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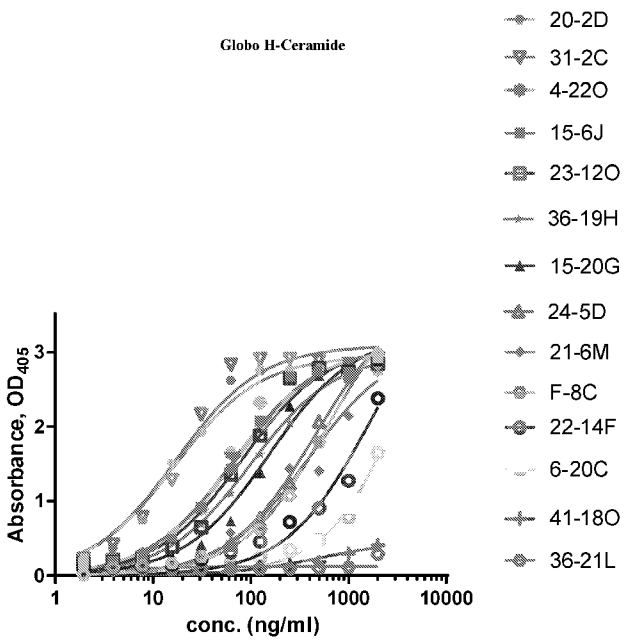
(54) Title: HUMAN ANTIBODIES, PHARMACEUTICAL COMPOSITIONS AND METHODS

FIG. 1A



(57) Abstract: Pharmaceutical composition comprising antibodies or antigen binding fragments thereof that bind to Globo H, stage-specific embryonic antigen 3 (SSEA-3) and stage-specific embryonic antigen 4 (SSEA-4) are disclosed herein, as well as methods of use thereof. Methods of use include, without limitation, cancer therapies and diagnostics. The antibodies of the disclosure can bind to certain cancer cell surfaces. Exemplary targets of the antibodies disclosed herein can include carcinomas, such as sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervix cancer, endometrial cancer, ovarian cancer, testical cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer.

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[Continued on next page]

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HUMAN ANTIBODIES, PHARMACEUTICAL COMPOSITIONS AND METHODS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the priority of U.S. Provisional Patent Application No. 62/368,407, filed July 29, 2016. The entirety of the aforementioned application is incorporated herein by reference.

FIELD

[0002] The present disclosure relates to human antibodies and binding fragments thereof to carbohydrate antigens, as well as nucleic acids encoding such antibodies, complementary nucleic acids, polypeptides, vectors, host cells and methods of making and using thereof, including pharmaceutical compositions comprising said antibody and/or binding fragments. Further, methods are provided for administering antibodies to a subject in an amount effective to inhibit cancer cells. Specifically, antibodies that bind to stage-specific embryonic antigen 3 (SSEA-3), stage-specific embryonic antigen 4 (SSEA-4) and Globo H are disclosed herein, as well as related compositions and methods of use. Methods of use include, without limitation, cancer therapies and diagnostics.

BACKGROUND OF THE INVENTION

[0003] Recent advances in the isolation, culture and expansion of human B cells are enabling the isolation of large numbers of human antibodies to be used for cancer diagnostics and therapeutics. For several decades, mouse monoclonal antibodies were isolated using the hybridoma technology. However, the therapeutic application of these antibodies was limited by induction of anti-mouse antibodies and autoreactivity. More recently, monoclonal antibodies have been isolated through phage display libraries produced from humans with a humoral response of interest (Mao S, *et al.* (1999) Proc Natl Acad Sci USA; 96:6953–6958.). Although this technique has produced numerous useful antibodies, its applicability is limited by differences in binding properties between antibodies expressed in bacterial and eukaryotic cells. In addition, phage display may result in heavy- and light-chain combinations that do not occur in the same B cell *in vivo*.

[0004] Numerous surface carbohydrates are expressed in malignant tumor cells. For example, the carbohydrate antigen Globo H (Fucα1→2 Galβ1→3 GalNAcβ1→3 Galα1→4

Galβ1→4 Glc) was first isolated as a ceramide-linked Glycolipid and identified in 1984 from breast cancer MCF-7 cells. (Bremer E G, *et al.* (1984) J Biol Chem 259:14773-14777). Previous studies have also shown that Globo H and stage-specific embryonic antigen 3 (2Gal β1→ 3GalNAcβ1→ 3Galα1→ 4Galβ1→ 4Glcβ1) (SSEA-3, also called Gb5) were observed on breast cancer cells and breast cancer stem cells (WW Chang *et al.* (2008) Proc Natl Acad Sci USA, 105(33): 11667-11672). In addition, SSEA-4 (stage-specific embryonic antigen-4) (Neu5Acα2→ 3Galβ1→ 3GalNAcβ1→ 3Galα1→ 4Galβ1→ 4Glcβ1) has been commonly used as a cell surface marker for pluripotent human embryonic stem cells and has been used to isolate mesenchymal stem cells and enrich neural progenitor cells (Kannagi R *et al.* (1983) EMBO J, 2:2355-2361). Thus, it is of great interest to identify glycan markers associated with and/or predictive of cancers, and develop human monoclonal antibodies against the markers for use in diagnosing and treating a broad spectrum of cancers.

SUMMARY OF THE INVENTION

[0005] Accordingly, the present disclosure is based on the discovery that Globo series antigens (Globo H, SSEA-3 and SSEA-4) are aberrantly expressed in a broad spectrum of cancers, but not on normal cells. Thus, human monoclonal antibodies to Globo series antigens (Globo H, SSEA-3 and SSEA-4) can address the unmet need for effective treatment and/or prevention for cancer. Cancer cells expressing Globo series antigens can include, but are not limited to, sarcoma, skin cancer, leukemia, lymphoma, brain cancer, lung cancer, breast cancer, oral cancer, esophageal cancer, stomach cancer, liver cancer, bile duct cancer, pancreatic cancer, colon cancer, kidney cancer, cervical cancer, ovarian cancer and prostate cancer.

[0006] In one aspect, the present disclosure is directed to antibodies or binding fragments thereof specific to Globo series antigens.

[0007] In order to generate anti-Globo series antigens human monoclonal antibodies, human B cells are isolated from peripheral blood of vaccinated subjects, plated at a density of one cell per well and cultured for secreted IgG production. The secreted IgGs are assayed for Globo H, SSEA-3 or SSEA-4 binding specificities. Genes encoding Ig VH, Ig Vκ or Ig Vλ from positive wells are recovered using RT-PCR and cloned into expression vectors for generating anti-Globo H, SSEA-3 or SSEA-4 human monoclonal antibody. In one

embodiment, the light chains of the antibody is kappa type. In one embodiment, the light chain of the antibody is lamda type.

[0008] In one aspect, the present disclosure provides an antibody, and/or an antigen-binding fragment thereof, comprising: a heavy chain variable domain (VH) comprising respective CDRs as disclosed herein and an amino acid sequence of at least about 80%, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97 98, or 99 % sequence homology to the amino acid sequences as disclosed herein and/or a light chain variable domain (VL) comprising respective CDRs as disclosed herein and an amino acid sequence of at least about 80% , 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97 98, or 99 % sequence homology to the amino acid sequences as disclosed herein respectively.

[0009] In one aspect, the preent disclosure provides an antibody, or an antigen-binding fragment thereof capable of targeting the Globo-Series carbohydrate antigen, comprising: three heavy chain CDRs and corresponding three light chain CDRs of each respective clones as disclosed herein such as the ones disclosed in Tables 1-28.

[0010] In another aspect, the present disclosure provides the antibody or antigen-binding fragment thereof comprising: the heavy chain variable domain comprising an amino acid sequence having at least about 80% identity to the full length heavy chain sequences of each clone as disclosed herein in Tables 1-28 further comprising the three corresponding heavy chain complementarity determining regions (CDRs), CDR1, CDR2 and CDR3 sequences of the said corresponding clone; and the light chain variable domain comprising an amino acid sequence having at least about 80% identity to the full length light chain sequences of said clone as disclosed herein in Tables 1-28 further comprising the three corresponding light chain complementarity determining regions (CDRs), CDR1, CDR2 and CDR3 sequences of said corresponding clone.

[0011] For example, the present disclosure provides an antibody, or an antigen-binding fragment thereof capable of targeting the Globo-Series carbohydrate antigen, comprising: a.three heavy chain CDRs of SEQ ID NOs: 257, 258 and 259 or conservatively modified amino acid substitutions; and/or b. three light chain CDRs of SEQ ID NOs: 260, 261, and 262 or conservatively modified amino acid substitutions. In another embodiment, the antibody or antigen-binding fragment thereof of the above, comprising: the light chain variable domain comprising an amino acid sequence having at least about 80% identity to SEQ ID NO: 3 further comprising the three heavy chain complementarity determining

regions (CDRs), CDR1, CDR2 and CDR3 (SEQ ID Nos 257, 258, 259); and/or the light chain variable domain comprising an amino acid sequence having at least about 80% identity to SEQ ID NO: 4 further comprising the three light chain complementarity determining regions (CDRs), CDR1, CDR2 and CDR3 (SEQ ID Nos: 260, 261, 262). The same can be repeated for each of the clones recited in Tables 1-28 with the respective full length heavy chain and light chain sequences of each clone and their respective corresponding heavy chain and light chain CDRs.

[0012] In certain embodiments, the antibody or antigen-binding fragment thereof is selected from: (a) a whole immunoglobulin molecule; (b) an scFv; (c) a Fab fragment; (d) an $F(ab')_2$; or (e) a disulfide linked Fv.

[0013] In certain embodiments, the antibody is an IgG or IgM.

[0014] In one aspect, the present disclosure provides a pharmaceutical composition, comprising:

an antibody or an antigen-binding fragment thereof; and at least one pharmaceutically acceptable carrier.

[0015] In certain embodiments, the pharmaceutical composition further comprising at least one additional therapeutic agent.

[0016] In one aspect, the present disclosure provides a method for inhibiting the proliferation of cancer cells, comprising the administering of an effective amount of an exemplary pharmaceutical composition to a subject in need thereof, wherein the proliferation of cancer cells is inhibited and/or decreased.

[0017] In certain embodiments, the present disclosure provides a method of treating cancer in a subject, the method comprising administering to a subject in need thereof an effective amount of the exemplary human antibody described herein.

[0018] In certain embodiments, the cancer is selected from the group consisting of sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophageal cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervical cancer, endometrial

cancer, ovarian cancer, testicular cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer.

[0019] In one aspect, the present disclosure provides a method for staging cancer in a subject, comprising:

(a) applying one or more antibodies that detect expression of Globo series antigens to a cell or tissue sample obtained from the subject;

(b) assaying the binding of the one or more antibodies to the cell or the tissue sample;

(c) comparing the binding with a normal control to determine the presence of the cancer in the subject; and

(d) categorizing disease progression stage based on relative levels of corresponding abtibody binding compared to normal baseline index.

[0020] In one aspect, the present disclosure provides a method for inhibiting the proliferation of cancer cells, comprising the administering of an effective amount of an pharmaceutical composition comprising an antibody or an antigen-binding fragment thereof targeting Globo-series carbohydrate antigens to a subject in need thereof, wherein the proliferation of cancer cells is inhibited. In one embodiment, the subject is human.

[0021] In one aspect, the present disclosure provides a method of treating cancer in a subject, the method comprising administering to the subject in need thereof an effective amount of the antibody or an antigen-binding fragment thereof targeting Globo-series carbohydrate antigens.

[0022] In one embodiment, the cancer is selected from the group consisting of sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervix cancer, endometrial cancer, ovarian cancer, testical cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer. In one embodiment, the subject is human.

[0023] In one aspect, the present disclosure provides a method for cancer diagnosis in a subject, comprising:

(a) Applying one or more antibodies or binding fragments as disclosed herein that detect expression of a panel of markers to a cell or sample obtained from the subject;

(b) Assaying the binding of the one or more antibodies to the cell or the sample; and

(c) Comparing the binding with a normal control to determine the presence of the cancer in the subject.

[0024] In one embodiment, the markers consisting of Globo-H, SSEA-3 or SSEA-4.

[0025] In one embodiment, the cancer is selected from the group consisting of sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervix cancer, endometrial cancer, ovarian cancer, testical cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer.

[0026] In one embodjment, the cell is cancer stem cell.

[0027] In another embodiment, the sample consists serum, blood, plasma, cells, cell medium, saliva, urine, lymph node fluid, tumor biopsy or tissue culture. In one embosdiment, the subject is human.

[0028] In one aspect, the present disclosure provides a method of imaging a subject comprising:

(a) Administering an effective amount of an antibody or an antigen-binding fragment thereof as disclosed herein wherein the antibody or an antigen-binding fragment is conjugated to an imaging agent; and (b) Detecting the imaging agent in the subject.

[0029] In one embodiment, the imaging agent is a fluorophore, a dye, an MRI contrast agent or a radionuclide.

[0030] In one embodiment, the subject has a cancer, the method further defined as a method of detecting a cancer metastasis. In one embodiment, the subject is human.

[0031] In one aspect, the present disclosure provides a method of isolating an antibody, or an antigen-binding fragment in a subject, comprising:

(a) Administering to the subject a therapeutically effective dose of Globo series antigens vaccine and a pharmaceutically acceptable carrier:

(b) Collecting a sample from the subject;

(c) Isolating B cells from the sample; and

(d) Cultivating and screening the B cells which bind to the Globo series antigens.

[0032] In one embodiment, the Globo series antigens comprising Globo-H, SSEA-3 or SSEA-4. In one embodiment, the subject is human.

[0033] In one embodiment, the sample consists serum, blood, plasma, cells, cell medium, lymph node fluid, tumor biopsy or tissue culture.

[0034] In one aspect, the present disclosure provides an antibody-drug conjugate (ADC) comprising a drug conjugated to an antibody or an antigen-binding fragment that binds Globo series antigens, wherein VH selected from SEQ ID No: 3, SEQ ID No: 7, SEQ ID No: 11, SEQ ID No: 15, SEQ ID No: 19, SEQ ID No: 23, SEQ ID No: 27, SEQ ID No: 31, SEQ ID No: 35, SEQ ID No: 39, SEQ ID No: 43, SEQ ID No: 47, SEQ ID No: 51, SEQ ID No: 55, , SEQ ID No: 59, SEQ ID No: 63, SEQ ID No: 67, SEQ ID No: 71, SEQ ID No: 75, SEQ ID No: 79, SEQ ID No: 83, SEQ ID No: 87, SEQ ID No: 91, SEQ ID No: 95, SEQ ID No: 99, SEQ ID No: 103, or SEQ ID No: 107 and VL selected from SEQ ID No: 4, SEQ ID No: 8, SEQ ID No: 12, SEQ ID No: 16, SEQ ID No: 20, SEQ ID No: 24, SEQ ID No: 28, SEQ ID No: 32, SEQ ID No: 36, SEQ ID No: 40, SEQ ID No: 44, SEQ ID No: 48, SEQ ID No: 52, SEQ ID No: 56, SEQ ID No: 60, SEQ ID No: 64, SEQ ID No: 68, SEQ ID No: 72, SEQ ID No: 76, SEQ ID No: 80, SEQ ID No: 84, SEQ ID No: 88, SEQ ID No: 92, SEQ ID No: 96, SEQ ID No: 100, SEQ ID No: 104, or SEQ ID No: 108.; and wherein the drug is covalently conjugated to the antibody or the antigen-binding fragment by a linker.

[0035] In one embodiment, the Globo series antigens comprising Globo-H, SSEA-3 or SSEA-4.

[0036] In one embodiment, the linker comprising a *p*-nitrophenyl linker, a 4-(4-N-maleimidomethyl) cyclohexane-1-carboxyl hydrazide (MMCCH) linker, a maleimidocaproyl (MC) linker or a maleimidomethyl cyclohexane-1-carboxylate (MCC) linker. In one embodiment, the drug is a chemical compound or a biological agent. In one embodiment, the drug is an anti-proliferative agent.

[0037] In one embodiment, the anti-proliferative agent is selected from cyclophosphamide, opiate, granulocyte colony-stimulating factor (GCSF), estrogen inhibitors (tamoxifen or Fareston), aromatase inhibitors (Arimidex, Aromasin or Femara), pituitary downregulators (Zoladex or Lupron), Novaldex (tamoxifen selective estrogen-receptor modulator), Evista (rolaxifene), Faslodex (estrogen receptor down-regulator), anticoagulant (Refludan), enzyme (Elitek), Hematopoietic growth factor, anti-neoplastic Agent (antimetabolites, miscellaneous cytotoxic agents, vinca alkaloid, Epipodophyllotoxins, Alkylating agents, Taxanes, Antitumor antibiotics, Camptothecins, Nitrosoureas), HER1/EGFR tyrosine kinase inhibitor (Tarceva), VEGF protein inhibitor (Avastin), HER-2/ErbB2 inhibitor (Tyverb/Tykerb), Interferon, Interleukin, Monoclonal antibody, or Glucocorticoid steroid.

