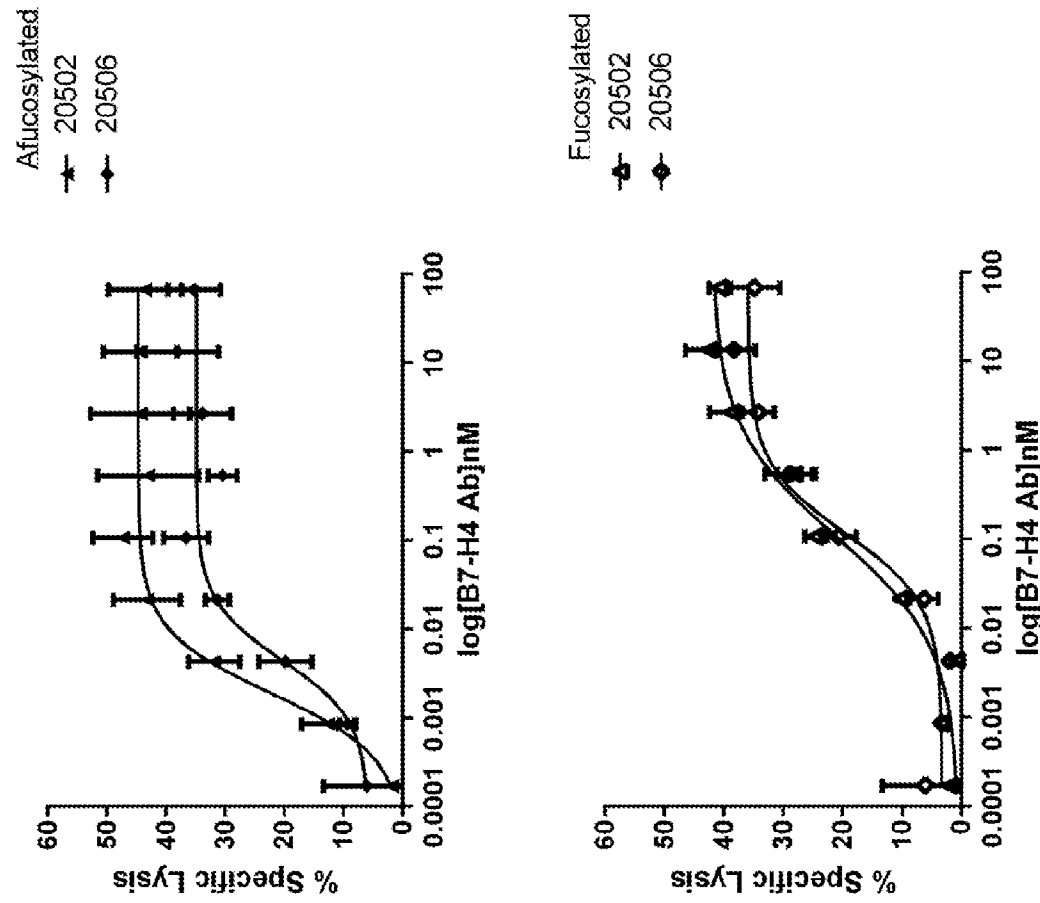


FIG. 7

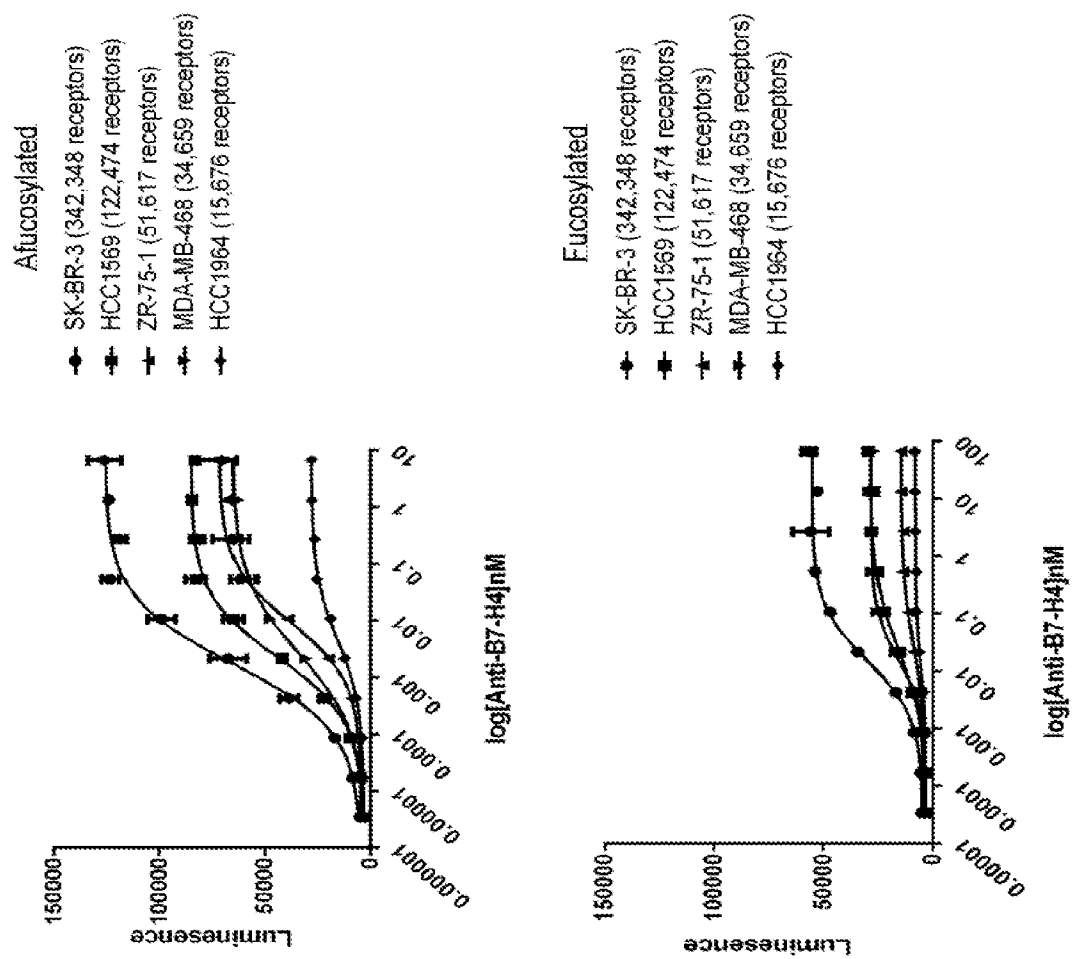


FIG. 8

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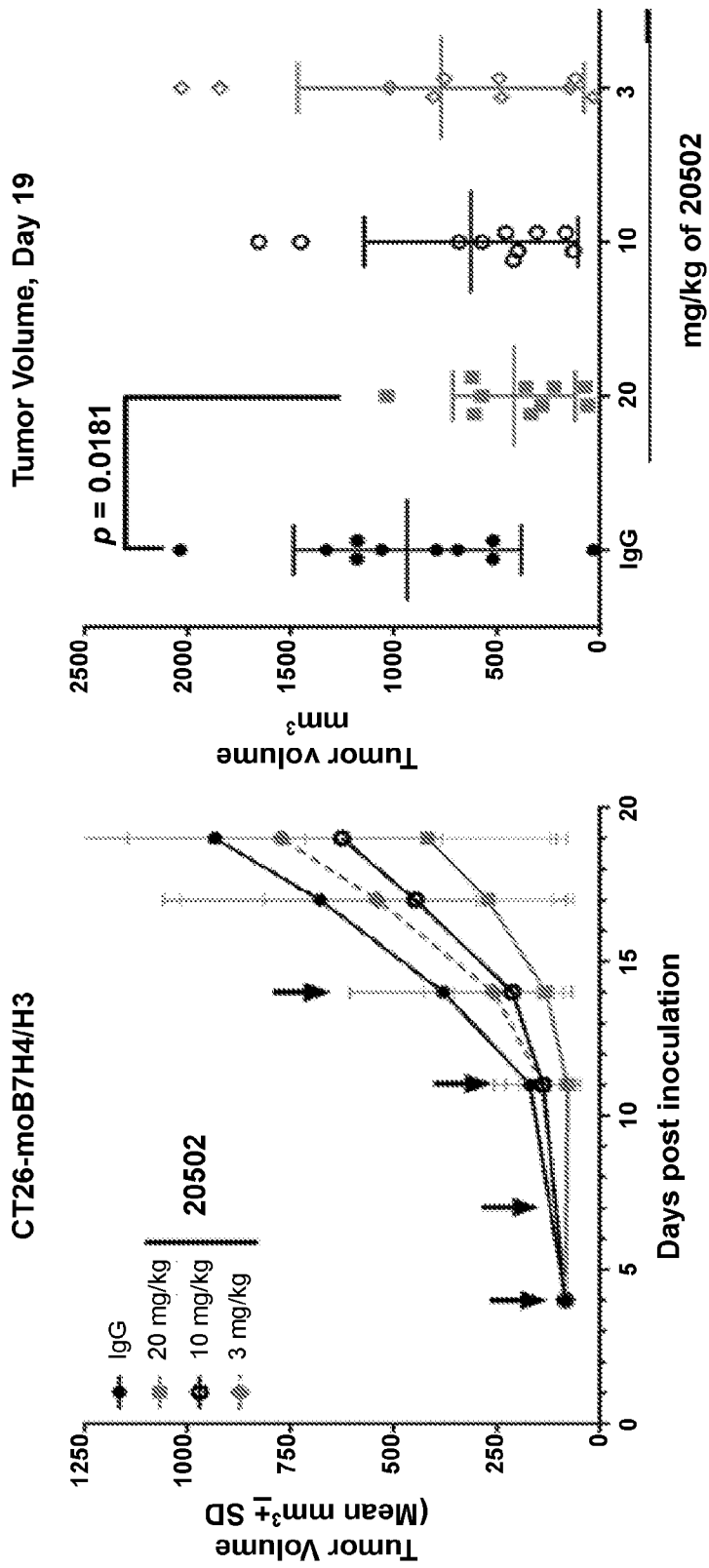


FIG. 9A

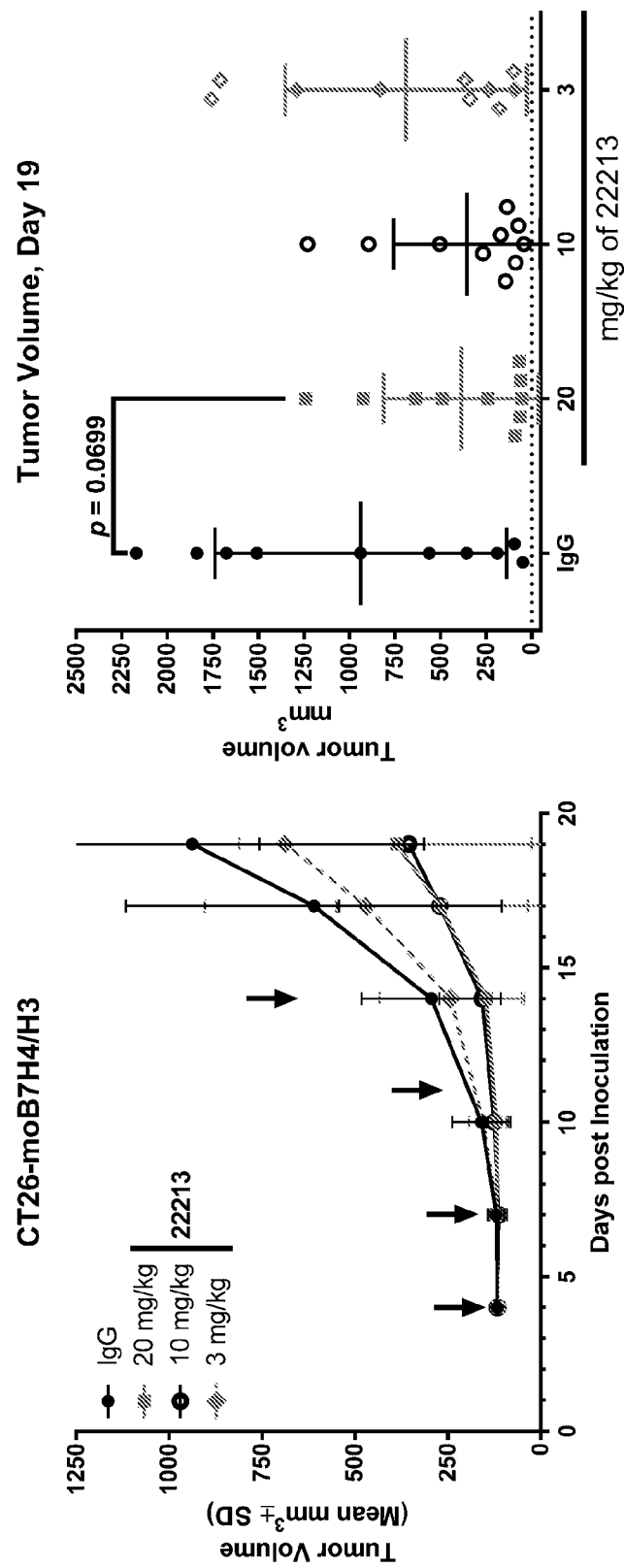


FIG. 9B

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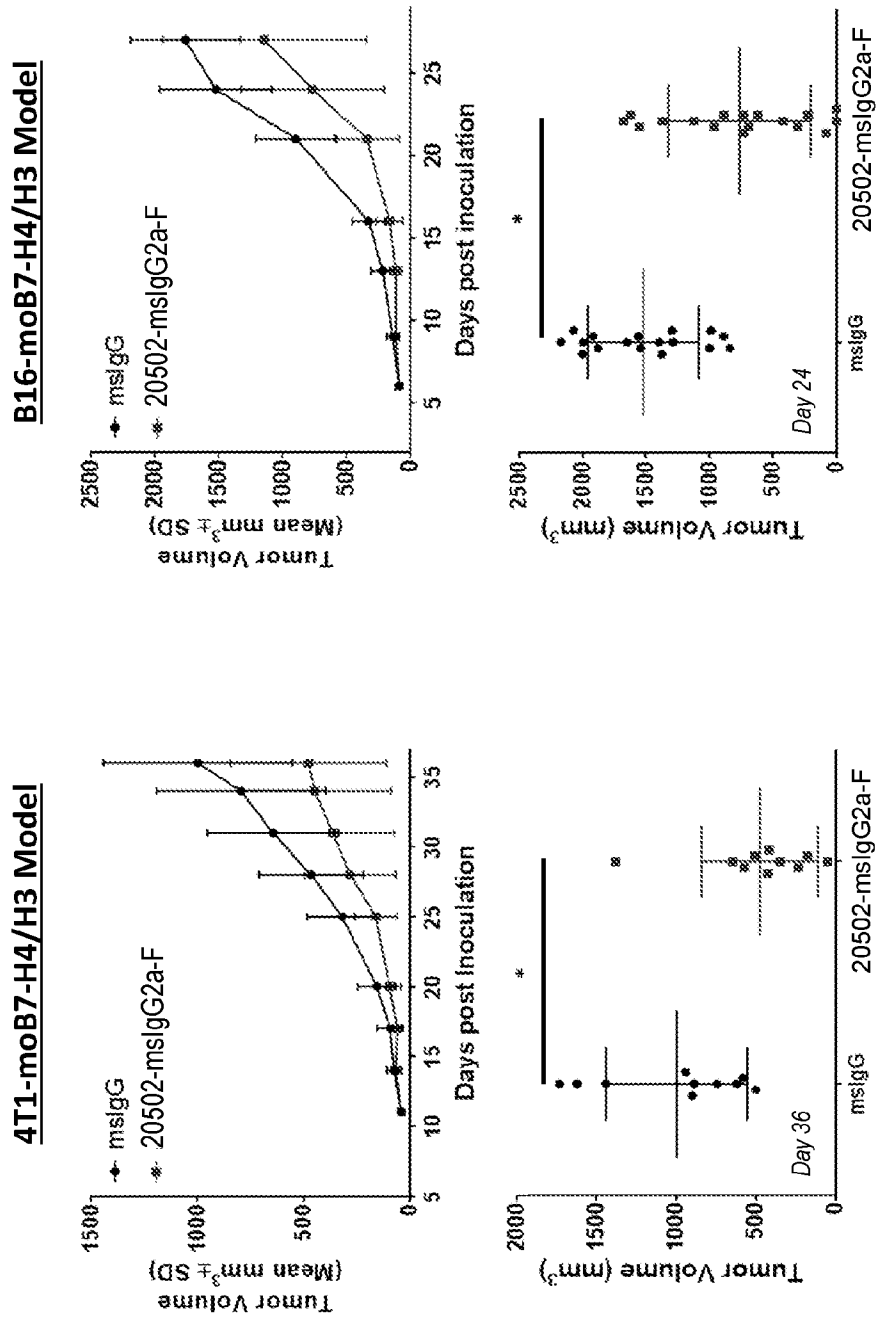


FIG. 10

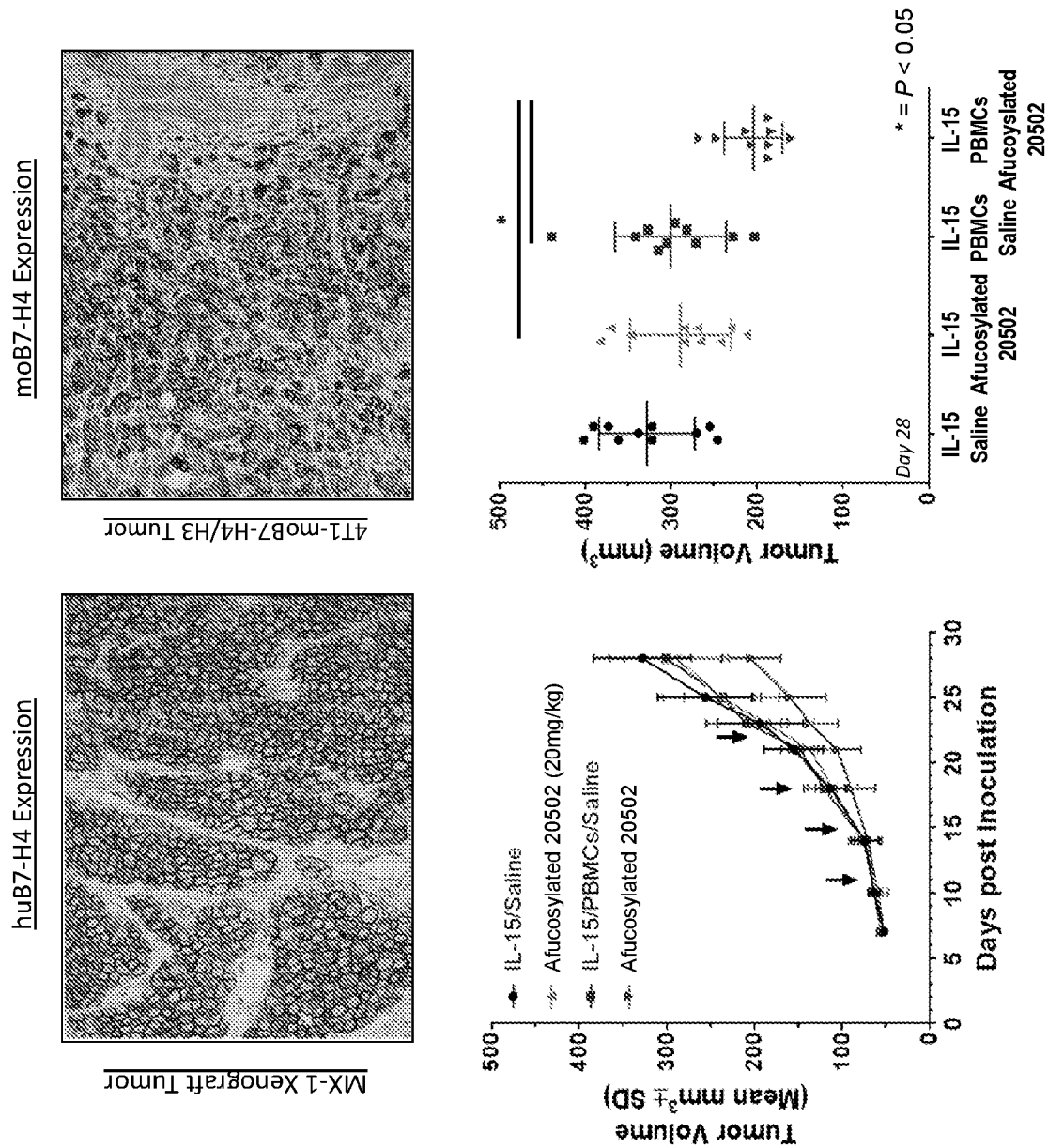


FIG. 11

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FIG. 12A 4T1-moB7H4/H3 Tumor Growth

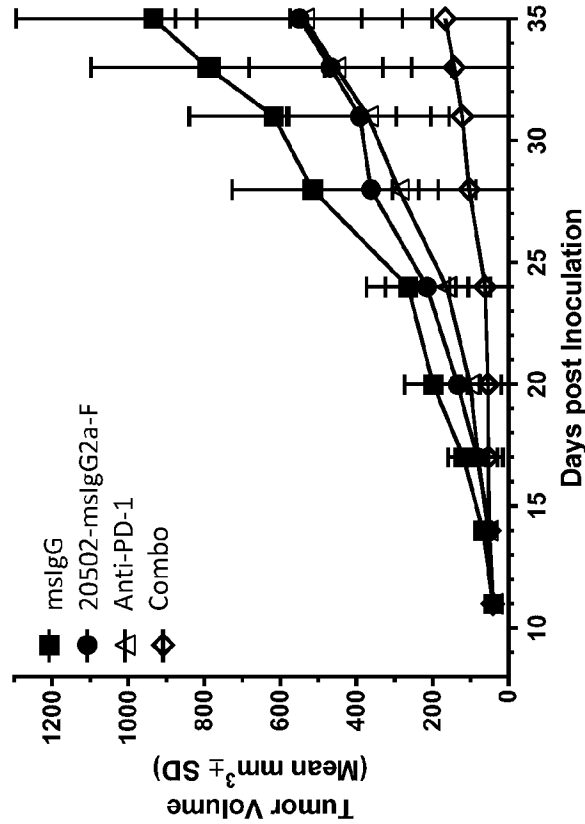


FIG. 12B

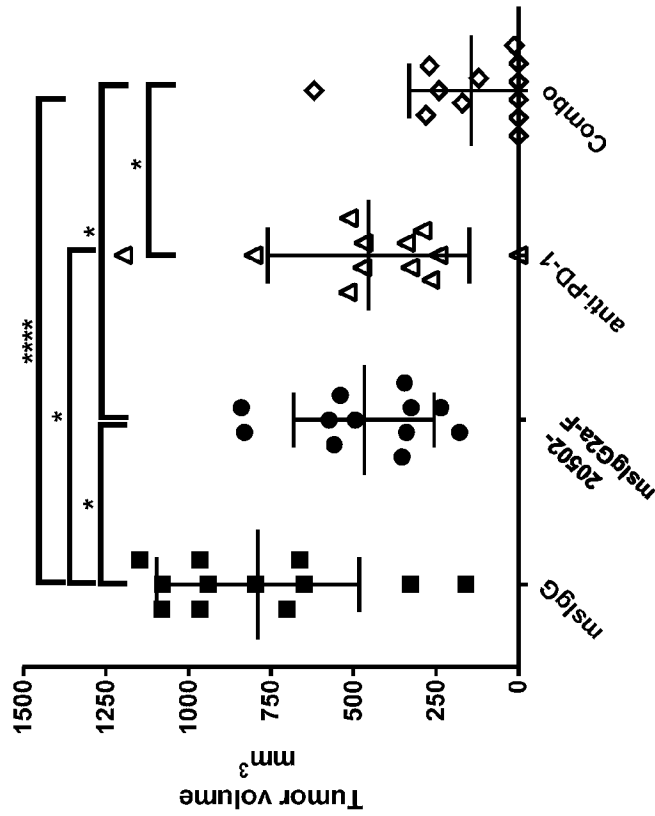
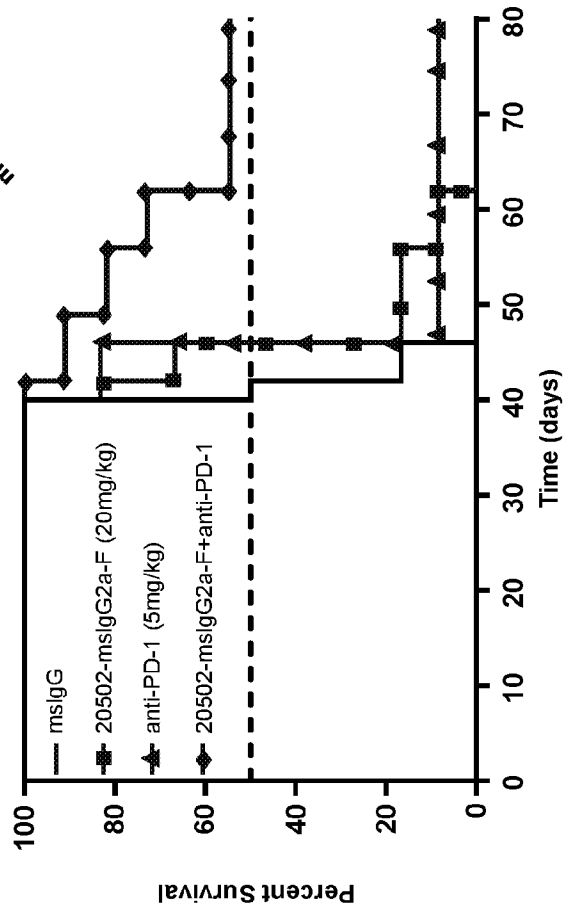