[0038] In one embodiment, the anti-proliferative agent is selected from erlotinib (TARCEVA); docetaxel (TAXOTERE); gemcitabine (GEMZAR); cisplatin; carboplatin; paclitaxel (TAXOL); trastuzumab (HERCEPTIN); temozolomide (TEMODAL); tamoxifen (NOLVADEX, ISTUBAL, VALODEX); doxorubicin (ADRIAMYCIN); oxaliplatin (ELOXATIN); bortezomib (VELCADE); sutent (SUNITINIB); letrozole (FEMARA); imatinib mesylate (GLEEVEC); MEK inhibitor (Exelixis); fulvestrant (FASLODEX); leucovorin (folinic acid); rapamycin (RAPAMUNE); lapatinib (TYKERB); lonafarnib (SARASAR); sorafenib (NEXAVAR); gefitinib (IRESSA); irinotecan (CAMPTOSAR); tipifarnib (ZARNESTRA); ABRAXANE (Cremophor-free); paclitaxel; vandetanib (ZACTIMA); chloranmbucil; temsirolimus (TORISEL); pazopanib; canfosfamide (TELCYTA); thiotepa; cyclosphosphamide (CYTOXAN, NEOSAR); 5-fluorouracil (5-FU); vinorelbine (NAVELBINE); novantrone; teniposide; edatrexate; daunomycin; aminopterin; capecitabine (XELODA); ibandronate; topoisomerase inhibitor RFS 2000; -difluoromethylornithine (DMFO); tamoxifen (NOLVADEX); raloxifene; droloxifene, 4-hydroxytamoxifen; trioxifene; keoxifene; onapristone; FARESTON (toremifine citrate); 4(5)-imidazoles; aminoglutethimide; MEGASE (megestrol acetate); AROMASIN (exemestane);

formestanie; fadrozole; RIVISOR® (vorozole); FEMARA (letrozole); ARIMIDEX (anastrozole); flutamide; nilutamide; bicalutamide; leuprolide; goserelin; troxacitabine (α-1,3-dioxolane nucleoside cytosine analog); lipid kinase inhibitor; oblimersen (GENASENSE); ANGIOZYME; ALLOVECTIN; LEUVECTIN; VAXID; PROLEUKIN; LURTOTECAN; ABARELIX; bevacizumab (AVASTIN); alemtuzumab (Campath); bevacizumab (AVASTIN); cetuximab (ERBITUX); panitumumab (VECTIBIX); rituximab (RITUXAN); pertuzumab (OMNITARG); trastuzumab (HERCEPTIN); tositumomab (Bexxar, Corixia); gemtuzumab; or ozogamicin (MYLOTARG).

[0039] In one aspect, the present disclosure provides a method of treating cancer in a subject, the method comprising administering to the subject in need thereof an effective amount of the ADC as disclosed herein.

[0040] In one embodiment, the cancer is selected from the group consisting of sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervix cancer, endometrial cancer, ovarian cancer, testical cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer. In one embodiment, the subject is human.

[0041] The details of one or more embodiments of the invention are set forth in the description below. Other features or advantages of the present invention will be apparent from the following drawings and detailed description of several embodiments, and also from the appending claims.

BRIEF DESCRIPTION OF THE FIGURES

[0042] A more complete understanding of the invention may be obtained by reference to the accompanying drawings, when considered in conjunction with the subsequent detailed description. The embodiments illustrated in the drawings are intended only to exemplify the invention and should not be construed as limiting the invention to the illustrated embodiments.

[0043] **Figure 1** shows the binding efficacy characterization between different human antibody clones by titration ELISA. **Figure 1A** uses Globo H-ceramide and **Figure 1B** uses Globo H-lipid as the coating antigens.

[0044] **Figure 2** shows the binding efficacy characterization between different human antibody clones by titration ELISA. **Figure 2A** uses SSEA-3-ceramide and **Figure 2B** uses SSEA-3-lipid as the coating antigens.

[0045] **Figure 3** shows the binding efficacy characterization between different human antibody clones by titration ELISA. **Figure 3A** uses SSEA-4-ceramide and **Figure 3B** uses SSEA-4-lipid as the coating antigens.

DETAILED DESCRIPTION OF THE INVENTION

[0046] Accordingly, antibody methods and compositions directed to the markers for use in diagnosing and treating a broad spectrum of cancers are provided. Anti-Globo series antigens human antibodies were developed and disclosed herein. Methods of use include, without limitation, cancer therapies and diagnostics. The antibodies described herein can bind to a broad spectrum of Globo series antigens-expressing cancer cells, thereby facilitating cancer diagnosis and treatment. Cells that can be targeted by the antibodies include carcinomas, such as those in skin, blood, lymph node, brain, lung, breast, mouse, esophagus, stomach, liver, bile duct, pancreas, colon, kidney, cervix, ovary, prostate cancer, etc.

Definitions

[0047] The practice of the present invention will employ, unless otherwise indicated, conventional techniques of molecular biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. See, for example, Molecular Cloning A Laboratory Manual, 2nd Ed., ed. by Sambrook, Fritsch and Maniatis (Cold Spring Harbor Laboratory Press, 1989); DNA Cloning, Volumes I and II (D. N. Glover ed., 1985); Culture Of Animal Cells (R. I. Freshney, Alan R. Liss, Inc., 1987); Immobilized Cells And Enzymes (IRL Press, 1986); B. Perbal, A Practical Guide To Molecular Cloning (1984); the treatise, Methods In Enzymology (Academic Press, Inc., N.Y.); Gene Transfer Vectors For Mammalian Cells (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); Methods In Enzymology, Vols. 154 and 155 (Wu *et al.* eds.), Immunochemical Methods In Cell And Molecular Biology (Mayer

and Walker, eds., Academic Press, London, 1987); Antibodies: A Laboratory Manual, by Harlow and Lane s (Cold Spring Harbor Laboratory Press, 1988); and Handbook Of Experimental Immunology, Volumes I-IV (D. M. Weir and C. C. Blackwell, eds., 1986).

[0048] As used herein, the term "glycan" refers to a polysaccharide, or oligosaccharide. Glycan is also used herein to refer to the carbohydrate portion of a glycoconjugate, such as a glycoprotein, glycolipid, glycopeptide, glycoproteome, peptidoglycan, lipopolysaccharide or a proteoglycan. Glycans usually consist solely of O-glycosidic linkages between monosaccharides. For example, cellulose is a glycan (or more specifically a glucan) composed of ß-1,4-linked D-glucose, and chitin is a glycan composed of ß-1,4-linked N-acetyl-D-glucosamine. Glycans can be homo or heteropolymers of monosaccharide residues, and can be linear or branched. Glycans can be found attached to proteins as in glycoproteins and proteoglycans. They are generally found on the exterior surface of cells. O- and N-linked glycans are very common in eukaryotes but may also be found, although less commonly, in prokaryotes. N-Linked glycans are found attached to the R-group nitrogen (N) of asparagine in the sequon. The sequon is a Asn-X-Ser or Asn-X-Thr sequence, where X is any amino acid except praline.

[0049] As used herein, the term "antigen" is defined as any substance capable of eliciting an immune response.

[0050] As used herein, the term "immunogenicity" refers to the ability of an immunogen, antigen, or vaccine to stimulate an immune response.

[0051] As used herein, the term "epitope" is defined as the parts of an antigen molecule which contact the antigen binding site of an antibody or a T cell receptor.

[0052] As used herein, the term "vaccine" refers to a preparation that contains an antigen, consisting of whole disease-causing organisms (killed or weakened) or components of such organisms, such as proteins, peptides, or polysaccharides, that is used to confer immunity against the disease that the organisms cause. Vaccine preparations can be natural, synthetic or derived by recombinant DNA technology.

[0053] As used herein, the term "antigen specific" refers to a property of a cell population such that supply of a particular antigen, or a fragment of the antigen, results in specific cell proliferation.

[0054] As used herein, the term "specifically binding," refers to the interaction between binding pairs (e.g., an antibody and an antigen). In various instances, specifically binding can be embodied by an affinity constant of about 10^{-6} moles/liter, about 10^{-7} moles/liter, or about 10^{-8} moles/liter, or less.

[0055] The phrase “substantially similar,” “substantially the same”, “equivalent”, or “substantially equivalent”, as used herein, denotes a sufficiently high degree of similarity between two numeric values (for example, one associated with a molecule and the other associated with a reference/comparator molecule) such that one of skill in the art would consider the difference between the two values to be of little or no biological and/or statistical significance within the context of the biological characteristic measured by said values (e.g., Kd values, anti-viral effects, etc.). The difference between said two values is, for example, less than about 50%, less than about 40%, less than about 30%, less than about 20%, and/or less than about 10% as a function of the value for the reference/comparator molecule.

[0056] The phrase “substantially reduced,” or “substantially different”, as used herein, denotes a sufficiently high degree of difference between two numeric values (generally one associated with a molecule and the other associated with a reference/comparator molecule) such that one of skill in the art would consider the difference between the two values to be of statistical significance within the context of the biological characteristic measured by said values (e.g., Kd values). The difference between said two values is, for example, greater than about 10%, greater than about 20%, greater than about 30%, greater than about 40%, and/or greater than about 50% as a function of the value for the reference/comparator molecule.

[0057] “Binding affinity” generally refers to the strength of the sum total of noncovalent interactions between a single binding site of a molecule (e.g., an antibody) 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 and antigen). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (Kd). Affinity can be measured by common methods known in the art, including those described herein. Low-affinity antibodies generally bind antigen slowly and tend to dissociate readily, whereas high-affinity antibodies generally bind antigen faster and tend to remain bound longer. A variety of methods of measuring binding affinity are known in the art, any of which can be used for purposes of the present invention. Specific illustrative embodiments are described in the following.

[0058] The term "vector," as used herein, is intended to refer to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments may be ligated. Another type of vector is a phage vector. Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) can be integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "recombinant expression vectors" (or simply, "recombinant vectors"). In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" may be used interchangeably as the plasmid is the most commonly used form of vector.

[0059] "Polynucleotide," or "nucleic acid," as used interchangeably herein, refer to polymers of nucleotides of any length, and include DNA and RNA. The nucleotides can be deoxyribonucleotides, ribonucleotides, modified nucleotides or bases, and/or their analogs, or any substrate that can be incorporated into a polymer by DNA or RNA polymerase, or by a synthetic reaction. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and their analogs. If present, modification to the nucleotide structure may be imparted before or after assembly of the polymer. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after synthesis, such as by conjugation with a label. Other types of modifications include, for example, "caps," substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as, for example, those with uncharged linkages (e.g., methyl phosphonates, phosphotriesters, phosphoamidates, carbamates, etc.) and with charged linkages (e.g., phosphorothioates, phosphorodithioates, etc.), those containing pendant moieties, such as, for example, proteins (e.g., nucleases, toxins, antibodies, signal peptides, ply-L-lysine, etc.), those with intercalators (e.g., acridine, psoralen, etc.), those containing chelators (e.g., metals, radioactive metals, boron, oxidative metals, etc.), those containing alkylators, those with modified linkages (e.g., alpha anomeric nucleic acids, etc.), as well as unmodified forms of the polynucleotides(s). Further, any of the hydroxyl groups

ordinarily present in the sugars may be replaced, for example, by phosphonate groups, phosphate groups, protected by standard protecting groups, or activated to prepare additional linkages to additional nucleotides, or may be conjugated to solid or semi-solid supports. The 5' and 3' terminal OH can be phosphorylated or substituted with amines or organic capping group moieties of from 1 to 20 carbon atoms. Other hydroxyls may also be derivatized to standard protecting groups. Polynucleotides can also contain analogous forms of ribose or deoxyribose sugars that are generally known in the art, including, for example, 2'-O-methyl-, 2'-O-allyl, 2'-fluoro- or 2'-azido-ribose, carbocyclic sugar analogs, α-anomeric sugars, epimeric sugars such as arabinose, xyloses or lyxoses, pyranose sugars, furanose sugars, sedoheptuloses, acyclic analogs and basic nucleoside analogs such as methyl riboside. One or more phosphodiester linkages may be replaced by alternative linking groups. These alternative linking groups include, but are not limited to, embodiments wherein phosphate is replaced by P(O)S ("thioate"), P(S)S ("dithioate"), (O)NR_2 ("amidate"), P(O)R, P(O)OR', CO or CH_2 ("formacetal"), in which each R or R' is independently H or substituted or unsubstituted alkyl (1-20C) optionally containing an ether (—O—) linkage, aryl, alkenyl, cycloalkyl, cycloalkenyl or araldyl. Not all linkages in a polynucleotide need be identical. The preceding description applies to all polynucleotides referred to herein, including RNA and DNA.

[0060] "Oligonucleotide," as used herein, generally refers to short, generally single-stranded, generally synthetic polynucleotides that are generally, but not necessarily, less than about 200 nucleotides in length. The terms "oligonucleotide" and "polynucleotide" are not mutually exclusive. The description above for polynucleotides is equally and fully applicable to oligonucleotides.

[0061] "Antibodies" (Abs) and "immunoglobulins" (Igs) are glycoproteins having the same structural characteristics. While antibodies exhibit binding specificity to a specific antigen, immunoglobulins include both antibodies and other antibody-like molecules which generally lack antigen specificity. Polypeptides of the latter kind are, for example, produced at low levels by the lymph system and at increased levels by myelomas.

[0062] The terms "antibody" and "immunoglobulin" are used interchangeably in the broadest sense and include monoclonal antibodies (e.g., full length or intact monoclonal antibodies), polyclonal antibodies, monovalent, multivalent antibodies, multispecific

antibodies (e.g., bispecific antibodies so long as they exhibit the desired biological activity) and may also include certain antibody fragments (as described in greater detail herein). An antibody can be chimeric, human and/or affinity matured.

[0063] The "variable region" or "variable domain" of an antibody refers to the amino-terminal domains of heavy or light chain of the antibody. These domains are generally the most variable parts of an antibody and contain the antigen-binding sites.

[0064] The term "variable" refers to the fact that certain portions of the variable domains differ extensively in sequence among antibodies and are used in the binding and specificity of each particular antibody for its particular antigen. However, the variability is not evenly distributed throughout the variable domains of antibodies. It is concentrated in three segments called complementarity-determining regions (CDRs) or hypervariable regions both in the light-chain and the heavy-chain variable domains. The more highly conserved portions of variable domains are called the framework (FR). The variable domains of native heavy and light chains each comprise four FR regions, largely adopting a beta-sheet configuration, connected by three CDRs, which form loops connecting, and in some cases forming part of, the beta-sheet structure. The CDRs in each chain are held together in close proximity by the FR regions and, with the CDRs from the other chain, contribute to the formation of the antigen-binding site of antibodies (see Kabat *et al.*, Sequences of Proteins of Immunological Interest, Fifth Edition, National Institute of Health, Bethesda, Md. (1991)). The constant domains are not involved directly in binding an antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody-dependent cellular toxicity.

[0065] Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, whose name reflects its ability to crystallize readily. Pepsin treatment yields an $F(ab')_2$ fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

[0066] "Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. In a two-chain Fv species, this region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. In a single-chain Fv species, one heavy- and one light-chain variable domain can be covalently linked by

a flexible peptide linker such that the light and heavy chains can associate in a "dimeric" structure analogous to that in a two-chain Fv species. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the VH-VL dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

[0067] The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab′ fragments differ from Fab fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab′-SH is the designation herein for Fab′ in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab′ fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

[0068] The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa (κ) and lambda (λ), based on the amino acid sequences of their constant domains.

[0069] Depending on the amino acid sequences of the constant domains of their heavy chains, antibodies (immunoglobulins) can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, and IgA_2. The heavy chain constant domains that correspond to the different classes of immunoglobulins are called α, δ, ε, γ, and μ, respectively. The subunit structures and three-dimensional configurations of different classes of immunoglobulins are well known and described generally in, for example, Abbas *et al.* Cellular and Mol. Immunology, 4th ed. (2000). An antibody may be part of a larger fusion molecule, formed by covalent or non-covalent association of the antibody with one or more other proteins or peptides.

[0070] The terms "full length antibody," "intact antibody" and "whole antibody" are used herein interchangeably, to refer to an antibody in its substantially intact form, not

antibody fragments as defined below. The terms particularly refer to an antibody with heavy chains that contain the Fc region.

[0071] "Antibody fragments" comprise only a portion of an intact antibody, wherein the portion retains at least one, and as many as most or all, of the functions normally associated with that portion when present in an intact antibody. In one embodiment, an antibody fragment comprises an antigen binding site of the intact antibody and thus retains the ability to bind antigen. In another embodiment, an antibody fragment, for example one that comprises the Fc region, retains at least one of the biological functions normally associated with the Fc region when present in an intact antibody, such as FcRn binding, antibody half life modulation, ADCC function and complement binding. In one embodiment, an antibody fragment is a monovalent antibody that has an in vivo half life substantially similar to an intact antibody. For example, such an antibody fragment may comprise an antigen binding arm linked to an Fc sequence capable of conferring in vivo stability to the fragment.

[0072] The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Thus, the modifier "monoclonal" indicates the character of the antibody as not being a mixture of discrete antibodies. Such monoclonal antibody typically includes an antibody comprising a polypeptide sequence that binds a target, wherein the target-binding polypeptide sequence was obtained by a process that includes the selection of a single target binding polypeptide sequence from a plurality of polypeptide sequences. For example, the selection process can be the selection of a unique clone from a plurality of clones, such as a pool of hybridoma clones, phage clones or recombinant DNA clones. In contrast to polyclonal antibody preparations which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody of a monoclonal antibody preparation is directed against a single determinant on an antigen. In addition to their specificity, the monoclonal antibody preparations are advantageous in that they are typically uncontaminated by other immunoglobulins. The modifier "monoclonal" indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies to be used in accordance with the

present invention may be made by a variety of techniques, including, for example, the hybridoma method (e.g., Kohler *et al.*, Nature, 256: 495 (1975); Harlow *et al.*, Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling *et al.*, in: Monoclonal Antibodies and T-Cell hybridomas 563-681 (Elsevier, N.Y., 1981)), recombinant DNA methods (see, e.g., U.S. Pat. No. 4,816,567), phage display technologies (See, e.g., Clackson *et al.*, Nature, 352: 624-628 (1991); Marks *et al.*, J. Mol. Biol. 222: 581-597 (1992); Sidhu *et al.*, J. Mol. Biol. 338(2): 299-310 (2004); Lee *et al.*, J. Mol. Biol. 340(5): 1073-1093 (2004); Fellouse, Proc. Natl. Acad. Sci. USA 101(34): 12467-12472 (2004); and Lee *et al.*, J. Immunol. Methods 284(1-2): 119-132 (2004), and technologies for producing human or human-like antibodies in animals that have parts or all of the human immunoglobulin loci or genes encoding human immunoglobulin sequences (see, e.g., WO98/24893; WO96/34096; WO96/33735; WO91/10741; Jakobovits *et al.*, Proc. Natl. Acad. Sci. USA 90: 2551 (1993); Jakobovits *et al.*, Nature 362: 255-258 (1993); Bruggemann *et al.*, Year in Immunol. 7:33 (1993); U.S. Pat. Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016; Marks *et al.*, Bio. Technology 10: 779-783 (1992); Lonberg *et al.*, Nature 368: 856-859 (1994); Morrison, Nature 368: 812-813 (1994); Fishwild *et al.*, Nature Biotechnol. 14: 845-851 (1996); Neuberger, Nature Biotechnol. 14: 826 (1996) and Lonberg and Huszar, Intern. Rev. Immunol. 13: 65-93 (1995).

[0073] The monoclonal antibodies herein specifically include "chimeric" antibodies in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (U.S. Pat. No. 4,816,567; and Morrison *et al.*, Proc. Natl. Acad. Sci. USA 81:6851-6855 (1984)).

[0074] Antibodies of the present invention can also include chimerized monoclonal antibodies generated from antibodies of the present invention.

[0075] The antibodies can be full-length or can comprise a fragment (or fragments) of the antibody having an antigen-binding portion, including, but not limited to, Fab, $F(ab')_2$, Fab', F(ab)', Fv, single chain Fv (scFv), bivalent scFv (bi-scFv), trivalent scFv (tri-scFv), Fd, dAb fragment (e.g., Ward *et al,* Nature, 341 :544-546 (1989)), an CDR, diabodies, triabodies,

tetrabodies, linear antibodies, single-chain antibody molecules, and multispecific antibodies formed from antibody fragments. Single chain antibodies produced by joining antibody fragments using recombinant methods, or a synthetic linker, are also encompassed by the present invention. Bird *et al.* Science, 1988, 242:423-426. Huston *et al*, Proc. Natl. Acad. Sci. USA, 1988, 85:5879-5883.

[0076] The antibodies or antigen-binding portions thereof of the present invention may be monospecific, bi-specific or multispecific.

[0077] All antibody isotypes are encompassed by the present invention, including IgG (e.g., IgG_1, IgG_2, IgG_3, IgG_4), IgM, IgA (IgA_1, IgA_2), IgD or IgE (all classes and subclasses are encompassed by the present invention). The antibodies or antigen-binding portions thereof may be mammalian (e.g., mouse, human) antibodies or antigen-binding portions thereof. The light chains of the antibody may be of kappa or lambda type.

[0078] Thus, anti-cancer antibodies of the present invention include in combination with a heavy chain or light chain variable region, a heavy chain or light chain constant region, a framework region, or any portion thereof, of non-murine origin, preferably of human origin, which can be incorporated into an antibody of the present invention.

[0079] Antibodies with a variable heavy chain region and a variable light chain region that are at least about 70%, at least about 75%, at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about 86%o, at least about 87%>, at least about 88%>, at least about 89%>, at least about 90%>, at least about 91 >, at least about 92%>, at least about 93%>, at least about 94%>, at least about 95%), at least about 96%>, at least about 97%>, at least about 98%>, at least about 99%> or about 100% homologous to the variable heavy chain region and variable light chain region of the antibody produced by the reference antibody, and can also bind to a carbohydrate antigen (e.g. Globo H, SSEA-3 or SSEA-4). Homology can be present at either the amino acid or nucleotide sequence level.

[0080] As used herein, substantially "homology" and/or "homologous sequences" of proteins of the invention include, without limitation, conservative amino acid substitutions, or for example alterations that do not effect the VH, VL or CDR domains of the antibodies, e.g., include scFv antibodies where a different linker sequence is used or antibodies where tag sequences or other components are added that do not contribute to the binding of antigen, or

alterations to convert one type or format of antibody molecule or fragment to another type or format of antibody molecule or fragment (e.g., conversion from Fab to scFv or vice versa), or the conversion of an antibody molecule to a particular class or subclass of antibody molecule (e.g., the conversion of an antibody molecule to IgG or a subclass thereof, e.g., IgG1 or IgG3).

[0081] A "conservative amino acid substitution", as used herein, is one in which the amino acid residue is replaced with another amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art, including basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., glycine, cysteine, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

[0082] Homology may be assessed by any convenient method. However, for determining the degree of homology between sequences, computer programs that make multiple alignments of sequences are useful, for instance Clustal W (Thompson et al., 1994). If desired, the Clustal W algorithm can be used together with BLOSUM 62 scoring matrix (Henikoff and Henikoff, 1992) and a gap opening penalty of 10 and gap extension penalty of 0.1, so that the highest order match is obtained between two sequences wherein at least 50% of the total length of one of the sequences is involved in the alignment. Other methods that may be used to align sequences are the alignment method of Needleman and Wunsch (1970), as revised by Smith and Waterman (1981) so that the highest order match is obtained between the two sequences and the number of identical amino acids is determined between the two sequences. Other methods to calculate the percentage identity between two amino acid sequences are generally art recognized and include, for example, those described by Carillo and Lipton (1988) and those described in Computational Molecular Biology, Lesk, e.d. Oxford University Press, New York, 1988, Biocomputing: Informatics and Genomics Projects.

[0083] Generally, computer programs can be employed for such calculations. Programs that compare and align pairs of sequences, like ALIGN (Myers and Miller, 1988), FASTA (Pearson and Lipman, 1988; Pearson, 1990) and gapped BLAST (Altschul et al., 1997),

BLASTP, BLASTN, or GCG (Devereux et al., 1984) are also useful for this purpose. Furthermore, the Dali server at the European Bioinformatics institute offers structure-based alignments of protein sequences (Holm, 1993; 1995; 1998).

[0084] The antibodies or antigen-binding portions may be peptides. Such peptides can include variants, analogs, orthologs, homologs and derivatives of peptides, that exhibit a biological activity, e.g., binding of a carbohydrate antigen. The peptides may contain one or more analogs of an amino acid (including, for example, non-naturally occurring amino acids, amino acids which only occur naturally in an unrelated biological system, modified amino acids from mammalian systems etc.), peptides with substituted linkages, as well as other modifications known in the art.

[0085] Also within the scope of the invention are antibodies or antigen-binding portions thereof in which specific amino acids have been substituted, deleted or added. In an exemplary embodiment, these alternations do not have a substantial effect on the peptide's biological properties such as binding affinity. In another exemplary embodiment, antibodies may have amino acid substitutions in the framework region, such as to improve binding affinity of the antibody to the antigen. In yet another exermplary embodiment, a selected, small number of acceptor framework residues can be replaced by the corresponding donor amino acids. The donor framework can be a mature or germline human antibody framework sequence or a consensus sequence. Guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie *et al.*, Science, 247: 1306-1310 (1990). Cunningham *et al*, Science, 244: 1081-1085 (1989). Ausubel (ed.), Current Protocols in Molecular Biology, John Wiley and Sons, Inc. (1994). T. Maniatis, E. F. Fritsch and J. Sambrook, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor laboratory, Cold Spring Harbor, N.Y. (1989). Pearson, Methods Mol. Biol. 243:307-31 (1994). Gonnet *et al.*, Science 256: 1443-45 (1992).

[0086] The antibody, or antigen-binding portion thereof, can be derivatized or linked to another functional molecule. For example, an antibody can be functionally linked (by chemical coupling, genetic fusion, noncovalent interaction, etc.) to one or more other molecular entities, such as another antibody, a detectable agent, a cytotoxic agent, a pharmaceutical agent, a protein or peptide that can mediate association with another molecule (such as a streptavidin core region or a polyhistidine tag), amino acid linkers, signal sequences, immunogenic carriers, or ligands useful in protein purification, such as

glutathione-S-transferase, histidine tag, and staphylococcal protein A. One type of derivatized protein is produced by crosslinking two or more proteins (of the same type or of different types). Suitable crosslinkers include those that are heterobifunctional, having two distinct reactive groups separated by an appropriate spacer (e.g., m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (e.g., disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, 111. Useful detectable agents with which a protein can be derivatized (or labeled) include fluorescent compounds, various enzymes, prosthetic groups, luminescent materials, bioluminescent materials, and radioactive materials. Non-limiting, exemplary fluorescent detectable agents include fluorescein, fluorescein isothiocyanate, rhodamine, and, phycoerythrin. A protein or antibody can also be derivatized with detectable enzymes, such as alkaline phosphatase, horseradish peroxidase, beta-galactosidase, acetylcholinesterase, glucose oxidase and the like. A protein can also be derivatized with a prosthetic group (e.g., streptavidin/biotin and avidin/biotin).

[0087] Nucleic acids encoding a functionally active variant of the present antibody or antigen-binding portion thereof are also encompassed by the present invention. These nucleic acid molecules may hybridize with a nucleic acid encoding any of the present antibody or antigen-binding portion thereof under medium stringency, high stringency, or very high stringency conditions. Guidance for performing hybridization reactions can be found in Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. 6.3.1-6.3.6, 1989, which is incorporated herein by reference. Specific hybridization conditions referred to herein are as follows: 1) medium stringency hybridization conditions: 6 X SSC at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 60°C; 2) high stringency hybridization conditions: 6 X SSC at about 45°C, followed by one or more washes in 0.2XSSC, 0.1% SDS at 65°C; and 3) very high stringency hybridization conditions: 0.5 M sodium phosphate, 7% SDS at 65°C, followed by one or more washes at 0.2XSSC, 1% SDS at 65°C.

[0088] A nucleic acid encoding the present antibody or antigen-binding portion thereof may be introduced into an expression vector that can be expressed in a suitable expression system, followed by isolation or purification of the expressed antibody or antigen-binding portion thereof. Optionally, a nucleic acid encoding the present antibody or antigen-binding portion thereof can be translated in a cell-free translation system. U.S. Patent No. 4,816,567. Queen *et al*, Proc Natl Acad Sci USA, 86: 10029-10033 (1989).

[0089] The present antibodies or antigen-binding portions thereof can be produced by host cells transformed with DNA encoding light and heavy chains (or portions thereof) of a desired antibody. Antibodies can be isolated and purified from these culture supernatants and/or cells using standard techniques. For example, a host cell may be transformed with DNA encoding the light chain, the heavy chain, or both, of an antibody. Recombinant DNA technology may also be used to remove some or all of the DNA encoding either or both of the light and heavy chains that is not necessary for binding, e.g., the constant region.

[0090] As used herein, "substantially purified" or "substantially isolated" refers to a molecule (e.g. a compound) in a state that it is separated from substantially all other molecules normally associated with it in its native state. Preferably, a substantially purified molecule is the predominant species present in a preparation. Particularly, a substantially purified molecule may be greater than 60% free, preferably 75% free, or 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 97.5%, 98%, 98.5%, 99%, or 99.5% free, or any range between any two recited percentages free from the other molecules (exclusive of solvent) present in the natural mixture.

[0091] The present nuceic acids can be expressed in various suitable cells, including prokaryotic and eukaryotic cells, e.g., bacterial cells, (e.g., *E. coli*), yeast cells, plant cells, insect cells, and mammalian cells. A number of mammalian cell lines are known in the art and include immortalized cell lines available from the American Type Culture Collection (ATCC). Non-limiting examples of the cells include all cell lines of mammalian origin or mammalian-like characteristics, including but not limited to, parental cells, derivatives and/or engineered variants of monkey kidney cells (COS, e.g., COS-1, COS-7), HEK293, baby hamster kidney (BHK, e.g., BHK21), Chinese hamster ovary (CHO), NSO, PerC6, BSC-1, human hepatocellular carcinoma cells (e.g., Hep G2), SP2/0, HeLa, Madin-Darby bovine kidney (MDBK), myeloma and lymphoma cells. The engineered variants include, e.g., glycan profile modified and/or site-specific integration site derivatives.

[0092] The present invention also provides for cells comprising the nucleic acids described herein. The cells may be a hybridoma or transfectant.

[0093] Alternatively, the present antibody or antigen-binding portion thereof can be synthesized by solid phase procedures well known in the art. Solid Phase Peptide Synthesis: A Practical Approach by E. Atherton and R. C. Sheppard, published by IRL at Oxford

University Press (1989). Methods in Molecular Biology, Vol. 35: Peptide Synthesis Protocols (ed. M. W.Pennington and B. M. Dunn), chapter 7. Solid Phase Peptide Synthesis, 2nd Ed., Pierce Chemical Co., Rockford, IL (1984). G. Barany and R. B. Merrifield, The Peptides: Analysis, Synthesis, Biology, editors E. Gross and J. Meienhofer, Vol. 1 and Vol. 2, Academic Press, New York, (1980), pp. 3-254. M. Bodansky, Principles of Peptide Synthesis, Springer-Verlag, Berlin (1984).

[0094] The term "hypervariable region", "HVR", or "HV", when used herein refers to the regions of an antibody variable domain which are hypervariable in sequence and/or form structurally defined loops. Generally, antibodies comprise six hypervariable regions; three in the VH (H1, H2, H3), and three in the VL (L1, L2, L3). A number of hypervariable region delineations are in use and are encompassed herein. The Kabat Complementarity Determining Regions (CDRs) are based on sequence variability and are the most commonly used (Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)). Chothia refers instead to the location of the structural loops (Chothia and Lesk J. Mol. Biol. 196:901-917 (1987)).

[0095] "Framework" or "FW" residues are those variable domain residues other than the hypervariable region residues as herein defined.

[0096] The term "variable domain residue numbering as in Kabat" or "amino acid position numbering as in Kabat," and variations thereof, refers to the numbering system used for heavy chain variable domains or light chain variable domains of the compilation of antibodies in Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991). Using this numbering system, the actual linear amino acid sequence may contain fewer or additional amino acids corresponding to a shortening of, or insertion into, a FR or HVR of the variable domain. For example, a heavy chain variable domain may include a single amino acid insert (residue 52a according to Kabat) after residue 52 of H2 and inserted residues (e.g. residues 82a, 82b, and 82c, etc. according to Kabat) after heavy chain FR residue 82. The Kabat numbering of residues may be determined for a given antibody by alignment at regions of homology of the sequence of the antibody with a "standard" Kabat numbered sequence.

[0097] "Single-chain Fv" or "scFv" antibody fragments comprise the VH and VL domains of antibody, wherein these domains are present in a single polypeptide chain. Generally, the

scFv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the scFv to form the desired structure for antigen binding. For a review of scFv see Pluckthun, in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

[0098] The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (VH) connected to a light-chain variable domain (VL) in the same polypeptide chain (VH-VL). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO93/1161; and Hollinger *et al.*, Proc. Natl. Acad. Sci. USA 90: 6444-6448 (1993).

[0099] A "human antibody" is one which possesses an amino acid sequence which corresponds to that of an antibody produced by a human and/or has been made using any of the techniques for making human antibodies as disclosed herein.

[00100] An "affinity matured" antibody is one with one or more alterations in one or more HVRs thereof which result in an improvement in the affinity of the antibody for antigen, compared to a parent antibody which does not possess those alteration(s). In one embodiment, an affinity matured antibody has nanomolar or even picomolar affinities for the target antigen. Affinity matured antibodies are produced by procedures known in the art. Marks *et al.* Bio/Technology 10:779-783 (1992) describes affinity maturation by VH and VL domain shuffling. Random mutagenesis of CDR and/or framework residues is described by: Barbas *et al.* Proc Nat. Acad. Sci. USA 91:3809-3813 (1994); Schier *et al.* Gene 169:147-155 (1995); Yelton *et al.* J. Immunol. 155:1994-2004 (1995); Jackson *et al.*, J. Immunol. 154(7):3310-9 (1995); and Hawkins *et al*, J. Mol. Biol. 226:889-896 (1992).

[00101] A "blocking" antibody or an "antagonist" antibody is one which inhibits or reduces biological activity of the antigen it binds. Certain blocking antibodies or antagonist antibodies substantially or completely inhibit the biological activity of the antigen.

[00102] An "agonist antibody", as used herein, is an antibody which mimics at least one of the functional activities of a polypeptide of interest.

[00103] A "disorder" is any condition that would benefit from treatment with an antibody of the invention. This includes chronic and acute disorders or diseases including those pathological conditions which predispose the mammal to the disorder in question. Non-limiting examples of disorders to be treated herein include cancer.

[00104] The terms "cell proliferative disorder" and "proliferative disorder" refer to disorders that are associated with some degree of abnormal cell proliferation. In one embodiment, the cell proliferative disorder is cancer.

[00105] "Tumor" as used herein, refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues. The terms "cancer," "cancerous," "cell proliferative disorder," "proliferative disorder" and "tumor" are not mutually exclusive as referred to herein.

[00106] The terms "cancer" and "cancerous" refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth/proliferation. Examples of cancer include, but are not limited to, carcinoma, lymphoma (e.g., Hodgkin's and non-Hodgkin's lymphoma), blastoma, sarcoma, and leukemia. More particular examples of such cancers include squamous cell cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, leukemia and other lymphoproliferative disorders, and various types of head and neck cancer.

[00107] As used herein, "treatment" refers to clinical intervention in an attempt to alter the natural course of the individual or cell being treated, and can be performed either for prophylaxis or during the course of clinical pathology. "Treating" or "treating" is referred to herein as administration of a therapeutic composition to a subject with the purpose to cure, alleviate, relieve, remedy, prevent, or ameliorate a disorder, symptoms of the disorder, a disease state secondary to the disorder, or predisposition toward the disorder. Desirable effects of treatment include preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, preventing or decreasing inflammation and/or tissue/organ damage, decreasing the rate of

disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. In some embodiments, antibodies of the invention are used to delay development of a disease or disorder.

[00108] An "individual" or a "subject" is a vertebrate. In certain embodiments, the vertebrate is a mammal. Mammals include, but are not limited to, farm animals (such as cows), sport animals, pets (such as cats, dogs, and horses), primates, mice and rats. In certain embodiments, the vertebrate is a human.

[00109] "Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, horses, cats, cows, etc. In certain embodiments, the mammal is human.

[00110] An "effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic or prophylactic result.

[00111] A "therapeutically effective amount" of a substance/molecule of the invention may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the substance/molecule, to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effects of the substance/molecule are outweighed by the therapeutically beneficial effects. A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result. Typically but not necessarily, since a prophylactic dose is used in subjects prior to or at an earlier stage of disease, the prophylactically effective amount would be less than the therapeutically effective amount.

Antibodies Targeting Globo Series Antigens

[00112] One aspect of the present disclosure features the new antibody targeting the Globo series antigens (Globo H, SSEA-3, SSEA-4).

[00113] Cancers expressing Globo series antigens (SSEA-4, Globo H or SSEA-3) include, but are not limited to, sarcoma, skin cancer, leukemia, lymphoma, brain cancer, lung cancer, breast cancer, oral cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, pancreas cancer, colon cancer, kidney cancer, cervix cancer, ovary cancer and prostate cancer.