FIG. 12C



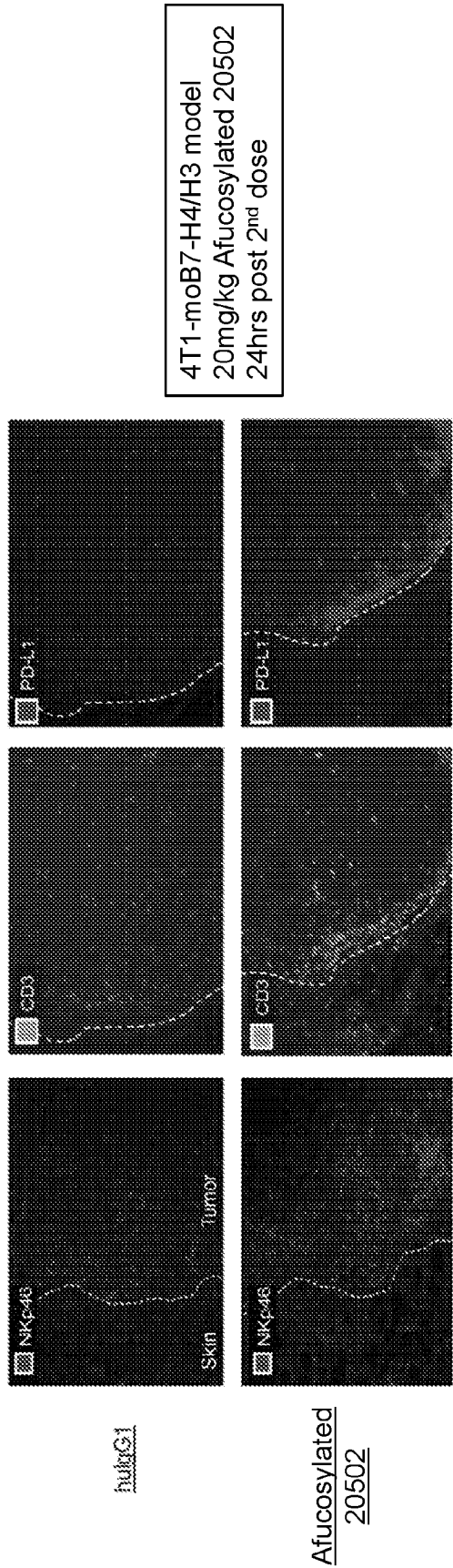


FIG. 13

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FIG. 14A

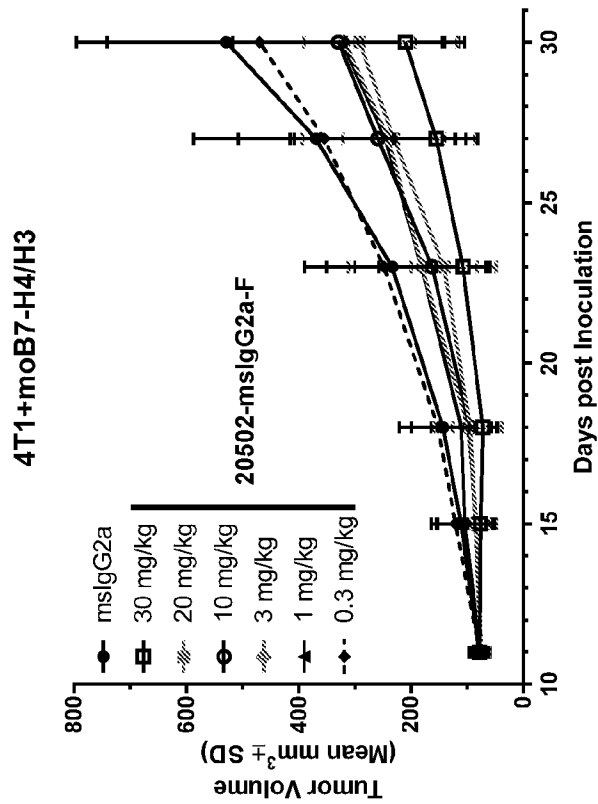
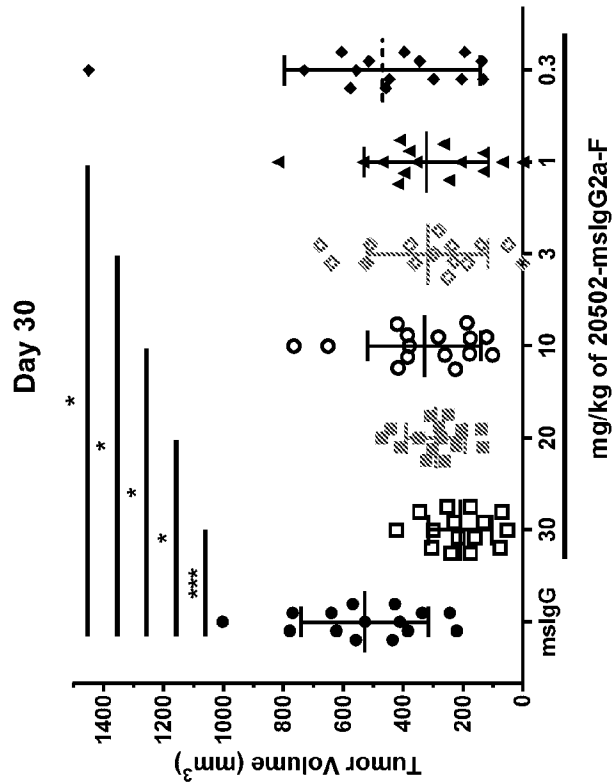


FIG. 14B



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FIG. 15B

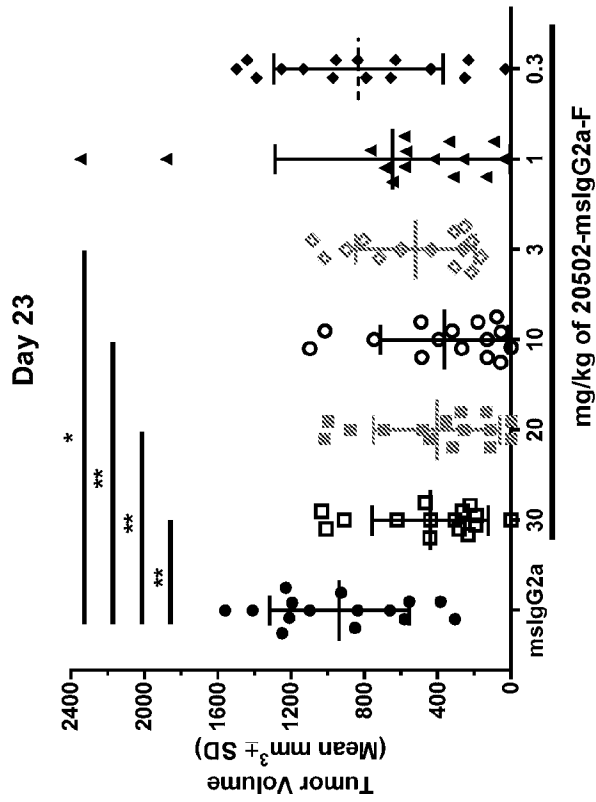
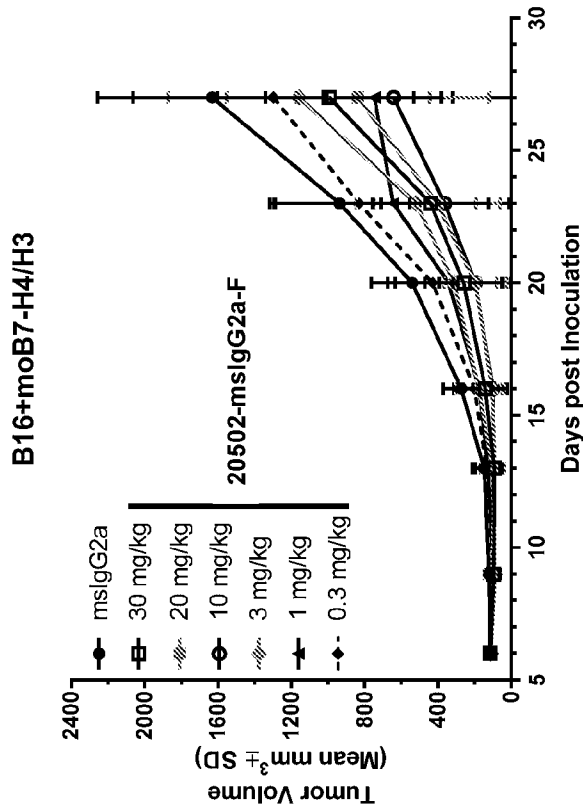


FIG. 15A



3986_009PC04_SL_ST25.txt
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<151> 2017-08-25

<150> 62/579,774

<151> 2017-10-31

<150> 62/607,810

<151> 2017-12-19

<150> 62/656,789

<151> 2018-04-12

<160> 469

<170> PatentIn version 3.5

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<212> PRT

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20 25 30

Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35 40 45

Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50 55 60

Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65 70 75 80

His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met

85

90

95

Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
 100 105 110

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
 115 120 125

Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
 130 135 140

Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
 145 150 155 160

Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
 165 170 175

Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
 180 185 190

Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
 195 200 205

Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
 210 215 220

Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
 225 230 235 240

Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
 245 250 255

Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu
 260 265 270

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 1 5 10 15

Phe Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
 20 25 30

Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
 35 40 45

Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
 50 55 60

Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Ile Gly Leu Val
 65 70 75 80

His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
 85 90 95

Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
 100 105 110

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
 115 120 125

Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
 130 135 140

Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
 145 150 155 160

Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
 165 170 175

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Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
180 185 190

Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
195 200 205

Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
210 215 220

Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225 230 235 240

Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
245 250 255

Lys Ala Ser Leu Cys Val Ser Ser Phe Leu Ala Ile Ser Trp Ala Leu
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Leu Pro Leu Ala Pro Tyr Leu Met Leu Lys
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20 25 30

Gly Lys His Phe Ile Thr Val Thr Thr Phe Thr Ser Ala Gly Asn Ile
35 40 45

Gly Glu Asp Gly Thr Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu

50

55

60

Asn Gly Ile Val Ile Gln Trp Leu Lys Glu Gly Ile Lys Gly Leu Val
 65 70 75 80

His Glu Phe Lys Glu Gly Lys Asp Asp Leu Ser Gln Gln His Glu Met
 85 90 95

Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Val Val Gly Asn
 100 105 110

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
 115 120 125

Thr Cys Tyr Ile Arg Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
 130 135 140

Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Ile Asn Val Asp Tyr Asn
 145 150 155 160

Ala Ser Ser Glu Ser Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
 165 170 175

Pro Thr Val Ala Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
 180 185 190

Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
 195 200 205

Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
 210 215 220

Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
 225 230 235 240

Thr Asp Ser Glu Val Lys Arg Arg Ser Gln Leu Gln Leu Leu Asn Ser
 245 250 255

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260

265

270

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 20 25 30

Gly Lys His Phe Ile Thr Val Thr Thr Phe Thr Ser Ala Gly Asn Ile
 35 40 45

Gly Glu Asp Gly Thr Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
 50 55 60

Asn Gly Ile Val Ile Gln Trp Leu Lys Glu Gly Ile Lys Gly Leu Val
 65 70 75 80

His Glu Phe Lys Glu Gly Lys Asp Asp Leu Ser Gln Gln His Glu Met
 85 90 95

Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Val Val Gly Asn
 100 105 110

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
 115 120 125

Thr Cys Tyr Ile His Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
 130 135 140

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Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Ile Asn Val Asp Tyr Asn
145 150 155 160

Ala Ser Ser Glu Ser Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
165 170 175

Pro Thr Val Ala Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
180 185 190

Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
195 200 205

Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
210 215 220

Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225 230 235 240

Thr Asp Ser Glu Val Lys Arg Arg Ser Gln Leu Glu Leu Leu Asn Ser
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Gly Pro Ser Pro Cys Val Ser Ser Val Ser Ala Ala Gly Trp Ala Leu
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Leu Ser Leu Ser Cys Cys Leu Met Leu Arg
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Ala	Arg	Glu	Gly	Ser	Tyr	Pro	Asn	Trp	Phe	Asp	Pro
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<400> 9

Gly Ala Ser Thr Arg Ala Thr

1 5

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Gln Gln Tyr His Ser Phe Pro Phe Thr
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 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
 20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro Trp Gly Gln

100

105

110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

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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
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Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Phe Pro Phe
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Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 13

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 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
 20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys

195

200

205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
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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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp

405

410

415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
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 435 440 445

Gly Lys
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 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 His Ser Phe Pro Phe
 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
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<213> Artificial Sequence

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Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro
1 5 10

<210> 18
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20500 VL CDR1

<400> 18

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 19
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20500 VL CDR2

<400> 19

Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 20
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Antibody 20500 VL CDR3

<400> 20

Gln Gln Tyr His Ser Phe Pro Phe Thr
 1 5

<210> 21

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20500 Variable Heavy Chain

<400> 21

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 Lys Ser Gly
 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Arg Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 22

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

<220>
 <223> Antibody 20500 Variable Light Chain

<400> 22

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 His Ser Phe Pro Phe
 85 90 95

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

<210> 23
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20500 Full-Length Heavy Chain

<400> 23

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 Lys Ser Gly

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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Arg Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro

435

440

445

Gly Lys
450

<210> 24

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20500 Full-Length Light Chain

<400> 24

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 His Ser Phe Pro Phe
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> 25
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20501 VH CDR1

<400> 25

Gly Ser Ile Lys Ser Gly Ser His Tyr Trp Gly
1 5 10

<210> 26
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20501 VH CDR2

<400> 26

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 27
<211> 12
<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20501 VH CDR3

<400> 27

Ala	Arg	Glu	Gly	Ser	Tyr	Pro	Asn	Trp	Leu	Asp	Pro
1				5					10		

<210> 28

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20501 VL CDR1

<400> 28

Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Asn	Leu	Ala
1				5					10	

<210> 29

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20501 VL CDR2

<400> 29

Gly	Ala	Ser	Thr	Arg	Ala	Thr
1				5		

<210> 30

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20501 VL CDR3

<400> 30

Gln	Gln	Tyr	His	Ser	Phe	Pro	Phe	Thr
1				5				

<210> 31
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20501 Variable Heavy Chain

<400> 31

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 Lys Ser Gly
 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Leu Asp Pro Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 32
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20501 Variable Light Chain

<400> 32

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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 His Ser Phe Pro Phe
85 90 95

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

<210> 33

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20501 Full-Length Heavy Chain

<400> 33

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 Lys Ser Gly
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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser

50

55

60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Leu Asp Pro Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu

260

265

270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
 435 440 445

Gly Lys
 450

<210> 34

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20501 Full-Length Light Chain

<400> 34

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 His Ser Phe Pro Phe
 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> 35
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VH CDR1

<400> 35

Gly Ser Ile Lys Ser Gly Ser Tyr Tyr Trp Gly
1 5 10

<210> 36
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VH CDR2

<400> 36

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 37
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VH CDR3

<400> 37

Ala Arg Glu Gly Ser Tyr Pro Asn Gln Phe Asp Pro

1

5

10

<210> 38
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VL CDR1

<400> 38

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 39
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VL CDR2

<400> 39

Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 40
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VL CDR3