[00114] "SSEA-4 moiety" is defined herein to be a glycan (i.e., a molecule containing a sugar moiety) that is SSEA-4 or a fragment or analog thereof. SSEA-4 is a glycan containing the hexasaccharide epitope (Neu5Acα2→ 3Galβ1→ 3GalNAcβ1→ 3Galα1→ 4Galβ1→ 4Glcβ1), and optionally, a non-sugar moiety. Its fragment is a glycan containing a fragment of the hexasaccharide epitope and, if applicable, the non-sugar moiety.

[00115] "Globo H moiety" is defined herein to be a glycan (i.e., a molecule containing a sugar moiety) that is Globo H or a fragment or analog thereof. Globo H is a glycan containing the hexasaccharide epitope (Fucα1→2 Galβ1→3 GalNAcβ1→3 Galα1→4 Galβ1→4 Glc), and optionally, a non-sugar moiety. Its fragment is a glycan containing a fragment of the hexasaccharide epitope and, if applicable, the non-sugar moiety.

[00116] "SSEA-3 moiety" is defined herein to be a glycan (i.e., a molecule containing a sugar moiety) that is SSEA-3 or a fragment or analog thereof. SSEA-3 is a glycan containing the pentasaccharide epitope (Galβ1→ 3GalNAcβ1→ 3Galα1→ 4Galβ1→ 4Glcβ1), and optionally, a non-sugar moiety. Its fragment is a glycan containing a fragment of the hexasaccharide epitope and, if applicable, the non-sugar moiety.

[00117] Exemplars and their amino acid and nucleic acid structures/sequences are provided below:

Table 1. Amino Acid and Nucleotide Sequences of Human Antibody 2-8M

SEQ ID NO	DESCRIPTION	SEQUENCE
1	2-8M VH nucleotide sequence	CAGCTGCAGTTGCAGGAGTCGGGCCCAGGACTGGT GAAGCCTGCGGAGACCCTGTCCCTCACCTGCTCTGT CTCCGGTGGCTACGTCACCATCAAGGATAATTATTG GGTCTGGTTCCGCCAGTCCCCAGGGAAGGAGCCGG AGTGGATTGGGAGTATGTCTTATAGTGGGAATGCCT ACTACAACCCGTCCCTCAAGAGTCGAGCCAGCATTT CCATAGACCGGTACAGGAACCAGTTCTCCCTGAGGT TGACTTCTGTGACCGCCGCAGACACGTCCATGTACT ACTGTGCGAGACGATCAGCAGCAGCTGGTGGGGGG AATGAATGGTTCGACCCCTGGGGCCAAGGAGCCCTT

		GTCACCGTCTCCTCA
2	2-8M VL nucleotide sequence	CAGTCTGCTTTGACGCAGCCGCCCTCAGTGTCTGCG GCCCCAGGACGGAAGGTCGACATCTCCTGCTCTGGA AGCACCTTCAATATTGGGAACAATTATGTGTCGTGG TACCGGCAGTTCCCAGGAACAGCCCCCAAACTCCTC ATTTATGACAATGATAAGCGACCCTCAGGCATTCCT GACCGATTCTCTGGCTCCAGGTTCGGCACGTCAGCC ACCCTGGGCATCACCGGACTCCAGACTGACGACGA GGCCATTTATTACTGCGCAACATGGGATAACAGACT GGATGCTGTGGTTTTCGGCGGGGGGACCGAGTTGAT CGTCCTT
3	2-8M VH amino acid sequence	QLQLQESGPGLVKPAETLSLTCSVSGGYVTIKDNYWV WFRQSPGKEPEWIGSMSYSGNAYYNPSLKSRASISIDR YRNQFSLRLTSVTAADTSMYYCARRSAAAGGGNEWF DPWGQGALVTVSS
4	2-8M VL amino acid sequence	QSALTQPPSVSAAPGRKVDISCSGSTFNIGNNYVSWYR QFPGTAPKLLIYDNDKRPSGIPDRFSGSRFGTSATLGIT GLQTDDEAIYYCATWDNRLDAVVFGGGTELIVL

Table 2. Amino Acid and Nucleotide Sequences of Antibody 6-8N

SEQ ID NO	DESCRIPTION	SEQUENCE
5	6-8N VH nucleotide sequence	GAGGTGCACCTGGTGGAGTCTGGGGGAGGCCTGGT AAACCCGGGGGGGTCCCTTAGACTCTCCTGTTCAGC CTCTGGCTTCGCTTTCACTACCGCCTGGATGACCTGG GCCCGCCAGGCTCCAGGGAAGGGACTGGAATGGAT TGGCCTTATTAAAAGCACAAATGATGGTGGGTCTAT AGACTACGCTGCACCCGTGCAAGGCAGATTCACCAT CTCAAGAGATGATTCAAAGAACACGATTTACCTCCA

		AATGAGCAGCCTCAAAGCCGAGGACTCAGCCGTCT ACTATTGTGCCACAAACGATGTTGTTCGGCTTCGAG GGGTTACCCCCCCCATACTTCTGTGGGGCCAGGGGA CCCTGATCACCGTCTCCTCA
6	6-8N VL nucleotide sequence	CAGCTTGTACTGACTCAATCGCCCTCAACCTCTGCCT CCCTGGGAGCCCCGGTCACACTCACCTGCACTCTGA GCAGTGGGCACCACAGCTACCCCGTCGCATGGCATC AGAAGCACCCAGAGAAGGGCCCTCGATACTTGATG AAGATTAACGGAGATGGCAGCCACACCAAGGGGGA CGGTATCCCTGATCGCTTCTCAGGCTCCAGCTCTGG GACTGGGCGCTATCTCACCATCTCCAGCCTCCAGTC TGAGGATGAGGCTGACTATTACTGTCAGACCTGGGC CACTGGATGGGTGTTCGGCGGAGGGACCAAACTGA CCGTCCTA
7	6-8N VH amino acid sequence	EVHLVESGGGLVNPGGSLRLSCSASGFAFTTAWMTW ARQAPGKGLEWIGLIKSTNDGGSIDYAAPVQGRFTISR DDSKNTIYLQMSSLKAEDSAVYYCATNDVVRLRGVTP PILLWGQGTLITVSS
8	6-8N VL amino acid sequence	QLVLTQSPSTSASLGAPVTLTCTLSSGHHSYPVAWHQ KHPEKGPRYLMKINGDGSHTKGDGIPDRFSGSSSGTGR YLTISSLQSEDEADYYCQTWATGWVFGGGTKLTVL

Table 3. Amino Acid and Nucleotide Sequences of Antibody 2-20G

SEQ ID NO	DESCRIPTION	SEQUENCE
9	2-20G VH nucleotide sequence	GAGTTGCAGTTGGTGGAGTCTGGGGGAAAGTTGGT AAATCCGGGGGGGTCCCTGAGACTCTCATGTGCAG CCTCTGGATTCACTTTCCCTAACGCCTGGTTTAACT GGGTCCGCCAGACTCCAGGGAGGGGGCTGGAGTG

		GGTTGCCCGTATTAAAAGTCATTCTGACGGTGGGA CAGCCGACTACGCTGCACCCGTGAAAGGCAGATTC ACCGTCTCAAGGGATGATTCAGAGAACATGGTGTT TCTGCAAATGAACCGCCTGCGTGCCGAGGACACAG CCGTTTATTATTGTACTACCTTGGAGATTTATCACC CTGTGGACGTCTGGGGCCAGGGGACCACGGTCGCC GTCTCCTCA
10	2-20G VL nucleotide sequence	GATGTTGTGCTGACTCAGTCTCCACTCTCCCTGTCC GTCACCCTTGGACAGCCGGCCTCCATCTCCTGCAG GTCCAGTCACAGCCTCCCAAGAGATGATGAATACT CCTACCTGAATTGGTTTCAGCAGAGGCCAGGCCAG TCTCCAAGGCGCCTAATTTATAGGGTTTCTAAGCG GGACTCTGGGGTCCCAGACAGATTCAGCGGCAGTG GGTCAGACACTTATTTCACACTGACAATCAGCAGG GTGGAGGCTGAGGATGTTGGAGTTTATTACTGCAT GCAAGGTACATACTGGCCCGGGACGTTCGGCCAAG GGACGAAGTTGGAAATCGAGCGA
11	2-20G VH amino acid sequence	ELQLVESGGKLVNPGGSLRLSCAASGFTFPNAWFNW VRQTPGRGLEWVARIKSHSDGGTADYAAPVKGRFT VSRDDSENMVFLQMNRLRAEDTAVYYCTTLEIYHPV DVWGQGTTVAVSS
12	2-20G VL amino acid sequence	DVVLTQSPLSLSVTLGQPASISCRSSHSLPRDDEYSYL NWFQQRPGQSPRRLIYRVSKRDSGVPDRFSGSGSDTY FTLTISRVEAEDVGVYYCMQGTYWPGTFGQGTKLEI ER

Table 4. Amino Acid and Nucleotide Sequences of Antibody 3-17I

SEQ ID NO	DESCRIPTION	SEQUENCE

13	3-17I VH nucleotide sequence	GAGGTGCACCTGGTGGAGTCTGGGGGAGGCCTCGT AAACCCGGGGGGGTCCCTTAGACTCTCCTGTACAG CCTCTGGATTCACTTTCATCACCGCCTGGATGACCT GGGCCCGCCAGGCTCCAGGGAGGGGGCTGGAGTG GATTGGACTTATTAAAAGCGGAAATGATGGTGGGG CTATAGAGTACGCTGCACCCGTGAAAGGCAGATTC ACCATCTCAAGAGATGATTCAAGGAATATGATTTA TCTACAAATGAATAATGTCAAAGCCGAGGACGCA GCCGTCTACTATTGTGCCACAAACGATGTTGCTTTG GTTTGGGGAGTTACCCCCCCCTTGCTTCTCTGGGGC CAGGGGACCCGGGTCACCGTCTCTTCA
14	3-17I VL nucleotide sequence	CAACTTGTGGTGACTCAATCGCCCTCTGCCTCTGCC TCCCTGGGAGGCTCGGTCAAGCTCACCTGCACTCT GAGCAGTGGGCACGGCAACTACCCCGTCGCATGGC ATCAGCTCCACCCAGCGAAGGGCCCTCGATACTTG ATGAAGCTTAATGCAGATGGCAGCCACATCAAGG GGGCCGGGATCACTGATCGCTTCTCAGGCTTCAGG TCTGGGGCTGAGCGCTACCTCACCATCTCCAGCCT CCAGTCTGAAGATGAGGCTGATTATTACTGTCAGA CCTGGGCCCCTGGATGGGTGCTCGGCGGAGGGACC AAGCTGACCGTCCTA
15	3-17I VH amino acid sequence	EVHLVESGGGLVNPGGSLRLSCTASGFTFITAWMTW ARQAPGRGLEWIGLIKSGNDGGAIEYAAPVKGRFTIS RDDSRNMIYLQMNNVKAEDAAVYYCATNDVALVW GVTPPLLLWGQGTRVTVSS
16	3-17I VL amino acid sequence	QLVVTQSPSASASLGGSVKLTCTLSSGHGNYPVAWH QLHPAKGPRYLMKLNADGSHIKGAGITDRFSGFRSG AERYLTISSLQSEDEADYYCQTWAPGWVLGGGTKLT VL

Table 5. Amino Acid and Nucleotide Sequences of Antibody B-21J

SEQ ID NO	DESCRIPTION	SEQUENCE
17	B-21J VH nucleotide sequence	CAGGTGCAACTGGTGGAGTGGGGGGGAGGCGTGG CCCAGCCTGGGACGTCCCTGAGGCTCACCTGTGAT GCGTCTGGATTCAGCTTCAGACATTATGGCATGCA CTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGT GGGTGGCAGTTATCTGGCATAATGGAAGAGACAG AGAGTATGCAGACTCCGTGAAGGGCCGCTTCACCA TCTCCAGAGACAATTCCAAGTACACCCTGTCTTTA CAAATGAACAGCCTGACAGTCGAAGACACGGCAT TATATTACTGCGGGAGAGATCGAGGTGAAGACGA GCCGATTGACTTTTGGGGCCAGGGAACCCTGGTCA CCGTCTCTTCA
18	B-21J VL nucleotide sequence	CAGGCTGTGCTGACTCAACCGTCTTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTCTCACCTGCACCTT GCGCAGTGGCCTCAGTGCTGGTCCCAAGTGGATAT ACTGGTACCAGCAGAGGGCAGGGAGTCCTCCCCA ATTTCTCCTGACATACAAATCAGACTCAGAAGAGC GGCGGAGCTCTGGACTCCCCAGCCGCTTCTCTGGA TCCAAGGATGGCTCGGCCAATGCAGGGATTTTACT CATCTCTGGGCTCCAATCTGAAGATGAGGCAGACT ATTACTGTGCGATTTGGCACAGCAACGTTGTCTTTT TCGGCGCAGGGACCAGGTTGACCGTCCTG
19	B-21J VH amino acid sequence	QVQLVEWGGGVAQPGTSLRLTCDASGFSFRHYGMH WVRQAPGKGLEWVAVIWHNGRDREYADSVKGRFTI SRDNSKYTLSLQMNSLTVEDTALYYCGRDRGEDEPI DFWGQGTLVTVSS
20	B-21J VL amino acid sequence	QAVLTQPSSLSASPGASASLTCTLRSGLSAGPKWIYW YQQRAGSPPQFLLTYKSDSEERRSSGLPSRFSGSKDG

		SANAGILLISGLQSEDEADYYCAIWHSNVVFFGAGTR LTVL

Table 6. Amino Acid and Nucleotide Sequences of Antibody F-18D

SEQ ID NO	DESCRIPTION	SEQUENCE
21	F-18D VH nucleotide sequence	GAGGTGCGCCTGGTGGAGTCTGGGGGAGGCTTAAT AGAGCCGGGGGGGTCTCTTAGACTCTCATGTGAAG CCTCTGGATTCGTTTTCACTACCGCCTGGATGAATT GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG GGTTGGCCGTATTAAGAGCAAAAATGAGGCTGAG ACAACAGACTACGCTGCACCCGTGAAAGGCAGATT CACCATCTCAAGAGATGATTCAAAGGACACATTGT ATCTGCAAATGAACAACCTGAAAACCGAAGACAC AGCCGTCTATTATTGTACCACACTTGAGACGTATT ACGAGTCCGACTTCTGGGGCCAGGGAGTCCTGGTC GCCGTCTCCTCA
22	F-18D VL nucleotide sequence	GATGTTGTGATGACTCAGTCTCCACTCTCCCTGACC GTCACTCTTGGACAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAAAGCCTCGCAGAGAGAGAAGAGGAC ATCTTGTTAAACTGGTATCACCAGGGGCCAGGCCA ATCTCCCAGGCGCCTAATTTATAGAGTTTCTAAGC GTGAGTCTGGGGTCCCAAATAAATTCAGCGGCAGT GTGTCAGGCACTGATTTCACCCTGAGAATCAGCAG GGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCA TGCAACGAACACACTGGCCTCAGACTTTTGGCCAG GGGACCAAGCTGGAGATCAGACGA
23	F-18D VH amino acid sequence	EVRLVESGGGLIEPGGSLRLSCEASGFVFTTAWMNW VRQAPGKGLEWVGRIKSKNEAETTDYAAPVKGRFTI

		SRDDSKDTLYLQMNNLKTEDTAVYYCTTLETYYESD FWGQGVLVAVSS
24	F-18D VL amino acid sequence	DVVMTQSPLSLTVTLGQPASISCRSSQSLAEREEDILL NWYHQGPGQSPRRLIYRVSKRESGVPNKFSGSVSGT DFTLRISRVEAEDVGVYYCMQRTHWPQTFGQGTKLE IRR

Table 7. Amino Acid and Nucleotide Sequences of Antibody J-5N

SEQ ID NO	DESCRIPTION	SEQUENCE
25	J-5N VH nucleotide sequence	CAGGTGCAGCTGGTGGAGTGGGGGGGAGGCGTGG TCCAGCCTGGGGGGTCCCTGAGACTTTGCTGTGCA GCGTCTGGATTCAGTTTAAGGAGTTTTGGCATGCA CTGGGTCCGTCAGGCTCCAGGCAAGGGGCTGGAAT GGGTGGCAGTTATTTGGCCCCGACGAAGTCAAATA CAATATGCAGACTCCGTGAAGGGCCGAGTCACCAT CTCCAGAGACGACTCTAGGAGTACGGTATGTCTGC AGATGAACAGCCTGAGAGTCGAGGACACGGCTCT CTATCGCTGTGCGAGAGACCCCGGTGAGGACAATC CCATAGATTACTGGGGCCAGGGAACCCTGGTCATC GTCTCCTCA
26	J-5N VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCTTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTCTCACCTGCACCTTC CTCAGCGGCATCAATGTTGGTCCCTACTGGATATA CTGGTACCAGCAAAAGCCAGGGAGTCCTCCCCAGT TTCTCCTGAGGTACAAGTCAGACTCAGATAAGCAC CAGGGCTCTGAAGTCCCCAGCCGCTTCTCTGGATC CAAAGATGCTTCGGCCAATGCAGGGATTTTACTCA TCTCTGGGCTCCAGTCTGAAGATGAGGCTGACTAT TACTGTATGATCTGGCACGTCAGCGGTGTGATTTTC

		GGCGGAGGGACCAAGCTGACCGTCCTA
27	J-5N VH amino acid sequence	QVQLVEWGGGVVQPGGSLRLCCAASGFSLRSFGMH WVRQAPGKGLEWVAVIWPRRSQIQYADSVKGRVTIS RDDSRSTVCLQMNSLRVEDTALYRCARDPGEDNPID YWGQGTLVIVSS
28	J-5N VL amino acid sequence	QAVLTQPSSLSASPGASASLTCTFLSGINVGPYWIYW YQQKPGSPPQFLLRYKSDSDKHQGSEVPSRFSGSKDA SANAGILLISGLQSEDEADYYCMIWHVSGVIFGGGTK LTVL