<400> 40

Gln Gln Tyr His Ser Phe Pro Phe Thr
1 5

<210> 41
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 Variable Heavy Chain

<400> 41

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 Lys 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Gln Phe Asp Pro Trp Gly Gln
 100 105 110

Gly Ile Leu Val Thr Val Ser Ser
 115 120

<210> 42

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20502 and 20502.1 Variable light chain

<400> 42

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 His Ser Phe Pro Phe
85 90 95

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

<210> 43

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20502.1 Full-Length Heavy Chain

<400> 43

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 Lys 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr

85

90

95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Gln Phe Asp Pro Trp Gly Gln
 100 105 110

Gly Ile Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
 435 440 445

Gly Lys
 450

<210> 44

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20502 and 20502.1 Full-Length Light Chain

<400> 44

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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 His Ser Phe Pro Phe
 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> 45
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22208 VH CDR1

<400> 45

Gly Ser Ile Lys Ser Gly Ser His Tyr Trp Gly
1 5 10

<210> 46
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22208 VH CDR2

<400> 46

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 47
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22208 VH CDR3

<400> 47

Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro
1 5 10

<210> 48
<211> 11
<212> PRT
<213> Artificial Sequence

<220>

<223> Antibody 22208 VL CDR1

<400> 48

Arg	Ala	Ser	Gln	Ser	Val	Ser	Thr	Asn	Leu	Ala
1				5					10	

<210> 49

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22208 VL CDR2

<400> 49

Asp	Ala	Ser	Ala	Arg	Val	Thr
1				5		

<210> 50

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22208 VL CDR3

<400> 50

Gln	Gln	Tyr	His	Ser	Phe	Pro	Phe	Thr
1				5				

<210> 51

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22208 Variable Heavy Chain

<400> 51

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	Lys	Ser	Gly

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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 52

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22208 Variable Light Chain

<400> 52

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 Thr Asn
 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 Ala Arg Val 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 His Ser Phe Pro Phe
85 90 95

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

<210> 53

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22208 Full-Length Heavy Chain

<400> 53

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 Lys Ser Gly
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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Trp Phe Asp Pro Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val

115

120

125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
 435 440 445

Gly Lys
 450

<210> 54
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 Full-Length Light Chain

<400> 54

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 Thr Asn
 20 25 30

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

Tyr Asp Ala Ser Ala Arg Val 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 His Ser Phe Pro Phe
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> 55
<211> 11
<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 VH CDR1

<400> 55

Gly Ser Ile Ser Ser Ser Ser Tyr Tyr Trp Gly
1 5 10

<210> 56

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 VH CDR2

<400> 56

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 57

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 VH CDR3

<400> 57

Ala Arg Glu Gly Ser Tyr Thr Thr Val Leu Asn Val
1 5 10

<210> 58

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 VL CDR1

<400> 58

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> 59
 <211> 7
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Antibody 15462 VL CDR2

 <400> 59

Gly Ala Ser Ser Arg Ala Thr
 1 5

<210> 60
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Antibody 15462 VL CDR3

 <400> 60

Gln Gln Ala Ala Ser Tyr Pro Leu Thr
 1 5

<210> 61
 <211> 120
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Antibody 15462 Variable Heavy Chain

 <400> 61

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
 20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser

50

55

60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Gly Ser Tyr Thr Thr Val Leu Asn Val Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 62

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 Variable Light Chain

<400> 62

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 Ala Ala Ser Tyr Pro
85 90 95

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

<210> 63
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15462 Full-length heavy chain

<400> 63

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Gly Ser Tyr Thr Thr Val Leu Asn Val Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser

145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
 435 440 445

Gly Lys
 450

<210> 64

<211> 215

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 Full-length light chain

<400> 64

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ala Ala Ser Tyr 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> 65

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 VH CDR1

<400> 65

Gly Ser Ile Gly Arg Gly Ser Tyr Tyr Trp Gly

1

5

10

<210> 66
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22213 VH CDR2

<400> 66

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 67
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22213 VH CDR3

<400> 67

Ala Arg Glu Gly Ser Tyr Thr Thr Val Leu Asn Val
1 5 10

<210> 68
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22213 VL CDR1

<400> 68

Arg Ala Ser Gln Ser Val Ala Ser Ser His Leu Ala
1 5 10

<210> 69
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22213 VL CDR2

<400> 69

Asp Ala Val Ser Arg Ala Thr
1 5

<210> 70

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 VL CDR3

<400> 70

Gln Gln Ala Ala Ser Tyr Pro Leu Thr
1 5

<210> 71

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 Variable Heavy Chain

<400> 71

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 Gly Arg 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr

85

90

95

Cys Ala Arg Glu Gly Ser Tyr Thr Thr Val Leu Asn Val Trp Gly Gln
 100 105 110

Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 72

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 Variable Light Chain

<400> 72

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 Ala Ser Ser
 20 25 30

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

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

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

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

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

<210> 73

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 Full-Length Heavy Chain

<400> 73

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 Gly Arg 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Thr Thr Val Leu Asn Val Trp Gly Gln
 100 105 110

Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro

180

185

190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
435 440 445

Gly Lys
450

<210>	74
<211>	215
<212>	PRT
<213>	Artificial Sequence

<220>
<223> Antibody 22213 Full-Length Light Chain

<400> 74

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 Ala Ser Ser
20 25 30

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

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ala Ala Ser Tyr 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> 75
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 VH CDR1

<400> 75

Gly Ser Ile Ser Ser Gly Gly Tyr Tyr Trp Ser
 1 5 10

<210> 76
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Antibody 15465 VH CDR2

<400> 76

Asn	Ile	Tyr	Tyr	Ser	Gly	Ser	Thr	Tyr	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5					10					15	

<210> 77

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15465 VH CDR3

<400> 77

Ala	Arg	Glu	Ser	Ser	Thr	Ile	Ser	Ala	Asp	Phe	Asp	Leu
1			5					10				

<210> 78

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15465 VL CDR1

<400> 78

Arg	Ala	Ser	Gln	Gly	Ile	Ser	Arg	Trp	Leu	Ala
1			5					10		

<210> 79

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15465 VL CDR2

<400> 79

Ala	Ala	Ser	Ser	Leu	Gln	Ser
1			5			

<210> 80

<211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 VL CDR3

<400> 80

Gln Gln Ala His Thr Phe Pro Tyr Thr
 1 5

<210> 81
 <211> 121
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 Variable Heavy Chain

<400> 81

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
 20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Ser Ser Thr Ile Ser Ala Asp Phe Asp Leu Trp Gly
 100 105 110

Arg Gly Thr Leu Val Thr Val Ser Ser

115

<210> 82
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 Variable Light Chain

<400> 82

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Arg Trp
20 25 30

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

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

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

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

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

<210> 83
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 Full-Length Heavy Chain

<400> 83

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln

1					5					10					15				
Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Ser	Ile	Ser	Ser	Gly				
			20				25						30						
Gly	Tyr	Tyr	Trp	Ser	Trp	Ile	Arg	Gln	His	Pro	Gly	Lys	Gly	Leu	Glu				
			35				40						45						
Trp	Ile	Gly	Asn	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						
Ser	Leu	Lys	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr				
			85				90						95						
Cys	Ala	Arg	Glu	Ser	Ser	Thr	Ile	Ser	Ala	Asp	Phe	Asp	Leu	Trp	Gly				
			100				105						110						
Arg	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser				
			115				120						125						
Val	Phe	Pro	Leu	Ala	Pro	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	Lys	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 Asp Glu Leu 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> 84
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 Full-Length Light Chain

<400> 84

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Arg Trp
 20 25 30

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

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

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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala His Thr Phe Pro Tyr
 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> 85
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20506 VH CDR1

<400> 85

Gly Ser Ile Ser His Gly Gly Tyr Tyr Trp Ser
1 5 10

<210> 86
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20506 VH CDR2

<400> 86

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 87
 <211> 13
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 VH CDR3

<400> 87

Ala Arg Glu Ser Ser Thr Ile Ser Ala Asp Phe Asp Leu
 1 5 10

<210> 88
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 VL CDR1

<400> 88

Arg Ala Ser Gln Gly Ile Ser Arg Trp Leu Ala
 1 5 10

<210> 89
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 VL CDR2

<400> 89

Ala Ala Ser Ser Leu Gln Ser
 1 5

<210> 90
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 VL CDR3

<400> 90

Gln Gln Ala His Thr Phe Pro Tyr Thr
1 5

<210> 91
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20506 Variable Heavy Chain

<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 Ala Ser Gly Gly Ser Ile Ser His Gly
20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Ser Ser Thr Ile Ser Ala Asp Phe Asp Leu Trp Gly
100 105 110

Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 92
<211> 107
<212> PRT
<213> Artificial Sequence

<220>

<223> Antibody 20506 Variable Light Chain

<400> 92

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Arg Trp
 20 25 30

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

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

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

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

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

<210> 93

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20506 Full-Length Heavy Chain

<400> 93

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 Ala Ser Gly Gly Ser Ile Ser His Gly
 20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu

35

40

45

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Ser Ser Thr Ile Ser Ala Asp Phe Asp Leu Trp Gly
 100 105 110

Arg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro 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 Lys 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 Asp Glu Leu 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> 94
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 Full-Length Light Chain

<400> 94

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Arg Trp
 20 25 30

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

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

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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala His Thr Phe Pro Tyr
 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> 95
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15483 VH CDR1

<400> 95

Gly Ser Ile Ser Ser Gly Gly Tyr Tyr Trp Ser
1 5 10

<210> 96
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15483 VH CDR2

<400> 96

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 97
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15483 VH CDR3

<400> 97

Ala Arg Gly Leu Ser Thr Ile Asp Glu Ala Phe Asp Pro
1 5 10

<210> 98

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 VL CDR1

<400> 98

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
1 5 10

<210> 99

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 VL CDR2

<400> 99

Lys Ala Ser Ser Leu Glu Ser
1 5

<210> 100

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 VL CDR3

<400> 100

Gln Gln Asp Asn Ser Tyr Pro Tyr Thr
1 5

<210> 101

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 Variable Heavy Chain

<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 Ser Ser Gly
20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 102

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 Variable Light Chain

<400> 102

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30

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

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

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

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

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

<210> 103

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 Full-Length Heavy Chain

<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 Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe

65					70						75				80
Ser	Leu	Lys	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr
				85					90					95	
Cys	Ala	Arg	Gly	Leu	Ser	Thr	Ile	Asp	Glu	Ala	Phe	Asp	Pro	Trp	Gly
			100					105					110		
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser
		115					120					125			
Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala
	130					135					140				
Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val
145					150					155					160
Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala
				165					170					175	
Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val
			180					185					190		
Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His
		195					200					205			
Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	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 Asp Glu Leu 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> 104
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Antibody 15483 Full-Length Light Chain

<400> 104

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

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

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

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

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Asn Ser Tyr Pro Tyr
 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> 105
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20513 VH CDR1

<400> 105

Gly Ser Ile Ser Asp Gly Ser Tyr Tyr Trp Ser
1 5 10

<210> 106
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20513 VH CDR2

<400> 106

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Arg Ser
1 5 10 15

<210> 107
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20513 VH CDR3

<400> 107

Ala Arg Gly Leu Ser Thr Ile Asp Glu Ala Phe Asp Pro
1 5 10

<210> 108

<211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20513 VL CDR1

<400> 108

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
 1 5 10

<210> 109
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20513 VL CDR2

<400> 109

Lys Ala Ser Ser Leu Glu Ser
 1 5

<210> 110
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20513 VL CDR3

<400> 110

Gln Gln Asp Asn Ser Tyr Pro Tyr Thr
 1 5

<210> 111
 <211> 121
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20513 Variable Heavy Chain

<400> 111

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 Asp Gly
 20 25 30
 Ser Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Arg Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Gly Leu Ser Thr Ile Asp Glu Ala Phe Asp Pro Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 112
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20513 Variable Light Chain

<400> 112

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

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

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

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

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

<210> 113
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20513 Full-Length Heavy Chain

<400> 113

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 Asp Gly
20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Arg Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Gly Leu Ser Thr Ile Asp Glu Ala Phe Asp Pro Trp Gly

100

105

110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys 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

305 310 320

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 Asp Glu Leu 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>	214
<212>	PRT
<213>	Artificial Sequence

<220>
<223> Antibody 20513 Full-Length Light Chain

<400> 114

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30

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

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

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

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Asn Ser Tyr Pro Tyr
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> 115
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22216 VH CDR1

<400> 115

Gly Ser Ile Ser Asp Gly Ser Tyr Tyr Trp Ser
 1 5 10

<210> 116
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22216 VH CDR2

<400> 116

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Arg Ser
 1 5 10 15

<210> 117
 <211> 13
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22216 VH CDR3

<400> 117

Ala Arg Gly Leu Ser Thr Ile Asp Glu Ala Phe Asp Pro
 1 5 10

<210> 118
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22216 VL CDR1

<400> 118

Arg Ala Ser Lys Ser Ile Ser Ser Trp Leu Ala
1 5 10

<210> 119
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 VL CDR2

<400> 119

Glu Ala Ser Ser Leu His Ser
1 5

<210> 120
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 VL CDR3

<400> 120

Gln Gln Asp Asn Ser Tyr Pro Tyr Thr
1 5

<210> 121
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 Variable Heavy Chain

<400> 121

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Asp Gly
20 25 30

Ser Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu

35

40

45

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Arg Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 122

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22216 Variable Light Chain

<400> 122

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Ser Trp
 20 25 30

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

Tyr Glu Ala Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

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

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

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

<210> 123
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 Full-Length Heavy Chain

<400> 123

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Asp Gly
20 25 30

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

Trp Ile Gly Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Arg Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala

130

135

140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys 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 Asp Glu Leu 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> 124
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22216 Full-Length Light Chain