Table 8. Amino Acid and Nucleotide Sequences of Antibody J-8G

SEQ ID NO	DESCRIPTION	SEQUENCE
29	J-8G VH nucleotide sequence	CAGGTGCAACTGGTGGAGTGGGGGGGAGGCGTGG TCCAGCCTGGGACGTCCCTGAGACTCACCTGTGAT GCGTCTGGATTCAGCTTCAGACATTATGGCATGCA CTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGT GGGTGGCAGTTATCTGGCATAATGGAAGAGATAA AGACTATGCAGACTCCGTGAAGGGCCGGTTCACCA TCTCCAGAGACAATTCCAAGTACACCCTGTCTTTA CAAATGAACAGCCTGACAGTCGAGGACACGGCAT TATATTACTGTGGGAGAGATCGAGGTGAAGACGA GCCGATTGACTTTTGGGGCCAGGGAACCCTGGTCA CCGTCTCCTCA
30	J-8G VL nucleotide sequence	CAGGCTGTGCTGACTCAACCGTCTTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTCTCACCTGCACCTT GCGCAGTGGCCTCAATGTTGGTCCCTACTGGATAT ACTGGTACCAGCAGAAGGCAGGGAGTCCTCCCCA ATTTCTCCTGAGATACAAATCAGACTCAGAAAAGC

		GGCGGAGCTCTGGAGTCCCCAGCCGCTTCTCTGGA TCCAAAGATGCCTCGGCCAATGCAGGGATTTTACT CATCTCTGGGCTCCAGTCTGAAGATGAGGCTGACT ATTATTGTGCGATTTGGCACAGCAATGCTGTCTTTT TCGGCGCAGGGACCAAGTTGACCGTCCTA
31	J-8G VH amino acid sequence	QVQLVEWGGGVVQPGTSLRLTCDASGFSFRHYGMH WVRQAPGKGLEWVAVIWHNGRDKDYADSVKGRFTI SRDNSKYTLSLQMNSLTVEDTALYYCGRDRGEDEPI DFWGQGTLVTVSS
32	J-8G VL amino acid sequence	QAVLTQPSSLSASPGASASLTCTLRSGLNVGPYWIYW YQQKAGSPPQFLLRYKSDSEKRRSSGVPSRFSGSKDA SANAGILLISGLQSEDEADYYCAIWHSNAVFFGAGTK LTVL

Table 9. Amino Acid and Nucleotide Sequences of Antibody 4-22O

SEQ ID NO	DESCRIPTION	SEQUENCE
33	4-22O VH nucleotide sequence	CAGGTGCAGATGGTGGAGTTTGGGGGAGGCATCTT CCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCG CGTCTGGATTCCCCTTCAGGTACTATGGTTTCCACT GGGTCCGCCAGACTCCAGGCAAGGGGCTGGAGTG GCTGGCAGTTGTATGGCACAATGGAAGGGAGACA TATTATGAAGACTCCGTGAAGGGGCGATTCACCAT CTCCAGAGACAATTACAAGAACACGCTGTATTTGC AAATGGACAGCCTGAGAGTCGAGGACACGGCTGT CTATCACTGTGCGAGAGATCGTGGTAGCGACGAAC CAATTGACTACTGGGGCCAGGGAGTTTTGGTCACC GTCTCCTCA

34	4-22O VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTATCACCTGCACCTT ACGCAGTGACCTCACTGTTGGTCCCTACTGGATGT ACTGGTACCAACAGAAGCCAGGGAGTCCTCCCCAA TTTCTCCTGAGGTACAAGTCAGACTCCGAAAAGTA TCAGGGCTCTGGAGTCCCCAGCCGCTTCTCTGGAT CCAAAGACGCTTCGGCCAATGCAGGGACTTTGCTC ATCTCTGGACTCCAGTCTGAAGATGAGGCTGACTA TTACTGTCAGACTTGGCACGCCAACACTGTGGTAT TTGGCGGAGGGACCAAGCTGACCGTCCTA
35	4-22O VH amino acid sequence	QVQMVEFGGGIFQPGGSLRLSCVASGFPFRYYGFHW VRQTPGKGLEWLAVVWHNGRETYYEDSVKGRFTIS RDNYKNTLYLQMDSLRVEDTAVYHCARDRGSDEPI DYWGQGVLVTVSS
36	4-22O VL amino acid sequence	QAVLTQPSSLSASPGASASITCTLRSDLTVGPYWMY WYQQKPGSPPQFLLRYKSDSEKYQGSGVPSRFSGSK DASANAGTLLISGLQSEDEADYYCQTWHANTVVFG GGTKLTVL

Table 10. Amino Acid and Nucleotide Sequences of Antibody 6-20C

SEQ ID NO	DESCRIPTION	SEQUENCE
37	6-20C VH nucleotide sequence	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTCTT CCAGCCGGGGGGGTCCCTGAGACTCTCCTGTGCAG CGTCTGGATTCAGTTTCAGGAGATTTGGTATGCATT GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG GCTGGCAGTTGTTTGGCATGATGGAAGGGAGACAC ACTATGGAGACTCCGTGAGGGGCCGATTCACCATC TCCAGAGACAACTCCATGCACATGGTGTTTTTGGA CATGTACAGCCTGAGGGTCGAGGACACGGCTCTAT

		ATCGCTGTGCGAGAGATCCTGGTCAGGACGAAGCC ATTGACTATTGGGGCCAGGGAGTCCTGGTCACCGT CTCGTCA
38	6-20C VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCTTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTCTCACCTGCACCTT ACACAGTGGCCTCACTGTTGGTCCCTATTGGATAT ACTGGTTCCGGCAGAAGCCAGGGAGTCCCCCCCAG TTTCTCCTCAGGTACAAATCCGACTCAGAGGAGTA CCGTGCCTCTGGAGTCCCCAGCCGCTTCTCTGGATC CAAAGATGCTTCGGCCAACTCAGGCATTTTACTCA TCTCTGGACCACAGTCTGAAGACGAGGCTGACTAT TACTGTATGACTTGGCACACCAACAAGGTAGTCTT CGGCGGAGGGACCACACTGACCGTCCTA
39	6-20C VH amino acid sequence	QVQLVESGGGVFQPGGSLRLSCAASGFSFRRFGMHW VRQAPGKGLEWLAVVWHDGRETHYGDSVRGRFTIS RDNSMHMVFLDMYSLRVEDTALYRCARDPGQDEAI DYWGQGVLVTVSS
40	6-20C VL amino acid sequence	QAVLTQPSSLSASPGASASLTCTLHSGLTVGPYWIYW FRQKPGSPPQFLLRYKSDSEEYRASGVPSRFSGSKDA SANSGILLISGPQSEDEADYYCMTWHTNKVVFGGGT TLTVL

Table 11. Amino Acid and Nucleotide Sequences of Antibody 12-14G

SEQ ID NO	DESCRIPTION	SEQUENCE
41	12-14G VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCCAGG CTTCTGGATACACCTTCACCAACTATGGTGTCAACT GGGTGCGACAGGCCACTGGACAAGGGCTTGAGTG

		GATGGGATGGATGAACACTAACAGTGGTGACACG GGTTATGCCCAGAAGTTCCAGGGCAGAGTCACCAT GACCAGGGACACCTCCATAAACACAGCCTACATGG AGCTGAGCGGACTGACATCTGAGGACACGGCCGTC TATTACTGTGCGCGAGCGTATTTTTTTGATTCGTGG AATAAGGGCAACTGGTTCGACCCCTGGGGCCAGG GAACCCCGGTCACCGTCTCCTCA
42	12-14G VL nucleotide sequence	CAGTCTGTGCTGACTCAGGCACCCTCAGTGTCTGG GACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTG GAGGCAGCTCCAACCTGGGAAGAAGTTATATATAT TGGTACCAACAGTTCCCAGGAACGGCCCCCAGAGT CCTCATTTATAAAAATAGTCAGCGGCCCTCAGGGG TCCCTGACCGATTCTCCGGCTCCAAGTCTGGCACCT CAGCCTCCCTGGCCATCAGTGGGCTCCGGTCCGAG GATGAGGCTCATTATTACTGTGCAGCATGGGATGA CAGCCTGAGTGGGTCTTGGGTGTTCGGCGGAGGGA CCAAGCTGACCGTCCTA
43	12-14G VH amino acid sequence	QVQLVQSGAEVKKPGASVKVSCQASGYTFTNYGVN WVRQATGQGLEWMGWMNTNSGDTGYAQKFQGRV TMTRDTSINTAYMELSGLTSEDTAVYYCARAYFFDS WNKGNWFDPWGQGTPVTVSS
44	12-14G VL amino acid sequence	QSVLTQAPSVSGTPGQRVTISCSGGSSNLGRSYIYWY QQFPGTAPRVLIYKNSQRPSGVPDRFSGSKSGTSASL AISGLRSEDEAHYYCAAWDDSLSGSWVFGGGTKLTV L

Table 12. Amino Acid and Nucleotide Sequences of Antibody 15-6J

SEQ ID NO	DESCRIPTION	SEQUENCE
45	15-6J VH nucleotide sequence	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTT CGAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCG CGTCTGGATTCTCCTTCAGGCATTATGGTATGCACT GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG GCTGGCAGTTGTATGGCATGATGGAAGGGAGACA CATTATGGAGACTCCGTGAAGGGGCGATTCACCAT CTCCAGAGACAATTACAAGAATACGCTGTTTTTGC AAATGGACAGCCTGAGAGTCGAGGACACGGCTGT CTATCACTGTGCGAGAGATCGTGGTAGCGACGAAC CTATTGACTACTGGGGCCAGGGAGTTTTGGTCACC GTCTCCTCA
46	15-6J VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTATCACCTGCACCTT ACGCAGTGACGTCACTGTTAGTCCCTGGACATACT GGTACCAACAGAAGCCAGGGAGTCCTCCCCGATTT CTCCTGAGATACAAATCAGACTCTGATAAGTATCA GGGCTCTGGAGTCCCCAGCCGCTTCTCTGGATCCA AAAATGCTTCGGCCAATGCAGCGATTTTACTCATC TCTGGGCTCCAGTCTGAAGATGAGGCTGACTATTA CTGTCAGACTTGGCACACCACCACTGTGGTATTTG GCGGAGGGACCAAGCTGACCGTCCTA
47	15-6J VH amino acid sequence	QVQLVEFGGGIFEPGGSLRLSCVASGFSFRHYGMHW VRQAPGKGLEWLAVVWHDGRETHYGDSVKGRFTIS RDNYKNTLFLQMDSLRVEDTAVYHCARDRGSDEPID YWGQGVLVTVSS
48	15-6J VL amino acid sequence	QAVLTQPSSLSASPGASASITCTLRSDVTVSPWTYWY QQKPGSPPRFLLRYKSDSDKYQGSGVPSRFSGSKNAS

		ANAAILLISGLQSEDEADYYCQTWHTTTVVFGGGTK LTVL

Table 13. Amino Acid and Nucleotide Sequences of Antibody 18-11C

SEQ ID NO	DESCRIPTION	SEQUENCE
49	18-11C VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAA GAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CGTCTGGATACACTTTCACCAGCTTTGGTATCAACT GGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTG GATGGGATGGATGAACTCCAACAGTGGTGATGCG GACTCTGCACAGAAGTTCCAGGGCAGACTCACTAT GACCACCGACACCTCCACAAGTACAGCCTACATGG AGCTGAGGAATCTGAGATCTGAGGACACGGCCGT ATATTATTGCGCGAGAATGAATTTCCGTGGTTCGA AGTGGGAGGTGAACTGGTTCGACCCCTGGGGCCAG GGAACCCTGATCACCGTCTCCTCA
50	18-11C VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTG GAAGCAGGTCCAACGTCGAAAGAAATTTTGTTTAC TGGTACCAGCAACTCCCAGGAACGGCCCCCAAACT TCTCATCTATATGAACAGTCAGCGGCCCTCAGGGG TCCCTGACCGATTCTCTGGCTCTCGTTCTGGCACCT CAGCCTCCCTGGCCATCACTGGGCTTCGGTCCGAG GATGAGGCTGACTATTATTGTGCAACTTGGGATGA CAATCTGAGAGGCTGGGTGTTCGGCGGAGGGACC AAGGTGACCGTCCTA

51	18-11C VH amino acid sequence	QVQLVQSGAEIKRPGASVKVSCKASGYTFTSFGINW VRQAPGQGLEWMGWMNSNSGDADSAQKFQGRLTM TTDTSTSTAYMELRNLRSEDTAVYYCARMNFRGSK WEVNWFDPWGQGTLITVSS
52	18-11C VL amino acid sequence	QSVVTQPPSASGTPGQRVTISCSGSRSNVERNFVYWY QQLPGTAPKLLIYMNSQRPSGVPDRFSGSRSGTSASL AITGLRSEDEADYYCATWDDNLRGWVFGGGTKVTV L

Table 14. Amino Acid and Nucleotide Sequences of Antibody 20-2D

SEQ ID NO	DESCRIPTION	SEQUENCE
53	20-2D VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAA GAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CGTCTGGATACACCTTCACCAGGTTCGGCATCAAC TGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTG GATGGGATGGATGAACTCCAACAGTGGTAATGCG GACTCTGCACAGAAGTTCCAGGGCAGACTCACTAT GACCACCGACACCTCCACAAGTACAGCCTACATGG AGCTGAGGAATCTAAGATCTGAGGACACGGCCGT ATATTATTGCGCGAGAATGAATTACCGTGGTTCGA AGTGGGAAATAAACTGGTTCGACCCCTGGGGCCAG GGAACCCTGATCACCGTCTCCTCA
54	20-2D VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGGTCACCATTTCCTGTTCTG GTAGCAGGTCCAACGTCCAAAGAAATTTTGTTTAC TGGTACCAGCAGCTCCCAGGAACGGCCCCCAAACT TCTCATCTATATGAACAATAACCGCCCCTCAGGGG TCCCTGACCGATTCTCTGGCTCTCATTCTGGCACCT CAGCCTCCCTGGCCATCACTGGGCTTCGGTCCGAG

		GATGAGGCTGATTATTATTGTGCTACTTGGGATGA CAATCTGAGAGGCTGGGTGTTCGGCGGAGGGACC AAGGTGACCGTCCTA
55	20-2D VH amino acid sequence	QVQLVQSGAEIKRPGASVKVSCKASGYTFTRFGINW VRQAPGQGLEWMGWMNSNSGNADSAQKFQGRLTM TTDTSTSTAYMELRNLRSEDTAVYYCARMNYRGSK WEINWFDPWGQGTLITVSS
56	20-2D VL amino acid sequence	QSVVTQPPSASGTPGQRVTISCSGSRSNVQRNFVYWY QQLPGTAPKLLIYMNNNRPSGVPDRFSGSHSGTSASL AITGLRSEDEADYYCATWDDNLRGWVFGGGTKVTV L

Table 15. Amino Acid and Nucleotide Sequences of Antibody 9-5L

SEQ ID NO	DESCRIPTION	SEQUENCE
57	9-5L VH nucleotide sequence	CAGGTGCACCTGGTGGAGTCTGGGGGAGACCTGGT CCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG CGTCTGGATTTACCCTCAAACGTTATGGCATTCACT GGGTCCGCCAGGCGCCAGGCAAGGGGCTGGAGTG GGTGGCAGTTACTTGGCATGATGGAAATATATACT ATGCAGACTCCGTGAAGGGCCGACTCACCGTCTCC AGAGACAGTTACAAGAACACGGTGGATCTACAAA TGAACAGCCTGAAAGTCGAGGACACGGCTCTATAT TACTGTGCGAGAGATGCCGGGCAAAATGCGCCCAT TGACCTCTGGGGCCACGGAACCCTGGTCACCGTCT CCTCA

58	9-5L VL nucleotide sequence	CAGGCTGTACTGACTCAGCCGTCTTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTCTCACCTGCACCTT ACCCAGTGGCATCAATGTTGCTACCCACTGGATAT ACTGGTACCAGCAGAAGCCTGGCAGTCCTCCCCAG TTTCTCCTGCGGTACAAATCAGACTCAGATATCCA ACACGGCTCTGGAGTCCCCAGCCGCTTCTCTGGAT CCAAAGATGCTTCGGCCAATGCCGCGATTTTAGTC GTCTCTGGTCTCCAGTCTGAGGATGAGGCTGACTA TTACTGTATGATTTGGTATTCCACCGCCGTGGTTTT CGGCGGAGGGACCAAGCTGACCGTCCTG
59	9-5L VH amino acid sequence	QVHLVESGGDLVQPGRSLRLSCAASGFTLKRYGIHW VRQAPGKGLEWVAVTWHDGNIYYADSVKGRLTVSR DSYKNTVDLQMNSLKVEDTALYYCARDAGQNAPID LWGHGTLVTVSS
60	9-5L VL amino acid sequence	QAVLTQPSSLSASPGASASLTCTLPSGINVATHWIYW YQQKPGSPPQFLLRYKSDSDIQHGSGVPSRFSGSKDA SANAAILVVSGLQSEDEADYYCMIWYSTAVVFGGGT KLTVL

Table 16. Amino Acid and Nucleotide Sequences of Antibody 15-20G

SEQ ID NO	DESCRIPTION	SEQUENCE
61	15-20G VH nucleotide sequence	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTT CCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCG CGTCTGGATTCTCCTTCAGGTATTATGGTTTCCACT GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG GCTGGCAGTTGTATGGCATGATGGAAGGGAGACA CATTATGGAGACTCCGTGAGGGGGCGATTCACCAT CTCCAGAGACAATTACAAGAACACGGTGTTTTTGG AAATGGACAGCCTGAGAGTCGAGGACACGGCTGT

		CTATCACTGTGCGAGAGATCGTGGTAGCGACGAAC CTATTGACTACTGGGGCCAGGGAGTTTTGGTCACC GTCTCCTCA
62	15-20G VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTATCACCTGCACCTT ACGCAGTGACCTCACTGTTAGTCCCTGGATATACT GGTACCAACAGAAGCCAGGGAGTCCTCCCCGATTT CTCCTGAAATACAAATCAGACTCCAATAACTACCA CGGCTCTGGAGTCCCCAGCCGCTTCTCTGGATCCA AAGATGCTTCGGCCAATGCAGCGATTTTACTCATC TCTGGACTCCAGTCTGAAGATGAGGCTGACTATTA CTGTCAGACTTGGCACACCACCACTGTGGTATTTG GCGGAGGGACCAAGCTGACCGTCCTA
63	15-20G VH amino acid sequence	QVQLVEFGGGIFQPGGSLRLSCVASGFSFRYYGFHW VRQAPGKGLEWLAVVWHDGRETHYGDSVRGRFTIS RDNYKNTVFLEMDSLRVEDTAVYHCARDRGSDEPID YWGQGVLVTVSS
64	15-20G VL amino acid sequence	QAVLTQPSSLSASPGASASITCTLRSDLTVSPWIYWY QQKPGSPPRFLLKYKSDSNNYHGSGVPSRFSGSKDAS ANAAILLISGLQSEDEADYYCQTWHTTTVVFGGGTK LTVL