<400> 124

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Ser Trp
 20 25 30

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

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Tyr Glu Ala Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Asn Ser Tyr Pro Tyr
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> 125
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15489 VH CDR1

<400> 125

Gly Ser Ile Ser Ser Tyr Tyr Trp Ser
1 5

<210> 126

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15489 VH CDR2

<400> 126

Tyr Ile Tyr Ser Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 127

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15489 VH CDR3

<400> 127

Ala Arg Gly Ser Gly Gln Tyr Ala Ala Pro Asp Tyr Gly Met Asp Val
1 5 10 15

<210> 128

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15489 VL CDR1

<400> 128

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
1 5 10

<210> 129

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15489 VL CDR2

<400> 129

Lys Ala Ser Ser Leu Glu Ser
1 5

<210> 130

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15489 VL CDR3

<400> 130

Gln Gln Asp Asn Ser Phe Pro Phe Thr
1 5

<210> 131

<211> 122

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15489 Variable Heavy Chain

<400> 131

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

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

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

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu

65 70 — — — 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Gly Ser Gly Gln Tyr Ala Ala Pro Asp Tyr Gly Met Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210>	132
<211>	107
<212>	PRT
<213>	Artificial Sequence

<220>
<223> Antibody 15489 Variable Light Chain

<400> 132

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30

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

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

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

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

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

<210> 133
 <211> 452
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 Full-Length Heavy Chain

<400> 133

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
 20 25 30

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

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

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
 65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

Arg Gly Ser Gly Gln Tyr Ala Ala Pro Asp Tyr Gly Met Asp Val Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
 130 135 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro

165

170

175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
 195 200 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
 210 215 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 225 230 235 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 260 265 270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 275 280 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 290 295 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 325 330 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 340 345 350

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
 355 360 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val

370

375

380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 385 390 395 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 405 410 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 435 440 445

Ser Pro Gly Lys
 450

<210> 134
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 Full-Length Light Chain

<400> 134

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

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

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

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

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Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Asn Ser Phe Pro Phe
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> 135
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20516 VH CDR1

<400> 135

Gly Ser Ile Ile Ser Tyr Tyr Trp Gly
1 5

<210> 136

<211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 VH CDR2

<400> 136

Tyr	Ile	Tyr	Ser	Ser	Gly	Ser	Thr	Ser	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5					10					15	

<210> 137
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 VH CDR3

<400> 137

Ala	Arg	Gly	Ser	Gly	Leu	Tyr	Ala	Ala	Pro	Asp	Tyr	Gly	Leu	Asp	Val
1				5					10					15	

<210> 138
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 VL CDR1

<400> 138

Arg	Ala	Ser	Gln	Ser	Ile	Ser	Ser	Trp	Leu	Ala
1				5					10	

<210> 139
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 VL CDR2

<400> 139

Lys Ala Ser Ser Leu Glu Ser

1 5

<210> 140
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 VL CDR3

<400> 140

Gln Gln Asp Asn Ser Phe Pro Phe Thr
 1 5

<210> 141
 <211> 122
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 Variable Heavy Chain

<400> 141

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ile Ser Tyr
 20 25 30

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

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

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
 65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

Arg Gly Ser Gly Leu Tyr Ala Ala Pro Asp Tyr Gly Leu Asp Val Trp

100

105

110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 142
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 Variable Light Chain

<400> 142

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

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

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

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

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

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

<210> 143
 <211> 452
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 Full-Length Heavy Chain

<400> 143

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ile Ser Tyr
 20 25 30

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

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

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
 65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

Arg Gly Ser Gly Leu Tyr Ala Ala Pro Asp Tyr Gly Leu Asp Val Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
 130 135 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
 165 170 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn

195

200

205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
 210 215 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 225 230 235 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 260 265 270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 275 280 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 290 295 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 325 330 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 340 345 350

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
 355 360 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 370 375 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 385 390 395 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr

405

410

415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 435 440 445

Ser Pro Gly Lys
 450

<210> 144
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 Full-Length Light Chain

<400> 144

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

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

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

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

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Asn Ser Phe Pro Phe
 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> 145
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 VH CDR1

<400> 145

Phe Thr Phe Ser Ser Tyr Ala Met Ser
 1 5

<210> 146
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 VH CDR2

<400> 146

Thr Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 147
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15472 VH CDR3

<400> 147

Ala Arg Gly Ala Gly His Tyr Asp Leu Val Gly Arg Tyr
1 5 10

<210> 148
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15472 VL CDR1

<400> 148

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 149
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15472 VL CDR2

<400> 149

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 150

<211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 VL CDR3

<400> 150

Gln Gln Leu Tyr Ser Leu Pro Pro Thr
 1 5

<210> 151
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 Variable Heavy Chain

<400> 151

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

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

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

Ser Thr Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Gly Ala Gly His Tyr Asp Leu Val Gly Arg Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser

115

<210> 152
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15472 Variable Light Chain

<400> 152

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

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

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

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

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

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

<210> 153
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15472 Full-Length Heavy Chain

<400> 153

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

1	5	10	15
Ser	Leu	Arg	Leu
	20		
Ser	Cys	Ala	Ala
		25	
Ser	Gly	Phe	Thr
			Phe
Ser	Ser	Tyr	
		30	
Ala	Met	Ser	Trp
	35		
Val	Arg	Gln	Ala
		40	
Pro	Gly	Lys	Gly
			45
Leu	Glu	Trp	Val
Ser	Thr	Ile	Ser
	50		
Gly	Ser	Gly	Gly
		55	
Ser	Thr	Tyr	Tyr
			60
Ala	Asp	Ser	Val
Lys	Gly	Arg	Phe
	65		
Thr	Ile	Ser	Arg
	70		
Asp	Asn	Ser	Lys
		75	
Asn	Thr	Leu	Tyr
			80
Leu	Gln	Met	Asn
			85
Ser	Leu	Arg	Ala
Glu	Asp	Thr	Ala
	90		
Val	Tyr	Tyr	Cys
		95	
Ala	Arg	Gly	Ala
		100	
Gly	His	Tyr	Asp
			105
Leu	Val	Gly	Arg
Tyr	Tyr	Trp	Gly
			110
Gln			
Gly	Thr	Leu	Val
	115		
Thr	Val	Ser	Ser
			120
Ala	Ser	Thr	Lys
Gly	Gly	Thr	Ala
			125
Pro	Ser	Val	
Phe	Pro	Leu	Ala
	130		
Pro	Ser	Ser	Lys
		135	
Ser	Thr	Ser	Gly
			140
Gly	Gly	Thr	Ala
Ala			
Leu	Gly	Cys	Leu
	145		
Val	Lys	Asp	Tyr
		150	
Phe	Pro	Glu	Pro
		155	
Val	Thr	Val	Ser
			160
Trp	Asn	Ser	Gly
			165
Ala	Leu	Thr	Ser
Gly	Val	His	Thr
	170		
Phe	Pro	Ala	Val
		175	
Leu	Gln	Ser	Ser
		180	
Gly	Leu	Tyr	Ser
			185
Leu	Ser	Ser	Val
Val	Thr	Val	Pro
		190	
Ser	Ser	Ser	Leu
		195	
Gly	Thr	Gln	Thr
			200
Tyr	Ile	Cys	Asn
			205
Val	Asn	His	Lys
Pro	Ser	Asn	Thr
Lys	Val	Asp	Lys
Lys	Val	Glu	Pro
Lys	Ser	Cys	Asp

210

215

220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
 435 440 445

Gly Lys
 450

<210> 154
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 Full-Length Light Chain

<400> 154

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
 20 25 30

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

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

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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Tyr Ser Leu Pro Pro
 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> 155
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15503 VH CDR1

<400> 155

Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5

<210> 156
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15503 VH CDR2

<400> 156

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 157
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VH CDR3

<400> 157

Ala	Arg	Val	Gly	Phe	Arg	Ala	Leu	Asn	Tyr
1				5					10

<210> 158
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VL CDR1

<400> 158

Arg	Ala	Ser	Gln	Asp	Ile	Ser	Ser	Trp	Leu	Ala
1				5						10

<210> 159
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VL CDR2

<400> 159

Ala	Ala	Ser	Ser	Leu	Gln	Ser
1				5		

<210> 160
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Antibody 15503 VL CDR3

<400> 160

Gln Gln Ala Thr Ser Tyr Pro Pro Trp Thr
 1 5 10

<210> 161

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15503 Variable Heavy Chain

<400> 161

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

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

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

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Val Gly Phe Arg Ala Leu Asn Tyr Trp Gly Gln Gly Thr Thr
 100 105 110

Val Thr Val Ser Ser
 115

<210> 162

<211> 108
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 Variable Light Chain

<400> 162

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Trp
 20 25 30

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

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

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

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

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

<210> 163
 <211> 447
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 Full-Length Heavy Chain

<400> 163

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

20

25

30

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

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Val Gly Phe Arg Ala Leu Asn Tyr Trp Gly Gln Gly Thr Thr
 100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
 115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
 130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
 145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 165 170 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
 180 185 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
 195 200 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
 210 215 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

435

440

445

<210> 164
 <211> 215
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 Full-Length Light Chain

<400> 164

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Trp
 20 25 30

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

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

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

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

Trp 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> 165
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15495 VH CDR1

<400> 165

Gly Thr Phe Ser Ser Tyr Ala Ile Ser
1 5

<210> 166
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15495 VH CDR2

<400> 166

Gly Ile Ile Pro Ile Phe Gly Thr Ala Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 167
<211> 13
<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VH CDR3

<400> 167

Ala Arg Gln Gln Tyr Asp Gly Arg Arg Tyr Phe Gly Leu
1 5 10

<210> 168

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VL CDR1

<400> 168

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 169

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VL CDR2

<400> 169

Ser Ala Ser Thr Arg Ala Thr
1 5

<210> 170

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VL CDR3

<400> 170

Gln Gln Val Asn Val Trp Pro Pro Thr
1 5

<210> 171
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15495 Variable Heavy Chain

<400> 171

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15

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

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Gln Gln Tyr Asp Gly Arg Arg Tyr Phe Gly Leu Trp Gly Arg
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 172
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15495 Variable Light Chain

<400> 172

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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 Ser 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 Val Asn Val Trp Pro Pro
85 90 95

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

<210> 173
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15495 Full-Length Heavy Chain

<400> 173

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

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

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Ser Tyr Ala Gln Lys Phe

50

55

60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gln Gln Tyr Asp Gly Arg Arg Tyr Phe Gly Leu Trp Gly Arg
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu

260

265

270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
 435 440 445

Gly Lys
 450

<210> 174

<211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15495 Full-Length Light Chain

<400> 174

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 Ser 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 Val Asn Val Trp Pro Pro
 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> 175
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15478 VH CDR1

<400> 175

Gly Thr Phe Ser Ser Tyr Ala Ile Ser
1 5

<210> 176
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15478 VH CDR2

<400> 176

Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 177
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15478 VH CDR3

<400> 177

Ala Arg Gly Gly Pro Trp Phe Asp Pro
1 5

<210> 178

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VL CDR1

<400> 178

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
1 5 10

<210> 179

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VL CDR2

<400> 179

Lys Ala Ser Ser Leu Glu Ser
1 5

<210> 180

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VL CDR3

<400> 180

Gln Gln Tyr Asn Ser Tyr Pro Pro Phe Thr
1 5 10

<210> 181

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 Variable Heavy Chain

<400> 181

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

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

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Thr Val Ser Ser
115

<210> 182

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 Variable Light Chain

<400> 182

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30

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

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

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

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

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

<210> 183
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15478 Full-Length Heavy Chain

<400> 183

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

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

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr

65		70		75		80									
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Gly	Gly	Pro	Trp	Phe	Asp	Pro	Trp	Gly	Gln	Gly	Thr	Leu	Val
			100					105					110		
Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala
		115					120					125			
Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu
	130					135					140				
Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly
145					150					155					160
Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser
				165					170					175	
Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu
			180					185					190		
Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr
		195					200					205			
Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr
	210					215					220				
Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	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	His	Glu	Asp	Pro	Glu	Val
			260					265					270		
Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr

275

280

285

Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp Lys Ser Arg Trp
 405 410 415

Gln Gln 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 Pro Gly Lys
 435 440 445

<210> 184

<211> 215

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 Full-Length Light Chain

<400> 184

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

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

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

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

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

Phe 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> 185
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15441 VH CDR1

<400> 185

Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5

<210> 186
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15441 VH CDR2

<400> 186

Ala Ile Ser Gly Ser Gly Gly Ser Thr Ser Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 187
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15441 VH CDR3

<400> 187

Ala Lys Pro Ser Leu Ala Thr Met Leu Ala Phe Asp Ile
1 5 10

<210> 188

<211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 VL CDR1

<400> 188

Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala
 1 5 10

<210> 189
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 VL CDR2

<400> 189

Asp Ala Ser Ser Leu Glu Ser
 1 5

<210> 190
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 VL CDR3

<400> 190

Gln Gln Ser Lys Ser Tyr Pro Arg Thr
 1 5

<210> 191
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 Variable Heavy Chain

<400> 191

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Ser Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Lys Pro Ser Leu Ala Thr Met Leu Ala Phe Asp Ile Trp Gly Gln
 100 105 110
 Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 192
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 Variable Light Chain

<400> 192

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

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

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

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

<210> 193

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15441 Full-Length Heavy Chain

<400> 193

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

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

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

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Ser Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Lys Pro Ser Leu Ala Thr Met Leu Ala Phe Asp Ile Trp Gly Gln

100

105

110

Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro 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 Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
435 440 445

Gly Lys
450

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<210> 194
<211> 214
<212> PRT
<213> Artificial Sequence
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<220>
<223> Antibody 15441 Full-Length Light Chain

<400> 194

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30

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

Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

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

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 195
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 VH CDR1