Table 17. Amino Acid and Nucleotide Sequences of Antibody 23-12O

SEQ ID NO	DESCRIPTION	SEQUENCE
65	23-12O VH nucleotide sequence	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTT CGAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCG CGTCTGGATTCTCCTTCAGGCATTATGGTATGCACT GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG

		GCTGGCAGTTGTATGGCATGATGGAAGGGAGACA CATTATGGAGACTCCGTGAAGGGGCGATTCACCAT CTCCAGAGACAATTACAAGAATACGCTGTTTTTGC AAATGGACAGCCTGAGAGTCGAGGACACGGCTGT CTATCACTGTGCGAGAGATCGTGGTAGCGACGAAC CTATTGACTACTGGGGCCAGGGAGTTTTGGTCACC GTCTCCTCA
66	23-12O VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTATCACCTGCACCTT ACGCAGTGACGTCACTGTTAGTCCCTGGACATACT GGTACCAACAGAAGCCAGGGAGTCCTCCCCAATTT CTCCTGAGATACAAATCAGACTCTGATAAGTATCA GGGCTCTGGAGTCCCCAGCCGCTTCTCTGGATCCA AAAATGCTTCGGCCAATGCAGCGATTTTACTCATC TCTGGGCTCCAGTCTGAAGATGAGGCTGACTATTA CTGTCAGACTTGGCACACCAACAATGTGGTATTTG GCGGAGGGACCAAGCTGACCGTCCTA
67	23-12O VH amino acid sequence	QVQLVEFGGGIFEPGGSLRLSCVASGFSFRHYGMHW VRQAPGKGLEWLAVVWHDGRETHYGDSVKGRFTIS RDNYKNTLFLQMDSLRVEDTAVYHCARDRGSDEPID YWGQGVLVTVSS
68	23-12O VL amino acid sequence	QAVLTQPSSLSASPGASASITCTLRSDVTVSPWTYWY QQKPGSPPQFLLRYKSDSDKYQGSGVPSRFSGSKNAS ANAAILLISGLQSEDEADYYCQTWHTNNVVFGGGTK LTVL

Table 18. Amino Acid and Nucleotide Sequences of Antibody 31-2C

SEQ ID NO	DESCRIPTION	SEQUENCE
69	31-2C VH nucleotide sequence	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTT CCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCG CGTCTGGATTCTCCTTCAGATATTATGGTTTCCACT GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG GCTGGCAGTTGTATGGCATGATGGAAGGGAGACA CATTATGGAGACTCCGTGAAGGGGCGATTCACCAT CTCCAGAGACAATTACAAGAACACGCTGTTTTTGC AAATGGACAGCCTGAGAGTCGAGGACACGGCTGT CTATCACTGTGCGAGAGATCGTGGTAGCGACGAAC CTATTGACTACTGGGGCCAGGGAGTTTTGGTCACC GTCTCCTCA
70	31-2C VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTATCACCTGCACCTT ACGCAGTGGCCTCACTGTTAGTCCCTGGATATACT GGTACCAACAGAAGCCAGGGAGTCCTCCCCAATTT CTCCTGAGATACAAATCAGACTCCGAAAACTACCG GGGCTCTGGAGTCCCCAGTCGCTTCTCTGGATCCA AAGAGGCTTCGGCCAATGCAGCGATTTTATTCATC TCTGGACTCCAGTCTGAAGATGAGGCTGACTATTA CTGTCAGACTTGGCACACCAGCACAGTGGTATTTG GCGGAGGGACCAAGCTGACCGTCCTA
71	31-2C VH amino acid sequence	QVQLVEFGGGIFQPGGSLRLSCVASGFSFRYYGFHW VRQAPGKGLEWLAVVWHDGRETHYGDSVKGRFTIS RDNYKNTLFLQMDSLRVEDTAVYHCARDRGSDEPID YWGQGVLVTVSS
72	31-2C VL amino acid sequence	QAVLTQPSSLSASPGASASITCTLRSGLTVSPWIYWY QQKPGSPPQFLLRYKSDSENYRGSGVPSRFSGSKEAS

		ANAAILFISGLQSEDEADYYCQTWHTSTVVFGGGTK LTVL

Table 19. Amino Acid and Nucleotide Sequences of Antibody 36-19H

SEQ ID NO	DESCRIPTION	SEQUENCE
73	36-19H VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAA GAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CGTCTGGATACATTTTCACCAACTTTGGCATCAACT GGGTGCGACAGGCCCCTGGTCAAGGGCTTGAGTGG ATGGGATGGATGAACTCCAAGTATGGTAATGCGGA CTCTGCACATAAGTTCCAGGACAGACTCACTATGA CCACCGACACCTCCACAAGTACAGCCTACATGGAG CTGAGAAATCTGAGATCTGAGGACACGGCCGTATA TTATTGCGCGAGAATGAATTACCGTGATTCGAAGT GGGACGTGAATTGGTTCGACCCCTGGGGCCAGGGA ACCCTGATCACCGTCTCCTCA
74	36-19H VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTG GAAGCAGGTCCAACGTCGAAAGAAATTTTGTTTAC TGGTACCAGCAGCTCCCAGGAACGGCCCCCAAACT TCTCATCTATATGAACAATCAGCGCCCCTCAGGGG TCCCTGACCGATTCTCTGGCTCTCGTTCTGGCACCT CAGCCTCCCTGGCCATCACTGGGCTTCGGTCCGAG GATGAGGCTGATTATTATTGTGCAGTTTGGGATGA CAATCTCAGAGGCTGGGTGTTCGGCGGAGGGACCG AGGTGACCGTCCTA

75	36-19H VH amino acid sequence	QVQLVQSGAEIKRPGASVKVSCKASGYIFTNFGINWV RQAPGQGLEWMGWMNSKYGNADSAHKFQDRLTMT TDTSTSTAYMELRNLRSEDTAVYYCARMNYRDSKW DVNWFDPWGQGTLITVSS
76	36-19H VL amino acid sequence	QSVVTQPPSASGTPGQRVTISCSGSRSNVERNFVYWY QQLPGTAPKLLIYMNNQRPSGVPDRFSGSRSGTSASL AITGLRSEDEADYYCAVWDDNLRGWVFGGGTEVTV L

Table 20. Amino Acid and Nucleotide Sequences of Antibody 36-21L

SEQ ID NO	DESCRIPTION	SEQUENCE
77	36-21L VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAA GAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CGTCTGGATACACTTTCACCGGCTTTGGTATCAACT GGGTGCGACAGGCCCCAGGACAGGGGCTTGAGTG GATGGGATGGATGAACTCCAACACTGGTGATGCGG ACTCTGCACAGAAGTTCCAGGGCAGACTCACTATG ACCACCGACACCTCCACAAGTACAGCCCACATGGA GCTGACGAATCTGGGATCTGAGGACACGGCCGTAT ACTATTGCGCGAGAATGAATTTCCTTGGTTCGAAG TGGGAGGTGAACTGGTTCGACCCCTGGGGCCAGGG AACCCTGATCACCGTCTCCTCA
78	36-21L VL nucleotide sequence	GATGTTGTGCTGACTCAGTCTCCACTCTCCCTGTCC GTCACCCTTGGACAGCCGGCCTCCATCTCCTGCAG GTCCAGTCACAGCCTCCCAAGAGATGATGAATACT CCTACCTGAATTGGTTTCAGCAGAGGCCAGGCCAG TCTCCAAGGCGCCTAATTTATAGGGTTTCTAAGCG GGACTCTGGGGTCCCAGACAGATTCAGCGGCAGTG GGTCAGACACTTATTTCACACTGACAATCAGCAGG

		GTGGAGGCTGAGGATGTTGGAGTTTATTACTGCAT GCAAGGTACATACTGGCCCGGGACGTTCGGCCAAG GGACGAAGTTGGAAATCGAGCGA
79	36-21L VH amino acid sequence	QVQLVQSGAEIKRPGASVKVSCKASGYTFTGFGINW VRQAPGQGLEWMGWMNSNTGDADSAQKFQGRLTM TTDTSTSTAHMELTNLGSEDTAVYYCARMNFLGSK WEVNWFDPWGQGTLITVSS
80	36-21L VL amino acid sequence	DVVLTQSPLSLSVTLGQPASISCRSSHSLPRDDEYSYL NWFQQRPGQSPRRLIYRVSKRDSGVPDRFSGSGSDTY FTLTISRVEAEDVGVYYCMQGTYWPGTFGQGTKLEI ER

Table 21. Amino Acid and Nucleotide Sequences of Antibody 41-18O

SEQ ID NO	DESCRIPTION	SEQUENCE
81	41-18O VH nucleotide sequence	GAGGTACAGCTGGTGGAGTCTGGGGGAGGCCTGG TCCAGCCTGGGGGGTCTCTGAGACTCTCCTGTGCA GCCTCTGGATTCACCTTTAATCACGATTGGATGACT TGGGTCCGCCAGGCTCCAGGGAAGGGTCTGGAGTG GGTGGCCAACATAATACAAGATGGAAGCGAAACA TACTATGTGGACTCTGTGAAGGGCCGATTCACCAT CTCCAGAGACAATGCCAAGAATTTACTGTATCTGC AGATGAACAGCCTGAGAGTCGAGGACACGGCTGT GTATTTCTGTGGCCGGAGTATGGACGTCTGGGGCC AAGGGACCACGGTCATCGTCTCCTCA
82	41-18O VL nucleotide sequence	CAGTCTGTGCTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTG GAAGCAGCTCCAACATCGGAAGTAATACTGTGAAC TGGTACCACCAGGTCCCAGGAACGGCCCCCAAACT

		CCTCATCTATACTGATAATCAGCGGCCCTCAGGGG TCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCT CAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTGAG GATGAAGGTGATTATTACTGTGCAGCGAGGGATGG CAGCCTGGATGTTTGGGTGTTCGGCGGAGGGACCA AAGTGACTGTCCTA
83	41-18O VH amino acid sequence	EVQLVESGGGLVQPGGSLRLSCAASGFTFNHDWMT WVRQAPGKGLEWVANIIQDGSETYYVDSVKGRFTIS RDNAKNLLYLQMNSLRVEDTAVYFCGRSMDVWGQ GTTVIVSS
84	41-18O VL amino acid sequence	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWY HQVPGTAPKLLIYTDNQRPSGVPDRFSGSKSGTSASL AISGLQSEDEGDYYCAARDGSLDVWVFGGGTKVTV L

Table 22. Amino Acid and Nucleotide Sequences of Antibody 5-14N

SEQ ID NO	DESCRIPTION	SEQUENCE
85	5-14N VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAA GAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CGTCTGGATACACTTTCACCAACTTTGGAATCAAC TGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTG GATGGGATGGATGAACTCCAGAACTGGTGATGCG GACTCTGCACAGAACTTCCAGGGCAGGCTCACTAT GACCACCGACACCTCCAGAAGTATAGCCTACATGG AGCTGACGCACCTGACCTCTGAGGACACGGCCGTA TATTATTGCGCGAGAATGAATTTCCTTGGTTCGAG GTGGGAGGTGAACTGGTTCGACCCCTGGGGCCAGG GAACCCTGATCACCGTCTCCTCA

86	5-14N VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGTGTCTGG GACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTG GAAGCAGGTCCAACGTCGAAAGAAATTTTTTTTAC TGGTATCAGCAATTCCCAGGAACGGCCCCCAAACT TCTCATCTATATGAACAGTCAGCGGCCCGCAGGGG TCCCTGACCGATTCTCTGGCTCTCGTTCTGGCACCT CAGTTTCCCTGGCCATCACTGGGCTTCGGTCCGAG GATGAGGCTGACTATTATTGTGCAACTTGGGATGA CAATCTGAGAGGCTGGGTGTTCGGCGGAGGGACC AAGGTGACCGTCCTA
87	5-14N VH amino acid sequence	QVQLVQSGAEIKRPGASVKVSCKASGYTFTNFGINW VRQAPGQGLEWMGWMNSRTGDADSAQNFQGRLTM TTDTSRSIAYMELTHLTSEDTAVYYCARMNFLGSRW EVNWFDPWGQGTLITVSS
88	5-14N VL amino acid sequence	QSVVTQPPSVSGTPGQRVTISCSGSRSNVERNFFYWY QQFPGTAPKLLIYMNSQRPAGVPDRFSGSRSGTSVSL AITGLRSEDEADYYCATWDDNLRGWVFGGGTKVTV L

Table 23. Amino Acid and Nucleotide Sequences of Antibody 11-19C

SEQ ID NO	DESCRIPTION	SEQUENCE
89	11-19C VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAA GCGGCCTGGGGCCTCAGTGAAGATCTCCTGCAAGG CGTCTGGATACATTTTCACCAGCTTTGGTATCAACT GGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTG GATGGGATGGATGAACTCCAACACTGGTGATGCGG ACTCTCTACAGAAGTTCCAGGGCAGACTCACCATG ACCACCGACACCTCCACAAGCACAGCCTACATGGA ATTGAGCAATCTGAGATCTGAAGACACGGCCGTAT

		ATTATTGCGCGAGAATGAATTTCCATGGTTCGAGG TGGGACGTGAACTGGTTCGACCCCTGGGGCCAGGG AACCCTGATCACCGTCTCCTCA
90	11-19C VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGGTCATCATCTCCTGTTCTG GAAGCGGGTCCAACGTCGAAAGAAATTCTGTTTAC TGGTACCAACAGTTCCCGGGAACGGCCCCCAAACT TCTCATCTACATGAGCAATAGGCGCCCCTCAGGGG TCCCTGACCGATTCTTTGGCTCTCGTTCTGGCACCT CAGCCTCCCTGGCCATCACTGGGCTTCGGCCCGAG GATGAGGCTGATTATTATTGTGCAGTTTGGGATGA CAGTCTGAGAGGCTGGGTATTCGGCGGAGGGACC AAGGTGACCGTCCTA
91	11-19C VH amino acid sequence	QVQLVQSGAEIKRPGASVKISCKASGYIFTSFGINWV RQAPGQGLEWMGWMNSNTGDADSLQKFQGRLTMT TDTSTSTAYMELSNLRSEDTAVYYCARMNFHGSRW DVNWFDPWGQGTLITVSS
92	11-19C VL amino acid sequence	QSVVTQPPSASGTPGQRVIISCSGSGSNVERNSVYWY QQFPGTAPKLLIYMSNRRPSGVPDRFFGSRSGTSASL AITGLRPEDEADYYCAVWDDSLRGWVFGGGTKVTV L

Table 24. Amino Acid and Nucleotide Sequences of Antibody F-8C

SEQ ID NO	DESCRIPTION	SEQUENCE
93	F-8C VH nucleotide sequence	CAGGTGCAGCTGGCGGAGTCTGGGGGAGGCGTGG TCCAGCCTGGGGGGTCCCTGAGACTTTCCTGTGCA GCGTCTGGATTCAGTCTCAAGAGTTATGGCATTCA CTGGGTCCGCCAGGCCCCAGGCAAGGGGCTGGAG

		TGGGTGGCAGTTATCTGGCCCCGACGAGATACACA GTATGCAGACTCCGTGAAGGGCCGAGTCACCATGT ACAGAGACGACTATAGGAATACGGTCTATCTACAG ATGAACAGCCTGAGATTCGATGACGCGGCTCTGTA TCGGTGTGCGAGAGATCGCGGTGAAGACAATCCCA TAGATTTCTGGGGCCAGGGAACCCTGGTCACCGTC TCCTCA
94	F-8C VL nucleotide sequence	CAGGCTGTGCTGACTCAGCCGTCTTCCCTCTCTGCA TCTCCTGGAGCATCAGCCAGTCTCACCTGCACCTT GCTCAGCGGCATCAATGTTGGTCCCTACTGGATAT ACTGGTATCAGCAGAAGGCAGGGAGTCCTCCCCAG TTTCTCCTCAGGTACAGGTCAGACTCAGATGAGGA GCAGGGCTCTGAGGTCCCCAGCCGCTTCTCTGGAT CCAAAGATGCCTCGGCCAATGCAGGGATTTTGGTC ATCTCTGGGCTCCAGTCTGAAGATGAAGCTGACTA TTACTGTATGATCTGGCACAGGACCGGTGTGATTT TCGGCGGAGGGACCAAGCTGACCGTCCTA
95	F-8C VH amino acid sequence	QVQLAESGGGVVQPGGSLRLSCAASGFSLKSYGIHW VRQAPGKGLEWVAVIWPRRDTQYADSVKGRVTMY RDDYRNTVYLQMNSLRFDDAALYRCARDRGEDNPI DFWGQGTLVTVSS
96	F-8C VL amino acid sequence	QAVLTQPSSLSASPGASASLTCTLLSGINVGPYWIYW YQQKAGSPPQFLLRYRSDSDEEQGSEVPSRFSGSKDA SANAGILVISGLQSEDEADYYCMIWHRTGVIFGGGTK LTVL

Table 25. Amino Acid and Nucleotide Sequences of Antibody 21-6M

SEQ ID NO	DESCRIPTION	SEQUENCE
97	21-6M VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTA AGAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAA GGCGTCTGGATACATTTTCACCAGCTTTGGTATCA ACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGA GTGGATGGGATGGATGAACTCCAACACTGGTGAT GCGGACTCTGTACAGAAGTTCCAGGGCAGACTCA CCATGACCACCGACCCCTCCACAAGTACAGCCTA TATGGAACTGAGGAATCTGAGATCTGACGACACG GCCGTATATTATTGCGCGAGAATGAACTTCTTTGG TTCGCAGTGGGAAGTGAACTGGTTCGACCCCTGG GGCCAGGGAACCCTGATCACCGTCTCCTCA
98	21-6M VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGATCACCATCTCCTGTTCTG GAAGCAGGTCCAACGTCGAAAGAAATTCTGTTTA CTGGTACCAGCAGCTCCGAGGAACGGCCCCCAAA CTTCTCATCTATATGAGCAATCAGCGCCCCTCAGG GGTCCCTGACCGATTCTCTGGCTCTCGTTCTGGCA CCTCAGCCTCCCTGGCCATCACTGGGCTTCGGTCC GAGGATGAGGCTGATTATTATTGTGCAGTTTGGG ATGACAATCTCAGAGGCTGGGTGTTCGGCGGAGG GACCGAGGTGACCGTCCTA
99	21-6M VH amino acid sequence	QVQLVQSGAEIKRPGASVKVSCKASGYIFTSFGINW VRQAPGQGLEWMGWMNSNTGDADSVQKFQGRLT MTTDPSTSTAYMELRNLRSDDTAVYYCARMNFFGS QWEVNWFDPWGQGTLITVSS
100	21-6M VL amino acid sequence	QSVVTQPPSASGTPGQRITISCSGSRSNVERNSVYWY QQLRGTAPKLLIYMSNQRPSGVPDRFSGSRSGTSASL

		AITGLRSEDEADYYCAVWDDNLRGWVFGGGTEVT VL

Table 26. Amino Acid and Nucleotide Sequences of Antibody 22-14F

SEQ ID NO	DESCRIPTION	SEQUENCE
101	22-14F VH nucleotide sequence	CCAGGTGCACCTGGTGCAGTCTGGGGCTGAGATT AAGAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCA AGGCGTCTGGATACACTTTCACCAGCTTTGGTATC AACTGGGTGCGACAGGCCCCTGGACAAGGGCTTG AGTGGATGGGATGGATGAACTCCAACAGTGGTGA TGCGGACTCTGCACAGAAGTTCCAGGGCAGACTC ACTATGACCACCGACACCTCCACAAGTACAGCCT ACATGGAGCTGAGGAATCTGAGATCTGAGGACAC GGCCGTATATTATTGCGCGAGAATGAATTTCCGTG GTTCGAAGTGGGAGGTGAACTGGTTCGACCCCTG GGGCCAGGGAACCCTGATCACCGTCTCCTCA
102	22-14F VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTG GAAGCAGGTCCAACGTCGAAAGAAATTTTGTTTA CTGGTACCAGCAACTCCCAGGAACGGCCCCCAAA CTTCTCATCTATATGAACAGTCAGCGGCCCTCAGG GGTCCCTGACCGATTCTCTGGCTCTCGTTCTGGCA CCTCAGCCTCCCTGGCCATCACTGGGCTTCGGTCC GAGGATGAGGCTGACTATTATTGTGCAACTTGGG ATGACAATCTGAGAGGCTGGGTGTTCGGCGGAGG GACCAAGGTGACCGTCCTA
103	22-14F VH amino acid sequence	QVHLVQSGAEIKRPGASVKVSCKASGYTFTSFGINW VRQAPGQGLEWMGWMNSNSGDADSAQKFQGRLT MTTDTSTSTAYMELRNLRSEDTAVYYCARMNFRGS

		KWEVNWFDPWGQGTLITVSS
104	22-14F VL amino acid sequence	QSVVTQPPSASGTPGQRVTISCSGSRSNVERNFVYW YQQLPGTAPKLLIYMNSQRPSGVPDRFSGSRSGTSAS LAITGLRSEDEADYYCATWDDNLRGWVFGGGTKV TVL

Table 27. Amino Acid and Nucleotide Sequences of Antibody 24-5D

SEQ ID NO	DESCRIPTION	SEQUENCE
105	24-5D VH nucleotide sequence	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTA AGAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAA GGCGTCTGGATACACCTTCACCAGATTTGGTATCA ACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGA GTGGATGGGATGGATGAACTCCAACACTGGTGAT GCGGACTCTGCACAGAAGTTCCAGGGCAGACTCA GTATGACCACCGACACCTCCACAAGTACAGCCTA CATGGAGCTGAAGAGTCTGACATCTGACGACACG GCCGTATATTTTTGCGCGAGAATGAATTACTGGGG GTCGAAGTGGGACGTGAACTGGTTCGACCCCTGG GGCCAGGGAACCCTGATCACCGTCTCCTCA
106	24-5D VL nucleotide sequence	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGG GACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTG GAAGAAGGACCAACGTGGAAAGAAATTCTGTCTA CTGGTACCAGCAGCTCCCAGGAACGGCCCCCAAA CTTCTCATCTATATGAGCAATAAGCGCCCCTCAGG GGTCCCTGACCGATTCTCCGGCTCTCGTTCTGGCA CCTCTGCCTCCCTGGCCATCACTGGGCTTCGGTCC GAGGATGAGGCTGATTATTATTGTGCAGTTTGGG ATGACAATCTGAGAGGCTGGGTGTTCGGCGGAGG

		GACCAAGGTGACCGTCCTA
107	24-5D VH amino acid sequence	QVQLVQSGAEIKRPGASVKVSCKASGYTFTRFGINW VRQAPGQGLEWMGWMNSNTGDADSAQKFQGRLS MTTDTSTSTAYMELKSLTSDDTAVYFCARMNYWGS KWDVNWFDPWGQGTLITVSS
108	24-5D VL amino acid sequence	QSVVTQPPSASGTPGQRVTISCSGRRTNVERNSVYW YQQLPGTAPKLLIYMSNKRPSGVPDRFSGSRSGTSAS LAITGLRSEDEADYYCAVWDDNLRGWVFGGGTKV TVL

Table 28. Amino Acid Sequences of twenty-seven antibodies complementarity-determining regions (CDRs)

SEQ ID NO	DESCRIPTION	SEQUENCE
109-111	15-6J CDR Heavy chain sequence (CDRH)	CDRH1: GFSFRHYGMH CDRH2: VVWHDGRETHYGDSV CDRH3: DRGSDEPIDY SEQ ID Nos: 109-111 (CDR 1, CDR2, CDR3 respectively)
112-114	15-6J CDR Light chain sequence (CDRL)	CDRL1: TLRSDVTVSPWTY CDRL2: KSDSDKYQGS CDRL3: QTWHTTTV SEQ ID Nos: 112-114 (CDR 1, CDR2, CDR3 respectively)

115-117	23-12O CDR Heavy chain sequence (CDRH)	CDRH1: GFSFRHYGMH CDRH2: VVWHDGRETHYGDSV CDRH3: DRGSDEPIDY SEQ ID Nos: 115-117 (CDR 1, CDR2, CDR3 respectively)
118-120	23-12O CDR Light chain sequence (CDRL)	CDRL1: TLRSDVTVSPWTY CDRL2: KSDSDKYQGS CDRL3: QTWHTSTV SEQ ID Nos: 118-120 (CDR 1, CDR2, CDR3 respectively)
121-123	31-2C CDR Heavy chain sequence (CDRH)	CDRH1: GFSFRYYGFH CDRH2: VVWHDGRETHYGDSV CDRH3: DRGSDEPIDY SEQ ID Nos: 121-123 (CDR 1, CDR2, CDR3 respectively)
124-126	31-2C CDR Light chain sequence (CDRL)	CDRL1: TLRSGLTVSPWIY CDRL2: KSDSENYRGS CDRL3: QTWHTSTV SEQ ID Nos: 124-126 (CDR 1, CDR2, CDR3 respectively)
127-129	15-20G CDR Heavy chain sequence (CDRH)	CDRH1: GFSFRYYGFH CDRH2: VVWHDGRETHYGDSV

		CDRH3: DRGSDEPIDY SEQ ID Nos: 127-129 (CDR 1, CDR2, CDR3 respectively)
130-132	15-20G CDR Light chain sequence (CDRL)	CDRL1: TLRSDLTVSPWIY CDRL2: KSDSNNYHGS CDRL3: QTWHTTTV SEQ ID Nos: 130-132 (CDR 1, CDR2, CDR3 respectively)
133-135	4-22O CDR Heavy chain sequence (CDRH)	CDRH1: GFPFRYYGFH CDRH2: VVWHNGRETYYEDSV CDRH3: DRGSDEPIDY SEQ ID Nos: 133-135 (CDR 1, CDR2, CDR3 respectively)
136-138	4-22O CDR Light chain sequence (CDRL)	CDRL1: TLRSDLTVGPYWMY CDRL2: KSDSEKYQGS CDRL3: QTWHANTV SEQ ID Nos: 136-138 (CDR 1, CDR2, CDR3 respectively)
139-141	6-20C CDR Heavy chain sequence (CDRH)	CDRH1: GFSFRRFGMH CDRH2: VVWHDGRETHYGDSV CDRH3: DPGQDEAIDY SEQ ID Nos: 139-141 (CDR 1, CDR2, CDR3 respectively)

142-144	6-20C CDR Light chain sequence (CDRL)	CDRL1: TLHSGLTVGPYWIY CDRL2: KSDSEEYRAS CDRL3: MTWHTNKV SEQ ID Nos: 142-144 (CDR 1, CDR2, CDR3 respectively)
145-147	J-5N CDR Heavy chain sequence (CDRH)	CDRH1: GFSLRSFGMH CDRH2: VIWPRRSQIQYADSV CDRH3: DPGEDNPIDY SEQ ID Nos: 145-147 (CDR 1, CDR2, CDR3 respectively)
148-150	J-5N CDR Light chain sequence (CDRL)	CDRL1: TFLSGINVGPYWIY CDRL2: KSDSDKHQGS CDRL3: MIWHVSGV SEQ ID Nos: 148-150 (CDR 1, CDR2, CDR3 respectively)
151-153	F-8C CDR Heavy chain sequence (CDRH)	CDRH1: GFSLKSYGIH CDRH2: VIWPRRDTQYADSV CDRH3: DRGEDNPIDF SEQ ID Nos: 151-153 (CDR 1, CDR2, CDR3 respectively)
154-156	F-8C CDR Light chain sequence (CDRL)	CDRL1: TLLSGINVGPYWIY CDRL2: RSDSDEEQGS

		CDRL3: MIWHRTGV SEQ ID Nos: 154-156 (CDR 1, CDR2, CDR3 respectively)
157-159	B-21J CDR Heavy chain sequence (CDRH)	CDRH1: GFSFRHYGMH CDRH2: VIWHNGRDREYADSV CDRH3: DRGEDEPIDF SEQ ID Nos: 157-159 (CDR 1, CDR2, CDR3 respectively)
160-162	B-21J CDR Light chain sequence (CDRL)	CDRL1: TLRSGLSAGPKWIY CDRL2: KSDSEERRSS CDRL3: AIWHSNVV SEQ ID Nos: 160-162 (CDR 1, CDR2, CDR3 respectively)
163-165	J-8G CDR Heavy chain sequence (CDRH)	CDRH1: GFSFRHYGMH CDRH2: VIWHNGRDKDYADSV CDRH3: DRGEDEPIDF SEQ ID Nos: 163-165 (CDR 1, CDR2, CDR3 respectively)
166-168	J-8G CDR Light chain sequence (CDRL)	CDRL1: TLRSGLNVGPYWIY CDRL2: KSDSEKRRSS CDRL3: AIWHSNAV SEQ ID Nos: 166-168 (CDR 1, CDR2, CDR3 respectively)

169-171	9-5L CDR Heavy chain sequence (CDRH)	CDRH1: GFTLKRYGIH CDRH2: VTWHDGNIYYADSV CDRH3: DAGQNAPIDL SEQ ID Nos: 169-171 (CDR 1, CDR2, CDR3 respectively)
172-174	9-5L CDR Light chain sequence (CDRL)	CDRL1: TLPSGINVATHWIY CDRL2: KSDSDIQHGS CDRL3: MIWYSTAV SEQ ID Nos: 172-174 (CDR 1, CDR2, CDR3 respectively)
175-177	2-20G CDR Heavy chain sequence (CDRH)	CDRH1: GFTFPNAWFN CDRH2: RIKSHSDGGTADYAAPV CDRH3: LEIYHPVDV SEQ ID Nos: 175-177 (CDR 1, CDR2, CDR3 respectively)
178-180	2-20G CDR Light chain sequence (CDRL)	CDRL1: RSSHSLPRDDEYSYLN CDRL2: RVSKRDS CDRL3: MQGTYWPGT SEQ ID Nos: 178-180 (CDR 1, CDR2, CDR3 respectively)
181-183	3-17I CDR Heavy chain sequence (CDRH)	CDRH1: GFTFITAWMT CDRH2: LIKSGNDGGAIEYAAPV

		CDRH3: NDVALVWGVTPPLLL SEQ ID Nos: 181-183 (CDR 1, CDR2, CDR3 respectively)
184-186	3-17I CDR Light chain sequence (CDRL)	CDRL1: TLSSGHGNYPVA CDRL2: NADGSHIKGA CDRL3: QTWAPGW SEQ ID Nos: 184-186 (CDR 1, CDR2, CDR3 respectively)
187-189	F-18D CDR Heavy chain sequence (CDRH)	CDRH1: GFVFTTAWMN CDRH2: RIKSKNEAETTDYAAPV CDRH3: LETYYESDF SEQ ID Nos: 187-189 (CDR 1, CDR2, CDR3 respectively)
190-192	F-18D CDR Light chain sequence (CDRL)	CDRL1: RSSQSLAEREEDILLN CDRL2: RVSKRES CDRL3: MQRTHWPQT SEQ ID Nos: 190-192 (CDR 1, CDR2, CDR3 respectively)
193-195	41-18O CDR Heavy chain sequence (CDRH)	CDRH1: GFTFNHDWMT CDRH2: NIIODGSETYYVDSV CDRH3: GRVSMDV SEQ ID Nos: 193-195 (CDR 1, CDR2, CDR3 respectively)

196-198	41-18O CDR Light chain sequence (CDRL)	CDRL1: SGSSSNIGSNTVN CDRL2: TDNQRPS CDRL3: AARDGSLDVW SEQ ID Nos: 196-198 (CDR 1, CDR2, CDR3 respectively)
199-201	18-11C CDR Heavy chain sequence (CDRH)	CDRH1: GYTFTSFGIN CDRH2: WMNSNSGDADSAQKF CDRH3: MNFRGSKWEVNWFDP SEQ ID Nos: 199-201 (CDR 1, CDR2, CDR3 respectively)
202-204	18-11C CDR Light chain sequence (CDRL)	CDRL1: SGSRSNVERNFVY CDRL2: MNSQRPS CDRL3: ATWDDNLRGW SEQ ID Nos: 202-204 (CDR 1, CDR2, CDR3 respectively)
205-207	22-14F CDR Heavy chain sequence (CDRH)	CDRH1: GYTFTSFGIN CDRH2: WMNSNSGDADSAQKF CDRH3: MNFRGSKWEVNWFDP SEQ ID Nos: 205-207 (CDR 1, CDR2, CDR3 respectively)
208-210	22-14F CDR Light chain sequence (CDRL)	CDRL1: SGSRSNVERNFVY CDRL2: MNSQRPS

		CDRL3: ATWDDNLRGW SEQ ID Nos: 208-210 (CDR 1, CDR2, CDR3 respectively)
211-213	20-2D CDR Heavy chain sequence (CDRH)	CDRH1: GYTFTRFGIN CDRH2: WMNSNSGNADSAQKF CDRH3: MNYRGSKWEINWFDP SEQ ID Nos: 211-213 (CDR 1, CDR2, CDR3 respectively)
214-216	20-2D CDR Light chain sequence (CDRL)	CDRL1: SGSRSNVQRNFVY CDRL2: MNNNRPS CDRL3: ATWDDNLRGW SEQ ID Nos: 214-216 (CDR 1, CDR2, CDR3 respectively)
217-219	36-21L CDR Heavy chain sequence (CDRH)	CDRH1: GYTFTGFGIN CDRH2: WMNSNTGDADSAQKF CDRH3: MNFLGSKWEVNWFDP SEQ ID Nos: 217-219 (CDR 1, CDR2, CDR3 respectively)
220-222	36-21L CDR Light chain sequence (CDRL)	CDRL1: RSSHSLPRDDEYSYLN CDRL2: RVSKRDS CDRL3: MQGTYWPGT SEQ ID Nos: 220-222 (CDR 1, CDR2, CDR3 respectively)

223-225	36-19H CDR Heavy chain sequence (CDRH)	CDRH1: GYIFTNFGIN CDRH2: WMNSKYGNADSAHKF CDRH3: MNYRDSKWDVNWFDP SEQ ID Nos: 223-225 (CDR 1, CDR2, CDR3 respectively)
226-228	36-19H CDR Light chain sequence (CDRL)	CDRL1: SGSRSNVERNFVY CDRL2: MNNQRPS CDRL3: AVWDDNLRGW SEQ ID Nos: 226-228 (CDR 1, CDR2, CDR3 respectively)
229-231	21-6M CDR Heavy chain sequence (CDRH)	CDRH1: GYIFTSFGIN CDRH2: WMNSNTGDADSVQKF CDRH3: MNFFGSQWEVNWFDP SEQ ID Nos: 229-231 (CDR 1, CDR2, CDR3 respectively)
232-234	21-6M CDR Light chain sequence (CDRL)	CDRL1: SGSRSNVERNSVY CDRL2: MSNQRPS CDRL3: AVWDDNLRGW SEQ ID Nos: 232-234 (CDR 1, CDR2, CDR3 respectively)
235-237	24-5D CDR Heavy chain sequence (CDRH)	CDRH1: GYTFTRFGIN CDRH2: WMNSNTGDADSAQKF

		CDRH3: MNYWGSKWDVNWFDP SEQ ID Nos: 235-237 (CDR 1, CDR2, CDR3 respectively)
238-240	24-5D CDR Light chain sequence (CDRL)	CDRL1: SGRRTNVERNSVY CDRL2: MSNKRPS CDRL3: AVWDDNLRGW SEQ ID Nos: 238-240 (CDR 1, CDR2, CDR3 respectively)
241-243	12-14G CDR Heavy chain sequence (CDRH)	CDRH1: GYTFTNYGVN CDRH2: WMNTNSGDTGYAQKF CDRH3: AYFFDSWNKGNWFDP SEQ ID Nos: 241-243 (CDR 1, CDR2, CDR3 respectively)
244-246	12-14G CDR Light chain sequence (CDRL)	CDRL1: SGGSSNLGRSYIY CDRL2: KNSQRPS CDRL3: AAWDDSLSGSW SEQ ID Nos: 244-246 (CDR 1, CDR2, CDR3 respectively)
247-249	2-8M CDR Heavy chain sequence (CDRH)	CDRH1: GGYVTIKDNYWV CDRH2: SMSYSGNAYYNPSL CDRH3: RSAAAGGGNEWFDP SEQ ID Nos: 247-249 (CDR 1, CDR2, CDR3 respectively)