<400> 195

Gly Ser Ile Ser Ser Ser Val Tyr Tyr Trp Ser
 1 5 10

<210> 196
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 VH CDR2

<400> 196

Ser Ile Leu Val Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
 1 5 10 15

<210> 197
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 VH CDR3

<400> 197

Ala Arg Ala Val Ser Phe Leu Asp Val
 1 5

<210> 198
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 VL CDR1

<400> 198

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 199
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20496 VL CDR2

<400> 199

Gly Ala Ser Ser Leu Gln Ser
1 5

<210> 200
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20496 VL CDR3

<400> 200

Gln Gln Ser Tyr Asp Pro Pro Trp Thr
1 5

<210> 201
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20496 Variable Heavy Chain

<400> 201

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

Val Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu

35

40

45

Trp Ile Gly Ser Ile Leu Val 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 Ala Val Ser Phe Leu Asp Val Trp Gly Gln Gly Thr Met
 100 105 110

Val Ile Val Ser Ser
 115

<210> 202

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20496 Variable Light Chain

<400> 202

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
 20 25 30

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

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

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

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

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

<210> 203
 <211> 447
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 Full-Length Heavy Chain

<400> 203

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

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

Trp Ile Gly Ser Ile Leu Val 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 Ala Val Ser Phe Leu Asp Val Trp Gly Gln Gly Thr Met
 100 105 110

Val Ile Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
 115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys

130

135

140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
 145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 165 170 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
 180 185 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
 195 200 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
 210 215 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
 225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
 245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
 260 265 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
 275 280 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
 290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
 305 310 315 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
 325 330 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro

340

345

350

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
 355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
 370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
 385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
 405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
 420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 435 440 445

<210> 204

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20496 Full-Length Light Chain

<400> 204

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
 20 25 30

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

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

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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Asp Pro 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> 205
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15461 VH FR1

<400> 205

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
20 25

<210> 206
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15461 VH FR2

<400> 206

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 207
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15461 VH FR3

<400> 207

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 208
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15461 VH FR4

<400> 208

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 209
 <211> 23
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15461 VL FR1

<400> 209

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
			20			

<210> 210
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15461 VL FR2

<400> 210

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr
1				5					10					15

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

<220>
 <223> Antibody 15461 VL FR3

<400> 211

Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 212

<211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15461 VL FR4

<400> 212

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 213
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15461 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 213
 cagctgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60
 acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120
 cagccccag ggaaggggct ggagtggatt gggaacatct attatagtgg gagcacctac 180
 tacaaccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240
 tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa 300
 ggatcttacc ccaattggtt tgatccatgg ggacagggta cattgggtcac cgtctcctca 360

<210> 214
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15461 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 214
 gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgtttagc agcaacttag cctggtacca gcagaaacct 120
 ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180

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aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag taccactcct tccctttcac ttttggcgga 300
gggaccaagg ttgagatcaa a 321

<210> 215
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20500 VH FR1

<400> 215

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
20 25

<210> 216
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20500 VH FR2

<400> 216

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 217
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20500 VH FR3

<400> 217

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 20 25 30

<210> 218
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20500 VH FR4

<400> 218

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 1 5 10

<210> 219
 <211> 23
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20500 VL FR1

<400> 219

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
 20

<210> 220
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20500 VL FR2

<400> 220

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
 1 5 10 15

<210> 221

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

<220>
 <223> Antibody 20500 VL FR3

<400> 221

Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5				10					15		

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 222
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20500 VL FR4

<400> 222

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5				10	

<210> 223
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20500 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 223

cagctgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc	60
acctgcactg tctctggtgg ctccatcaag agtggtagtc actactgggg ctggatccgc	120
cagccccag ggaaggggct ggagtggatt gggaacatct attatagtgg gagcacctac	180
tacaaccgt ccctcaggag tcgagtcacc atatccgtag acacgtccaa gaaccagttc	240
tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagggaa	300
ggatcttacc ccaattggtt tgatccatgg ggacagggta cattgggtcac cgtctcctca	360

<210> 224
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20500 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 224
 gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct 120
 ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
 aggttcagtg gcagtgggtc tgggacagag ttactctca ccatcagcag cctgcagtct 240
 gaagattttg cagtttatta ctgtcagcag taccactcct tccctttcac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 225
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20501 VH FR1

<400> 225
 Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
 20 25

<210> 226
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20501 VH FR2

<400> 226

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 227
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20501 VH FR3

<400> 227

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 228
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20501 VH FR4

<400> 228

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 229
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20501 VL FR1

<400> 229

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

20

<210> 230
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20501 VL FR2

<400> 230

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 231
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20501 VL FR3

<400> 231

Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 232
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20501 VL FR4

<400> 232

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5					10

<210> 233
 <211> 360
 <212> DNA

<213> Artificial Sequence

<220>

<223> Antibody 20501 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 233

cagctgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc	60
acctgcactg tctctggtgg ctccatcaag agtggtagtc actactgggg ctggatccgc	120
cagccccag ggaaggggct ggagtggatt gggaacatct attatagtgg gagcacctac	180
tacaaccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc	240
tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa	300
ggatcttacc ccaattgggtt ggatccatgg ggacagggta cattgggtcac cgtctcctca	360

<210> 234

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Antibody 20501 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 234

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc	60
ctctcctgca gggccagtca gagtggttagc agcaacttag cctggtacca gcagaaacct	120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc	180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct	240
gaagattttg cagtttatta ctgtcagcag taccactcct tccctttcac ttttggcgga	300
gggaccaagg ttgagatcaa a	321

<210> 235

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20502.1 VH FR1

<400> 235

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
20 25

<210> 236
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VH FR2

<400> 236

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 237
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VH FR3

<400> 237

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 238
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502.1 VH FR4

<400> 238

Trp Gly Gln Gly Ile Leu Val Thr Val Ser Ser

1

5

10

<210> 239
 <211> 23
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20502 and 20502.1 VL FR1

<400> 239

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
 20

<210> 240
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20502 and 20502.1 VL FR2

<400> 240

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
 1 5 10 15

<210> 241
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20502 and 20502.1 VL FR3

<400> 241

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
 1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Ser Glu Asp Phe Ala Val Tyr Tyr Cys
 20 25 30

<210> 242
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody20502 and 20502.1 VL FR4

<400> 242

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5					10

<210> 243
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20502.1 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 243

cagctgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc	60
acctgcactg tctctggtgg ctccatcaag agtggtagtt actactgggg ctggatccgc	120
cagccccag ggaaggggct ggagtggatt gggaacatct attatagtgg gagcacctac	180
tacaaccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc	240
tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa	300
ggatcttacc ccaatcagtt tgatccatgg ggacagggta tattggtcac cgtctcctca	360

<210> 244
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20502 and 20502.1 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 244

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc	60
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct	120

ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
 aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
 gaagattttg cagtttatta ctgtcagcag taccactcct tccctttcac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 245
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 VH FR1

<400> 245

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
 20 25

<210> 246
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 VH FR2

<400> 246

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
 1 5 10

<210> 247
 <211> 30
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 VH FR3

<400> 247

Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys

1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 248
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22208 VH FR4

<400> 248

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 249
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22208 VL FR1

<400> 249

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
20

<210> 250
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22208 VL FR2

<400> 250

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
1 5 10 15

<210> 251
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 VL FR3

<400> 251

Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 252
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 VL FR4

<400> 252

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5					10

<210> 253
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 253

cagctgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc	60
acctgcactg tctctggtgg ctccatcaag agtggtagtc actactgggg ctggatccgc	120
cagccccag ggaaggggct ggagtggatt gggaacatct attatagtgg gagcacctac	180
tacaaccgt ccctcaagag tcgagtcacc atgtccgtag acacgtccaa gaaccagttc	240
tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa	300

ggatcttacc ccaattgggtt tgatccatgg ggacagggta cattgggtcac cgtctcctca 360

<210> 254
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 22208 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 254
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 ctctcctgca gggccagtca gtccgttagc accaacttag cctgggtacca gcagaaacct 120
 ggccaggctc ccaggctcct catctatgac gcatccgcca gggtcactgg tatcccagcc 180
 aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
 gaagattttg cagtttatta ctgtcagcag taccactcct tccctttcac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 255
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15462 VH FR1

<400> 255

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
 20 25

<210> 256
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15462 VH FR2

<400> 256

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 257

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 VH FR3

<400> 257

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 258

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 VH FR4

<400> 258

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
1 5 10

<210> 259

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15462 VL FR1

<400> 259

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
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<210> 260
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15462 VL FR2

<400> 260

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
1 5 10 15

<210> 261
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15462 VL FR3

<400> 261

Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
20 25 30

<210> 262
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15462 VL FR4

<400> 262

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> 263

<211> 360
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Antibody 15462 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 263
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 cagccccag ggaaggggct ggagtggatt gggaacatct attatagtgg gagcacctac 180
 tacaaccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240
 tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa 300
 ggatcttaca caaccgtgtt aaacgtatgg ggtcagggta caatggtcac cgtctcctca 360

<210> 264
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Antibody 15462 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 264
 gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120
 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtg ttactgtcag caggccgcca gttaccctct cacttttggc 300
 ggagggacca aggttgagat caaa 324

<210> 265
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Antibody 22213 VH FR1

<400> 265

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
20 25

<210> 266

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 VH FR2

<400> 266

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 267

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 VH FR3

<400> 267

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 268

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22213 VH FR4

<400> 268

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
1 5 10

<210> 269
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22213 VL FR1

<400> 269

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys
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<210> 270
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22213 VL FR2

<400> 270

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
1 5 10 15

<210> 271
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22213 VL FR3

<400> 271

Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys

<210> 272
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22213 VL FR4

<400> 272

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 273
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 22213 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 273
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 cagccccag ggaaggggct ggagtggatt gggaacatct attatagtgg gagcacctac 180
 tacaaccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240
 tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa 300
 ggatcttaca caaccgtgtt aaacgtatgg ggtcagggta caatgggtcac cgtctcctca 360

<210> 274
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 22213 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 274
 gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

3986_009PC04_SL_ST25.txt

ctctcctgca gggccagtca gagtgttgcc agcagccact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatctat gacgcagtca gcagggccac tggcatccca 180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagtgtg ttactgtcag caggccgcca gttaccctct cacttttggc 300
ggagggacca aggttgagat caaa 324

<210> 275
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 VH FR1

<400> 275

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
20 25

<210> 276
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 VH FR2

<400> 276

Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 277
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 VH FR3

<400> 277

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 278
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 VH FR4

<400> 278

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 279
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 VL FR1

<400> 279

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys
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<210> 280
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15465 VL FR2

<400> 280

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr

1 5 10 15

<210> 281
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 VL FR3

<400> 281

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
 20 25 30

<210> 282
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 VL FR4

<400> 282

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 283
 <211> 363
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 Variable Heavy Chain-Encoding Polynucleotide
 Sequence

<400> 283
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 acctgtactg tctctggtgg ctccatcagc agtggtggtt actactggag ctggatccgc 120
 cagcaccag ggaagggcct ggagtggatt gggaacatct attacagtgg gagcacctac 180
 tacaaccggt ccctcaagag tcgagttacc atatcagtag acacgtctaa gaaccagttc 240

tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa 300
 tctagcacca tatctgccga cttcgaccta tgggggagag gtaccttggt caccgtctcc 360
 tca 363

<210> 284
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15465 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 284
 gacatccaga tgaccagtc tccatcttcc gtgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgtc gggcgagtca ggggtattagc aggtgggtag cctgggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
 gaagattttg caacttatta ctgtcagcag gcacacacct tcccttacac ttttggcgga 300
 gggaccaagg ttgatcaaa a 321

<210> 285
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 VH FR1

<400> 285

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 Ala Ser Gly
 20 25

<210> 286
 <211> 14
 <212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20506 VH FR2

<400> 286

Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 287

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20506 VH FR3

<400> 287

Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 288

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20506 VH FR4

<400> 288

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 289

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20506 VL FR1

<400> 289

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys
20

<210> 290
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20506 VL FR2

<400> 290

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> 291
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20506 VL FR3

<400> 291

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

<210> 292
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20506 VL FR4

<400> 292

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

1

5

10

<210> 293
 <211> 363
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 293
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 acctgtactg cctctggtgg ctccatcagc catggtgggt actactggag ctggatccgc 120
 cagcaccag ggaagggcct ggagtggatt gggaacatct attacagtgg gagcacctac 180
 tacaatccgt ccctcaagag tcgagttacc atgtcagtag acacgtctaa gaaccagttc 240
 tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagaa 300
 tctagcacca tatctgccga cttcgacctt tgggggagag gtaccttggt caccgtctcc 360
 tca 363

<210> 294
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20506 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 294
 gacatccaga tgaccagtc tccatcttcc gtgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgct gggcgagtca ggggtattagc aggtgggttag cctgggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
 gaagattttg caacttatta ctgtcagcag gcacacacct tcccttacac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 295

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

<220>
 <223> Antibody 15483 VH FR1

<400> 295

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
			20					25	

<210> 296
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15483 VH FR2

<400> 296

Trp	Ile	Arg	Gln	His	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Ile	Gly
1				5					10				

<210> 297
 <211> 30
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15483 VH FR3

<400> 297

Arg	Val	Thr	Ile	Ser	Val	Asp	Thr	Ser	Lys	Asn	Gln	Phe	Ser	Leu	Lys
1				5					10					15	

Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			20					25					30

<210> 298
 <211> 11
 <212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 VH FR4

<400> 298

Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 299

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 VL FR1

<400> 299

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1				5					10					15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
						20

<210> 300

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 VL FR2

<400> 300

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 301

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15483 VL FR3

<400> 301

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
 1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys
 20 25 30

<210> 302
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15483 VL FR4

<400> 302

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 303
 <211> 363
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15483 Variable Heavy Chain-Encoding Polynucleotide
 Sequence

<400> 303
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 cagcaccag ggaagggcct ggagtggatt gggaacatct attacagtgg gagcacctac 180
 tacaaccgt ccctcaagag tcgagttacc atatcagtag acacgtctaa gaaccagttc 240
 tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagaggg 300
 ttgagcacca tagacgaggc attcgacca tggggacagg gtacattggt caccgtctcc 360
 tca 363

<210> 304
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Antibody 15483 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 304

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gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggatatca gcagaaacca    120
gggaaagccc ctaagctcct gatctataaa gcctccagtt tggaaagtgg ggtcccatca    180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct    240
gatgattttg caacttatta ctgccagcag gacaacagtt acccttacac ttttggcgga    300
gggaccaagg ttgagatcaa a                                              321

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<210> 305

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20513 VH FR1

<400> 305

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Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1           5           10           15

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
          20           25

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<210> 306

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20513 VH FR2

<400> 306

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Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp Ile Gly
1           5           10

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<210> 307

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

<220>
 <223> Antibody 20513 VH FR3

<400> 307

Arg	Val	Thr	Met	Ser	Val	Asp	Thr	Ser	Lys	Asn	Gln	Phe	Ser	Leu	Lys
1				5					10					15	

Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			20					25					30

<210> 308
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20513 VH FR4

<400> 308

Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 309
 <211> 23
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20513 VL FR1

<400> 309

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1				5					10					15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 310
 <211> 15
 <212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20513 VL FR2

<400> 310

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 311

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20513 VL FR3

<400> 311

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
			20					25					30		

<210> 312

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20513 VL FR4

<400> 312

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5					10

<210> 313

<211> 363

<212> DNA

<213> Artificial Sequence

<220>

<223> Antibody 20513 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 313
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cagcaccag ggaagggcct ggagtggatt gggaacatct attacagtgg gagcacctac 180
tacaaccgt ccctcaggag tcgagttacc atgtcagtag acacgtctaa gaaccagttc 240
tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagaggg 300
ttgagcacca tagacaggc attcgacca tggggacagg gtacattggt caccgtctcc 360
tca 363

<210> 314
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Antibody 20513 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 314
gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctataaa gcctccagtt tggaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240
gatgattttg caacttatta ctgccagcag gacaacagtt acccttacac ttttggcgga 300
gggaccaagg ttgagatcaa a 321

<210> 315
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 VH FR1

<400> 315
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
20 25

<210> 316
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 VH FR2

<400> 316

Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 317
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 VH FR3

<400> 317

Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 318
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 22216 VH FR4

<400> 318

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 319

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

<220>
 <223> Antibody 22216 VL FR1

<400> 319

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1				5					10					15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 320
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22216 VL FR2

<400> 320

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 321
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 22216 VL FR3

<400> 321

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
			20					25					30		

<210> 322
 <211> 10
 <212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 22216 VL FR4

<400> 322

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5					10

<210> 323

<211> 363

<212> DNA

<213> Artificial Sequence

<220>

<223> Antibody 22216 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 323

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcacagac cctgtccctc	60
acctgtactg tctctggtgg ctccatcagc gatggtagtt actactggag ctggatccgc	120
cagcaccag ggaagggcct ggagtggatt gggaacatct attacagtgg gagcacctac	180
tacaaccgt ccctcaggag tcgagttacc atgtcagtag acacgtctaa gaaccagttc	240
tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagaggg	300
ttgagcacca tagacgaggc attcgacca tggggacagg gtacattggt caccgtctcc	360
tca	363

<210> 324

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Antibody 22216 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 324

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc	60
atcacttgcc gggccagtaa aagtattagt tcctggttgg cctggatatca gcagaaacca	120
ggaaaagccc ctaagctcct gatctatgaa gcctcctcct tgcacagtgg ggtcccatca	180

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aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccagcag gacaacagtt acccttacac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 325
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 VH FR1

<400> 325

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
 20 25

<210> 326
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 VH FR2

<400> 326

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
 1 5 10

<210> 327
 <211> 30
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 VH FR3

<400> 327

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
 1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 20 25 30

<210> 328
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 VH FR4

<400> 328

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 1 5 10

<210> 329
 <211> 23
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 VL FR1

<400> 329

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys
 20

<210> 330
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 VL FR2

<400> 330

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
 1 5 10 15

<210> 331

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

<220>
 <223> Antibody 15489 VL FR3

<400> 331

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
			20					25					30		

<210> 332
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 VL FR4

<400> 332

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5					10

<210> 333
 <211> 366
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 333

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc	60
acctgcactg tctctggtgg ctccatcagt agttactact ggagctggat ccggcagccc	120
ccaggggaagg gactggagtg gattgggtat atctatagta gtgggagcac caactacaac	180
ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg	240
aagctgagtt ctgtgaccgc cgcagacacg gcggtgtact actgcgccag aggctctgga	300
cagtatgcag ctcctgatta tggaatggac gtatggggcc agggaacaac tgtcaccgtc	360

tcctca 366

<210> 334
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15489 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 334
 gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggccagtca gagtattagt agctggttgg cctggatatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctataaa gcctccagtt tggaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccagcag gacaatagct tccctttcac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 335
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 VH FR1

<400> 335
 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
 20 25

<210> 336
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20516 VH FR2

<400> 336

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 337

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20516 VH FR3

<400> 337

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 338

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20516 VH FR4

<400> 338

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1 5 10

<210> 339

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20516 VL FR1

<400> 339

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys
20

<210> 340
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20516 VL FR2

<400> 340

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> 341
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20516 VL FR3

<400> 341

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

<210> 342
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20516 VL FR4

<400> 342

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> 343

<211> 366
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Antibody 20516 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 343
 caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60
 acctgcactg tctctggtgg ctccatcatt agttactact ggggggtggat ccggcagccc 120
 ccagggaagg gactggagtg gattgggtat atctattcta gtgggagcac ctcgtacaac 180
 ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240
 aagctgagtt ctgtgaccgc cgagacacg gcggtgtact actgcgccag aggctctgga 300
 ctgtatgcag ctcctgatta tggacttgac gtatggggtc aggaacaac tgtcacctgc 360
 tcctca 366

<210> 344
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Antibody 20516 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 344
 gacatccaga tgaccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggccagtca gagtattagt agctggttgg cctgggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctataaa gcctccagtt tggaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccagcag gacaatagct tccctttcac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 345
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Antibody 15472 VH FR1

<400> 345

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
20 25

<210> 346

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15472 VH FR2

<400> 346

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
1 5 10

<210> 347

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15472 VH FR3

<400> 347

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
1 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 348

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15472 VH FR4

<400> 348

Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 349

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15472 VL FR1

<400> 349

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1				5					10					15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
						20

<210> 350

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15472 VL FR2

<400> 350

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 351

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15472 VL FR3

<400> 351

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
 20 25 30

<210> 352
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 VL FR4

<400> 352

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 353
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 353
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 tcctgtgcag cctctggatt caccttttagc agctatgccg tgagctgggt ccgccaggct 120
 ccagggaagg ggctggagtg ggtctcaacc attagtggta gtggtggtag cacatactac 180
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240
 ctgcaaatga acagcctgag agccgaggac acggcggtgt actactgcgc cagaggtgcc 300
 ggacactacg acctcgtcgg acgatactgg ggacagggta cattgggtcac cgtctcctca 360

<210> 354
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15472 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 354

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gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
 aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
 gaagattttg caacttacta ctgtcagcaa ctatacagtc tccctcctac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 355
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VH FR1

<400> 355

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
 20 25

<210> 356
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VH FR2

<400> 356

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
 1 5 10

<210> 357
 <211> 30
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VH FR3

<400> 357

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
1 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 358

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15503 VH FR4

<400> 358

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1 5 10

<210> 359

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15503 VL FR1

<400> 359

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys
20

<210> 360

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15503 VL FR2

<400> 360

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
 1 5 10 15

<210> 361
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VL FR3

<400> 361

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
 20 25 30

<210> 362
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 VL FR4

<400> 362

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 363
 <211> 351
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 363
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 tcctgtgcag cctctggatt cacctttagc agctatgcc a tgagctgggt ccgccaggct 120
 ccagggaagg ggctggagtg ggtctcagct attagtggtg gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240
 ctgcaaatac acagcctgag agccgaggac acggcgggtg actactgcgc cagagtggga 300
 ttcagagcat taaactactg gggacagggt acaactgtca ccgtctcctc a 351

<210> 364
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15503 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 364
 gacatccagt tgaccagtc tccatcttcc gtgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgct gggcgagtca ggatattagc agctgggttag cctgggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
 gaagattttg caacttatta ctgtcagcag gcaaccagtt accctccttg gacttttggc 300
 ggagggacca aggttgagat caaa 324

<210> 365
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15495 VH FR1

<400> 365

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly
 20 25

<210> 366
 <211> 14
 <212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VH FR2

<400> 366

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
1 5 10

<210> 367

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VH FR3

<400> 367

Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 368

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VH FR4

<400> 368

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 369

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15495 VL FR1

<400> 369

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
20

<210> 370
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15495 VL FR2

<400> 370

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
1 5 10 15

<210> 371
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15495 VL FR3

<400> 371

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Ser Glu Asp Phe Ala Val Tyr Tyr Cys
20 25 30

<210> 372
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 15495 VL FR4

<400> 372

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

1

5

10

<210> 373
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15495 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 373
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 tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120
 cctggacaag ggcttgagt gatgggaggg atcatcccta tctttggtac agcaagctac 180
 gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac 240
 atggagctga gcagcctgag atctgaggac acggcgggtgt actactgcgc aagacagcaa 300
 tacgacggta gacgatactt cggcctatgg gggagaggta ccttggtcac cgtctcctca 360

<210> 374
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15495 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 374
 gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagggttagc agcaacttag cctggtacca gcagaaacct 120
 ggccaggctc ccaggctcct catctatagc gcatccacca gggccactgg tatcccagcc 180
 aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
 gaagattttg cagtttatta ctgtcagcag gtcaacgtct ggcctcctac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 375
 <211> 26
 <212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VH FR1

<400> 375

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ser
1				5					10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly
			20					25	

<210> 376

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VH FR2

<400> 376

Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly
1				5					10				

<210> 377

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VH FR3

<400> 377

Arg	Val	Thr	Ile	Thr	Ala	Asp	Glu	Ser	Thr	Ser	Thr	Ala	Tyr	Met	Glu
1				5					10					15	

Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			20					25					30

<210> 378

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VH FR4

<400> 378

Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 379

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VL FR1

<400> 379

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1				5					10					15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 380

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VL FR2

<400> 380

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 381

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15478 VL FR3

<400> 381

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr

1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys
 20 25 30

<210> 382
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15478 VL FR4

<400> 382

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 383
 <211> 348
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15478 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 383
 caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60
 tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120
 cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac agcaaaactac 180
 gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac 240
 atggagctga gcagcctgag atctgaggac acggcggtgt actactgcgc cagaggtggg 300
 ccttggtttg atccatgggg acagggtaca ttggtcaccg tctcctca 348

<210> 384
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15478 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 384
 gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggccagtca gagtattagt agctggttgg cctggatatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctataaa gcctccagtt tggaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccagcag tacaatagct accctccttt cacttttggc 300
 ggagggacca aggttgagat caaa 324

<210> 385
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 VH FR1

<400> 385
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
 20 25

<210> 386
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 VH FR2

<400> 386
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
 1 5 10

<210> 387
 <211> 30
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Antibody 15441 VH FR3

<400> 387

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr	Leu	Gln
1				5					10					15	

Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			20					25					30

<210> 388

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15441 VH FR4

<400> 388

Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 389

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15441 VL FR1

<400> 389

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1				5					10					15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 390

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15441 VL FR2

<400> 390

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5				10					15	

<210> 391

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15441 VL FR3

<400> 391

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr
1				5				10					15		

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
			20					25					30		

<210> 392

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 15441 VL FR4

<400> 392

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
1				5				10	

<210> 393

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> Antibody 15441 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 393

gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgccca tgagctgggt ccgccaggct 120

```

ccaggaagg ggctggagtg ggtctcagct attagtggta gtggtgtag cacatcctac      180
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat      240
ctgcaaatga acagcctgag agccgaggac acggcggtgt actactgcgc caagccttct      300
ttggcaacaa tgttagcctt cgatatctgg ggtcagggtg caatgggtcac cgtctcctca      360

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<210> 394
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 15441 Variable Light Chain-Encoding Polynucleotide Sequence

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<400> 394
gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggatatca gcagaaacca      120
gggaaagccc ctaagctcct gatctatgat gcctccagtt tggaaagtgg ggtcccatca      180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct      240
gatgatcttg caacttatta ctgccagcag tccaaaagtt accctaggac ttttggcgga      300
gggaccaagg ttgagatcaa a                                              321

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<210> 395
 <211> 26
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 VH FR1

<400> 395

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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
      20           25

```

<210> 396

<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20496 VH FR2

<400> 396

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 397
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20496 VH FR3

<400> 397

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
20 25 30

<210> 398
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20496 VH FR4

<400> 398

Trp Gly Gln Gly Thr Met Val Ile Val Ser Ser
1 5 10

<210> 399
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20496 VL FR1

<400> 399

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 400

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20496 VL FR2

<400> 400

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5				10						15

<210> 401

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20496 VL FR3

<400> 401

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5				10						15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
			20				25						30		

<210> 402

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Antibody 20496 VL FR4

<400> 402

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> 403
 <211> 351
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 Variable Heavy Chain-Encoding Polynucleotide Sequence

<400> 403
 cagctgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60
 acctgcactg tctctggtgg ctccatcagc agtagtggtt actactggag ttggatccgc 120
 cagccccag ggaaggggtt ggagtggatt gggagtatcc tggtagtgagg gagcacctac 180
 tacaaccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240
 tccctgaagc tgagttctgt gaccgccgca gacacggcgg tgtactactg cgccagagct 300
 gtatccttct tagacgtatg gggtcagggt acaatgggtca tcgtctcctc a 351

<210> 404
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Antibody 20496 Variable Light Chain-Encoding Polynucleotide Sequence

<400> 404
 gacatccaga tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatggt gcatccagtt tgcaaagtgg ggtcccatca 180
 aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
 gaagattttg caacttacta ctgtcagcaa agctacgacc ccccttggac ttttggcgga 300
 gggaccaagg ttgagatcaa a 321

<210> 405

<211> 107
 <212> PRT
 <213> Homo sapiens

<400> 405

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 100 105

<210> 406
 <211> 321
 <212> DNA
 <213> Homo sapiens

<400> 406

cggaccgtgg ctgcaccatc tgtcttcac ttcccgccat ctgatgagca gttgaaatct 60
 ggaactgcct ctgttggtg cctgctgaat aacttctatc ccagagaggc caaagtacag 120
 tggaaggtgg ataacgccct ccaatcgggt aactcccagg agagtgtcac agagcaggac 180
 agcaaggaca gcacctacag cctcagcagc accctgacgc tgagcaaagc agactacgag 240
 aaacacaaag tctacgcctg cgaagtcacc catcagggcc tgagctcgcc cgtcaciaag 300
 agcttcaaca ggggagagtg t 321

<210> 407
 <211> 330
 <212> PRT
 <213> Homo sapiens

<400> 407

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

Lys 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

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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 Asp Glu
225 230 235 240

Leu 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
325 330

<210> 408

<211> 990

<212> DNA

<213> Homo sapiens

<400> 408

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctgggtcaag gactacttcc ccgaaccggt gacgggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

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ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg caccagacc      240
tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc      300
aaatcttgtg acaaaaactca cacatgcccc ccgtgcccag cacctgaact cctggggggga      360
ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccctt      420
gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg      480
tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac      540
agcacgtacc ggggtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag      600
gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc      660
aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag      720
ctgaccaaga accaggctcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc      780
gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg      840
ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg      900
cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg      960
cagaagagcc tctccctgtc tccgggtaaa      990

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<210> 409
 <211> 493
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> B7-H4-huIgG1

<400> 409

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Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1           5           10          15

```

```

Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20          25          30

```

```

Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35          40          45

```

```

Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu

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50

55

60

Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65 70 75 80

His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85 90 95

Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100 105 110

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
115 120 125

Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
130 135 140

Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
145 150 155 160

Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
165 170 175

Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
180 185 190

Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
195 200 205

Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
210 215 220

Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225 230 235 240

Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
245 250 255

Lys Ala Ser Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys

260

265

270

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
 275 280 285

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
 290 295 300

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
 305 310 315 320

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
 325 330 335

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
 340 345 350

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
 355 360 365

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
 370 375 380

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
 385 390 395 400

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
 405 410 415

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
 420 425 430

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
 435 440 445

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
 450 455 460

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

465 470 480

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
485 490

<210>	410
<211>	385
<212>	PRT
<213>	Artificial Sequence

<220>
<223> B7-H4 IgV-huIgG1

<400> 410

Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1 5 10 15

Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20 25 30

Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35 40 45

Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50 55 60

Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65 70 75 80

His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85 90 95

Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100 105 110

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
115 120 125

Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
130 135 140

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Tyr Lys Thr Gly Ala Phe Ser Gly Ser Glu Pro Lys Ser Ser Asp Lys
145 150 155 160

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
165 170 175

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
180 185 190

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
195 200 205

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
210 215 220

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
225 230 235 240

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
245 250 255

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
260 265 270

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
275 280 285

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
290 295 300

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
305 310 315 320

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
325 330 335

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
340 345 350

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 355 360 365

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 370 375 380

Lys
 385

<210> 411
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 411

Ser Gly Ser Val Phe Ser Ile Asp Ala Met
 1 5 10

<210> 412
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 412

Leu Ser Gly Ile Ser Ser Ala Lys
 1 5

<210> 413
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 413

Tyr Ala Asp Val Ser Thr Gly Trp Gly Arg Asp Ala His Gly Tyr Trp

1 5 10 15

<210> 414
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 414

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Glu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Val Phe Ser Ile Asp
 20 25 30

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

Ala Val Leu Ser Gly Ile Ser Ser Ala Lys Tyr Ala Ala Ser Ala Pro
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
 65 70 75 80

Gln Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Tyr
 85 90 95

Ala Asp Val Ser Thr Gly Trp Gly Arg Asp Ala His Gly Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val
 115

<210> 415
 <211> 479
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 415

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Glu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Val Phe Ser Ile Asp
 20 25 30

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

Ala Val Leu Ser Gly Ile Ser Ser Ala Lys Tyr Ala Ala Ser Ala Pro
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
 65 70 75 80

Gln Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Tyr
 85 90 95

Ala Asp Val Ser Thr Gly Trp Gly Arg Asp Ala His Gly Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Lys Pro Gly Gly Ser Gly Gly Ser Glu
 115 120 125

Val Gln Leu Leu Glu Ser Gly Gly Gly Glu Val Gln Pro Gly Gly Ser
 130 135 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Val Phe Ser Ile Asp Ala
 145 150 155 160

Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val Ala
 165 170 175

Val Leu Ser Gly Ile Ser Ser Ala Lys Tyr Ala Ala Ser Ala Pro Gly
 180 185 190

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu Gln

195

200

205

Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Tyr Ala
 210 215 220

Asp Val Ser Thr Gly Trp Gly Arg Asp Ala His Gly Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Leu Val Thr Val Lys Pro Gly Gly Gly Gly Asp Lys Thr His
 245 250 255

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
 260 265 270

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
 275 280 285

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
 290 295 300

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
 305 310 315 320

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
 325 330 335

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
 340 345 350

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
 355 360 365

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
 370 375 380

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
 385 390 395 400

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn

405

410

415

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
 420 425 430

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
 435 440 445

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
 450 455 460

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 465 470 475

<210> 416
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 416

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
 1 5 10

<210> 417
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 417

Asp Lys Thr His Thr Cys Pro Pro Cys
 1 5

<210> 418
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>

<223> GITR Antibody

<400> 418

Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
1 5 10

<210> 419

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> GITR Antibody

<400> 419

Gly Gly Ser Gly Gly Ser
1 5

<210> 420

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> GITR Antibody

<400> 420

Gly Gly Ser Gly Gly Ser Gly Gly Ser
1 5

<210> 421

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> GITR Antibody

<400> 421

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser
1 5 10

<210> 422

<211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 422

Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ser
1				5				10					15	

<210> 423
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 423

Gly	Gly	Gly	Gly
1			

<210> 424
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 424

Gly	Gly	Gly	Gly	Gly
1			5	

<210> 425
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> GITR Antibody

<400> 425

Gly	Gly	Gly	Gly	Gly	Gly

1

5

<210> 426
 <211> 208
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD80

<400> 426

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
 1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
 20 25 30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
 35 40 45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
 50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
 65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
 85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
 100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
 115 120 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
 130 135 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
 145 150 155 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
 165 170 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
 180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
 195 200 205

<210> 427
 <211> 440
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD80

<400> 427

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
 1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
 20 25 30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
 35 40 45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
 50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
 65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
 85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
 100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys

115

120

125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
 130 135 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
 145 150 155 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
 165 170 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
 180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
 195 200 205

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
 210 215 220

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
 225 230 235 240

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 245 250 255

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
 260 265 270

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
 275 280 285

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 290 295 300

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
 305 310 315 320

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro

325

330

335

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
 340 345 350

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 355 360 365

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 370 375 380

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 385 390 395 400

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 405 410 415

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 420 425 430

Ser Leu Ser Leu Ser Pro Gly Lys
 435 440

<210> 428
 <211> 440
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD80

<400> 428

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
 1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
 20 25 30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
 35 40 45

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Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
115 120 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
130 135 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145 150 155 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
165 170 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
210 215 220

Pro Glu Phe Glu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
225 230 235 240

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
245 250 255

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Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
260 265 270

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
275 280 285

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
290 295 300

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
305 310 315 320

Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
325 330 335

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
340 345 350

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
355 360 365

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
370 375 380

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
385 390 395 400

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
405 410 415

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
420 425 430

Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> 429

<211> 122

<212> PRT

<213> Artificial Sequence

<220>

<223> CD80

<400> 429

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
20 25 30

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

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

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 430

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> CD80

<400> 430

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

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

Gly Asp Asn Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
35 40 45

Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys His Leu Ser Asn
85 90 95

Glu Asp Leu Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 431
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> GITR Antibody

<400> 431

Gly Tyr Thr Phe Thr Asp Asn Tyr Met Ile
1 5 10

<210> 432
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CD80

<400> 432

Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 433
 <211> 13
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD80

<400> 433

Glu	Ser	Pro	Tyr	Phe	Ser	Asn	Leu	Tyr	Val	Met	Asp	Tyr
1				5					10			

<210> 434
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD80

<400> 434

Lys	Ala	Ser	Gln	Ser	Val	Asp	Tyr	Asp	Gly	Asp	Asn	Tyr	Met	Asn
1				5					10					15

<210> 435
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD80

<400> 435

Ala	Ala	Ser	Asn	Leu	Glu	Ser
1				5		

<210> 436
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>

<223> CD80

<400> 436

His Leu Ser Asn Glu Asp Leu Ser Thr
 1 5

<210> 437

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> CD80

<400> 437

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
 20 25 30

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

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

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr

130

135

140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
 165 170 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
 195 200 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
 210 215 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro
 225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
 260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr

340

345

350

Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
 435 440 445

Lys

<210> 438
 <211> 218
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD80

<400> 438

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 Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Asn Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45

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Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys His Leu Ser Asn
85 90 95

Glu Asp Leu Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 439
<211> 268
<212> PRT
<213> Homo sapiens

<400> 439

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Thr Leu Val Val Gly Val Val Gly Gly Leu Leu Gly Ser
145 150 155 160

Leu Val Leu Leu Val Trp Val Leu Ala Val Ile Cys Ser Arg Ala Ala
165 170 175

Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly Gln Pro Leu Lys Glu Asp
180 185 190

Pro Ser Ala Val Pro Val Phe Ser Val Asp Tyr Gly Glu Leu Asp Phe
195 200 205

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Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro Cys Val Pro Glu
210 215 220

Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly Met Gly Thr Ser
225 230 235 240

Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly Pro Arg Ser Ala Gln Pro
245 250 255

Leu Arg Pro Glu Asp Gly His Cys Ser Trp Pro Leu
260 265

<210> 440
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-1 heavy chain variable region

<400> 440

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> 441
 <211> 327
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy chain constant region

<400> 441

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

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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> 442
<211> 107
<212> PRT
<213> Artificial Sequence

<220>

<223> PD-1 light chain variable region

<400> 442

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

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

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

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

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
 85 90 95

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

<210> 443

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> PD-1 light chain constant region

<400> 443

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 100 105

<210> 444
 <211> 30
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy FR1

<400> 444

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser
 20 25 30

<210> 445
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy CDR1

<400> 445

Asn Ser Gly Met His
 1 5

<210> 446
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy FR2

<400> 446

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
 1 5 10

<210> 447
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy CDR2

<400> 447

Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys
 1 5 10 15

Gly

<210> 448
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy FR3

<400> 448

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe Leu Gln
 1 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Thr
 20 25 30

<210> 449
 <211> 4

<212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy CDR3

<400> 449

Asn Asp Asp Tyr
 1

<210> 450
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 heavy FR4

<400> 450

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 1 5 10

<210> 451
 <211> 23
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 light FR1

<400> 451

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
 20

<210> 452
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-1 light CDR1

<400> 452

Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Tyr	Leu	Ala
1				5					10	

<210> 453

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> PD-1 light FR2

<400> 453

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 454

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> PD-1 light CDR2

<400> 454

Asp	Ala	Ser	Asn	Arg	Ala	Thr
1				5		

<210> 455

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> PD-1 light FR3

<400> 455

Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 456
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-1 light CDR3

<400> 456

Gln Gln Ser Ser Asn Trp Pro Arg Thr
1 5

<210> 457
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-1 light FR4

<400> 457

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> 458
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502 VH CDR1

<400> 458

Gly Ser Ile Lys Ser Gly Ser Tyr Tyr Trp Gly
1 5 10

<210> 459
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502 VH CDR2

<400> 459

Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Arg Ser
1 5 10 15

<210> 460
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502 VH CDR3

<400> 460

Ala Arg Glu Gly Ser Tyr Pro Asn Gln Phe Asp Pro
1 5 10

<210> 461
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502 VL CDR1

<400> 461

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 462
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody 20502 VL CDR2

<400> 462

Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 463
<211> 9
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<213> Artificial Sequence

<220>

<223> Antibody 20502 VL CDR3

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Gln Gln Tyr His Ser Phe Pro Phe Thr
1 5

<210> 464

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<212> PRT

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<220>

<223> Antibody 20502 Variable Heavy Chain

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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 Lys 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Arg Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Gln Phe Asp Pro Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 465

<211> 26

<212> PRT
 <213> Artificial Sequence

<220>
 <223> Antibody 20502 VH FR1

<400> 465

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
 20 25

<210> 466
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 <212> PRT
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<220>
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<400> 466

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
 1 5 10

<210> 467
 <211> 30
 <212> PRT
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<220>
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<400> 467

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
 1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 20 25 30

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<223> Antibody 20502 VH FR4

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Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<210> 469

<211> 450

<212> PRT

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<223> Antibody 20502 Full Length Heavy Chain

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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 Lys 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 Asn Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60

Leu Arg Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Glu Gly Ser Tyr Pro Asn Gln Phe Asp Pro Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

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Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 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 His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 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 Ala Leu Pro Ala Pro Ile Glu
 325 330 335

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Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu 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 Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln 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 Pro
 435 440 445

Gly Lys
 450