250-252	2-8M CDR Light chain sequence (CDRL)	CDRL1: SGSTFNIGNNYVS CDRL2: DNDKRPS CDRL3: ATWDNRLDAV SEQ ID Nos: 250-252 (CDR 1, CDR2, CDR3 respectively)
253-255	6-8N CDR Heavy chain sequence (CDRH)	CDRH1: GFAFTTAWMT CDRH2:LIKSTNDGGSIDYAAPV CDRH3: NDVVRLRGVTPPILL SEQ ID Nos: 253-255 (CDR 1, CDR2, CDR3 respectively)
256-258	6-8N CDR Light chain sequence (CDRL)	CDRL1: TLSSGHHSYPVA CDRL2: NGDGSHTKGDG CDRL3: QTWATGW SEQ ID Nos: 256-258 (CDR 1, CDR2, CDR3 respectively)
259-261	5-14N CDR Heavy chain sequence (CDRH)	CDRH1: GYIFTNFGIN CDRH2: WMNSRTGDADSAQNF CDRH3: MNFLGSRWEVNWFDP SEQ ID Nos: 259-261 (CDR 1, CDR2, CDR3 respectively)
262-264	5-14N CDR Light chain sequence (CDRL)	CDRL1: SGSRSNVERNFFY CDRL2: MNSQRPAG

		CDRL3: ATWDDNLRGW SEQ ID Nos: 262-264 (CDR 1, CDR2, CDR3 respectively)
265-267	11-19C CDR Heavy chain sequence (CDRH)	CDRH1: GYIFTSFGIN CDRH2: WMNSNTGDADSLQKF CDRH3: MNFHGSRWDVNWFDP SEQ ID Nos: 265-267 (CDR 1, CDR2, CDR3 respectively)
268-270	11-19C CDR Light chain sequence (CDRL)	CDRL1: SGSGSNVERNSVY CDRL2: MSNRPRSG CDRL3: AVWDDSLRGW SEQ ID Nos: 268-270 (CDR 1, CDR2, CDR3 respectively)

[00118] One aspect of the present disclosure features the new antibodies specific to SSEA-4. The anti-SSEA-4 antibody binds to Neu5Acα2→ 3Galβ1→ 3GalNAcβ1→ 3Galα 1→ 4Galβ1→ 4Glcβ1.

[00119] One aspect of the present disclosure features the new antibodies specific to SSEA-3. The anti-SSEA-3 antibody binds to 2Galβ1→ 3GalNAcβ1→ 3Galα1→ 4Galβ1→ 4Glcβ1.

[00120] One aspect of the present disclosure features the new antibodies specific to Globo H. The anti-Globo H antibody binds to Fucα1→2 Galβ1→3 GalNAcβ1→3 Galα1→4 Galβ1 →4 Glc.

[00121] Any of the antibodies described herein can be a full length antibody or an antigen-binding fragment thereof. In some examples, the antigen binding fragment is a Fab fragment, a $F(ab')_2$ fragment, or a single-chain Fv fragment. In some examples, the antigen binding fragment is a Fab fragment, a $F(ab')_2$ fragment, or a single-chain Fv fragment. In some examples, the antibody is a human antibody, a chimeric antibody, or a single-chain antibody.

[00122] Any of the antibodies described herein has one or more characteristics of: (a) is a recombinant antibody, a monoclonal antibody, a chimeric antibody, a human antibody, an antibody fragment, a bispecific antibody, a monospecific antibody, a monovalent antibody, an IgG_1 antibody, an IgG_2 antibody, or derivative of an antibody; (b) is a human, murine, or chimeric antibody, antigen-binding fragment, or derivative of an antibody; (c) is a single-chain antibody fragment, a multibody, a Fab fragment, and/or an immunoglobulin of the IgG, IgM, IgA, IgE, IgD isotypes and/or subclasses thereof; (d) has one or more of the following characteristics: (i) mediates ADCC and/or CDC of cancer cells; (ii) induces and/or promotes apoptosis of cancer cells; (iii) inhibits proliferation of target cells of cancer cells; (iv) induces and/or promotes phagocytosis of cancer cells; and/or (v) induces and/or promotes the release of cytotoxic agents; (e) specifically binds the tumor-associated carbohydrate antigen, which is a tumor-specific carbohydrate antigen; (f) does not bind an antigen expressed on non-cancer cells, non-tumor cells, benign cancer cells and/or benign tumor cells; and/or (g) specifically binds a tumor-associated carbohydrate antigen expressed on cancer stem cells and on normal cancer cells.

[00123] Preferably the binding of the antibodies to their respective antigens is specific. The term "specific" is generally used to refer to the situation in which one member of a binding pair will not show any significant binding to molecules other than its specific binding partner (s) and e.g. has less than about 30%, preferably 20%, 10%, or 1 % cross-reactivity with any other molecule other than those specified herein.

Immunization of Host Animals and Hybridoma Technology

[00124] In one embodiment, the present invention provides for a method for making a hybridoma that expresses an antibody that specifically binds to a carbohydrate antigen (e.g., Globo H). The method contains the following steps: immunizing an animal with a composition that includes a carbohydrate antigen (e.g., Globo H); isolating splenocytes from the animal; generating hybridomas from the splenocytes; and selecting a hybridoma that

produces an antibody that specifically binds to Globo H. Kohler and Milstein, Nature, 256: 495, 1975. Harlow, E. and Lane, D. Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1988.

[00125] In one embodiment, carbohydrate antigen is used to immunize mice subcutaneously. One or more boosts may or may not be given. The titers of the antibodies in the plasma can be monitored by, e.g., ELISA (enzyme-linked immunosorbent assay) or flow cytometry. Mice with sufficient titers of anti-carbohydrate antigen antibodies are used for fusions. Mice may or may not be boosted with antigen 3 days before sacrifice and removal of the spleen. The mouse splenocytes are isolated and fused with PEG to a mouse myeloma cell line. The resulting hybridomas are then screened for the production of antigen-specific antibodies. Cells are plated, and then incubated in selective medium. Supematants from individual wells are then screened by ELISA for human anti-carbohydrate antigen monoclonal antibodies. The antibody secreting hybridomas are replated, screened again, and if still positive for anti-carbohydrate antigen antibodies, can be subcloned by limiting dilution.

[00126] Exemplary Polyclonal antibodies against the anti-Globo series antigens antibodies may be prepared by collecting blood from the immunized mammal examined for the increase of desired antibodies in the serum, and by separating serum from the blood by any conventional method. Polyclonal antibodies include serum containing the polyclonal antibodies, as well as the fraction containing the polyclonal antibodies may be isolated from the serum.

[00127] Polyclonal antibodies are generally raised in host animals (e.g., rabbit, mouse, horse, or goat) by multiple subcutaneous (sc) or intraperitoneal (ip) injections of the relevant antigen and an adjuvant. It may be useful to conjugate the relevant antigen to a protein that is immunogenic in the species to be immunized, e.g., keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, or soybean trypsin inhibitor using a bifunctional or derivatizing agent, for example, maleimidobenzoyl sulfosuccinimide ester (conjugation through cysteine residues), N-hydroxysuccinimide (through lysine residues), glutaraldehyde, succinic anhydride, $SOCl_2$, etc.

[00128] Any mammalian animal may be immunized with the antigen for producing the desired antibodies. In general, animals of Rodentia, Lagomorpha, or Primates can be used.

Animals of Rodentia include, for example, mouse, rat, and hamster. Animals of Lagomorpha include, for example, rabbit. Animals of Primates include, for example, a monkey of Catarrhini (old world monkey) such as Macaca fascicularis, rhesus monkey, baboon, and chimpanzees.

[00129] Methods for immunizing animals with antigens are known in the art. Intraperitoneal injection or subcutaneous injection of antigens is a standard method for immunization of mammals. More specifically, antigens may be diluted and suspended in an appropriate amount of phosphate buffered saline (PBS), physiological saline, etc. If desired, the antigen suspension may be mixed with an appropriate amount of a standard adjuvant, such as Freund's complete adjuvant, made into emulsion, and then administered to mammalian animals. Animals are immunized against the antigen, immunogenic conjugates, or derivatives by combining 1 mg or 1 μg of the peptide or conjugate (for rabbits or mice, respectively) with 3 volumes of Freund's incomplete adjuvant.

[00130] Animals can be boosted until the titer plateaus by several administrations of antigen mixed with an appropriately amount of Freund's incomplete adjuvant every 4 to 21 days. Animals are boosted with 1/5 to 1/10 the original amount of peptide or conjugate in Freund's complete adjuvant by subcutaneous injection at multiple sites. Seven to 14 days later the animals are bled and the serum is assayed for antibody titer. An appropriate carrier may also be used for immunization. After immunization as above, serum is examined by a standard method for an increase in the amount of desired antibodies. Preferably, the animal is boosted with the conjugate of the same antigen, but conjugated to a different protein and/or through a different cross-linking reagent. Conjugates also can be made in recombinant cell culture as protein fusions. Also, aggregating agents such as alum are suitably used to enhance the immune response.

[00131] In some embodiments, antibodies can be made by the conventional hybridoma technology. Kohler *et al.*, Nature, 256:495 (1975). In the hybridoma method, a mouse or other appropriate host animal, such as a hamster or rabbit, is immunized as hereinabove described to elicit lymphocytes that produce or are capable of producing antibodies that can specifically bind to the protein used for immunization. Alternatively, lymphocytes may be immunized in vitro.

[00132] To prepare monoclonal antibodies, immune cells are collected from the mammal immunized with the antigen and checked for the increased level of desired antibodies in the serum as described above, and are subjected to cell fusion. The immune cells used for cell fusion are preferably obtained from spleen. Other preferred parental cells to be fused with the above immunocyte include, for example, myeloma cells of mammalians, and more preferably myeloma cells having an acquired property for the selection of fused cells by drugs.

[00133] Preferred myeloma cells are those that fuse efficiently, support stable high-level production of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. Among these, preferred myeloma cell lines are murine myeloma lines, such as those derived from MOPC-21 and MPC-11 mouse tumors available from the Salk Institute Cell Distribution Center, San Diego, Calif. USA, and SP-2 cells available from the American Type Culture Collection, Rockville, Md. USA. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, J. Immunol., 133:3001 (1984); Brodeur *et al.*, Monoclonal Antibody Production Techniques and Applications, pp. 51-63 (Marcel Dekker, Inc., New York, 1987)).

[00134] The above immunocyte and myeloma cells can be fused according to known methods, for example, the method of Milstein *et al.* (Galfre *et al.*, Methods Enzymol. 73:3-46, 1981). Lymphocytes are fused with myeloma cells using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, Monoclonal Antibodies: Principles and Practice, pp.59-103 (Academic Press, 1986)). Resulting hybridomas obtained by the cell fusion may be selected by cultivating them in a standard selection medium, such as HAT medium (hypoxanthine, aminopterin, and thymidine containing medium). The cell culture is typically continued in the HAT medium for several days to several weeks, the time being sufficient to allow all the other cells, with the exception of the desired hybridoma (non-fused cells), to die. Then, the standard limiting dilution is performed to screen and clone a hybridoma cell producing the desired antibody.

[00135] The hybridoma cells thus prepared are seeded and grown in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells. For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture

medium for the hybridomas typically include hypoxanthine, aminopterin, and thymidine (HAT medium), which substances prevent the growth of HGPRT-deficient cells.

[00136] Culture medium in which hybridoma cells are growing is assayed for production of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay. Measurement of absorbance in enzyme-linked immunosorbent assay (ELISA), enzyme immunoassay (EIA), radioimmunoassay (RIA), and/or immunofluorescence may be used to measure the antigen binding activity of the antibody of the invention. In ELISA, the antibody of the present invention is immobilized on a plate, protein of the invention is applied to the plate, and then a sample containing a desired antibody, such as culture supernatant of antibody producing cells or purified antibodies, is applied. Then, a secondary antibody that recognizes the primary antibody and is labeled with an enzyme, such as alkaline phosphatase, is applied, and the plate is incubated. Next, after washing, an enzyme substrate, such as p-nitrophenyl phosphate, is added to the plate, and the absorbance is measured to evaluate the antigen binding activity of the sample. A fragment of the protein, such as a C-terminal or N-terminal fragment may be used in this method.

[00137] Applying any of the conventional methods, including those described above, hybridoma cells producing antibodies that bind to epitopes described herein can be identified and selected for further characterization.

[00138] After hybridoma cells are identified that produce antibodies of the desired specificity, affinity, and/or activity, the clones may be subcloned by limiting dilution procedures and grown by standard methods (Goding, Monoclonal Antibodies: Principles and Practice, pp.59-103 (Academic Press, 1986)). Suitable culture media for this purpose include, for example, D-MEM or RPMI-1640 medium. The monoclonal antibodies secreted by the subclones are suitably separated from the culture medium, ascites fluid, or serum by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

[00139] In addition, the hybridoma cells may be grown *in vivo* as ascites tumors in an animal. For example, the obtained hybridomas can be subsequently transplanted into the abdominal cavity of a mouse and the ascites are harvested.

[00140] The obtained monoclonal antibodies can be purified by, for example, ammonium sulfate precipitation, a protein A or protein G column, DEAE ion exchange chromatography, or an affinity column to which the protein of the present invention is coupled. The antibody of the present invention can be used not only for purification and detection of the protein of the present invention, but also as a candidate for agonists and antagonists of the protein of the present invention. In addition, this antibody can be applied to the antibody treatment for diseases related to the protein of the present invention.

Activity Assays

[00141] Antibodies of the invention can be characterized for their physical/chemical properties and biological functions by various assays known in the art.

[00142] Antibodies, or antigen-binding fragments, variants or derivatives thereof of the present disclosure can also be described or specified in terms of their binding affinity to an antigen. The affinity of an antibody for a carbohydrate antigen can be determined experimentally using any suitable method (see, e.g., Berzofsky *et al*, "Antibody- Antigen Interactions," In Fundamental Immunology, Paul, W. E., Ed., Raven Press: New York, N.Y. (1984); Kuby, Janis Immunology, W. H. Freeman and Company: New York, N.Y. (1992); and methods described herein). The measured affinity of a particular antibody-carbohydrate antigen interaction can vary if measured under different conditions {e.g., salt concentration, pH). Thus, measurements of affinity and other antigen-binding parameters (e.g., K_D, K_a, Ka) are preferably made with standardized solutions of antibody and antigen, and a standardized buffer.

[00143] The present antibodies or antigen-binding portions thereof have *in vitro* and *in vivo* therapeutic, prophylactic, and/or diagnostic utilities. For example, these antibodies can be administered to cells in culture, e.g., *in vitro* or *ex vivo*, or to a subject, e.g., *in vivo*, to treat, inhibit, prevent relapse, and/or diagnose cancer.

[00144] Purified antibodies can be further characterized by a series of assays including, but not limited to, N-terminal sequencing, amino acid analysis, non-denaturing size exclusion high pressure liquid chromatography (HPLC), mass spectrometry, ion exchange chromatography and papain digestion.

[00145] Where necessary, antibodies are analyzed for their biological activity. In some embodiments, antibodies of the invention are tested for their antigen binding activity. The antigen binding assays that are known in the art and can be used herein include without limitation any direct or competitive binding assays using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, fluorescent immunoassays, chemiluminescent immunoassays, nanoparticle immunoassays, aptamer immunoassays, and protein A immunoassays.

Uses

[00146] An antibody of the invention may be used in, for example, *in vitro*, *ex vivo* and *in vivo* therapeutic methods. Antibodies of the invention can be used as an antagonist to partially or fully block the specific antigen activity *in vitro*, *ex vivo* and/or *in vivo*. Moreover, at least some of the antibodies of the invention can neutralize antigen activity from other species. Accordingly, antibodies of the invention can be used to inhibit a specific antigen activity, e.g., in a cell culture containing the antigen, in human subjects or in other mammalian subjects having the antigen with which an antibody of the invention cross-reacts (e.g. chimpanzee, baboon, marmoset, cynomolgus and rhesus, pig or mouse). In one embodiment, an antibody of the invention can be used for inhibiting antigen activities by contacting the antibody with the antigen such that antigen activity is inhibited. In one embodiment, the antigen is a human protein molecule.

[00147] "Administering" is referred to herein as providing a therapeutic composition of the invention to a patient. By way of example and not limitation, composition administration, e.g., injection, may be performed by intravenous (i.v.) injection, sub- cutaneous (s.c.) injection, intradermal (i.d.) injection, intraperitoneal (i.p.) injection, or intramuscular (i.m.) injection. One or more such routes may be employed. Parenteral administration can be, for example, by bolus injection or by gradual perfusion over time. Alternatively, or concurrently, administration may be by the oral route or nasal route. Additionally, administration may also be by surgical deposition of a bolus or positioning of a medical device.

[00148] In one embodiment, an antibody of the invention can be used in a method for inhibiting an antigen in a subject suffering from a disorder in which the antigen activity is detrimental, comprising administering to the subject an antibody of the invention such that

the antigen activity in the subject is inhibited. In one embodiment, the antigen is a human protein molecule and the subject is a human subject. Alternatively, the subject can be a mammal expressing the antigen with which an antibody of the invention binds. Still further the subject can be a mammal into which the antigen has been introduced (e.g., by administration of the antigen or by expression of an antigen transgene). An antibody of the invention can be administered to a human subject for therapeutic purposes. Moreover, an antibody of the invention can be administered to a non-human mammal expressing an antigen with which the antibody cross-reacts (e.g., a primate, pig or mouse) for veterinary purposes or as an animal model of human disease. Regarding the latter, such animal models may be useful for evaluating the therapeutic efficacy of antibodies of the invention (e.g., testing of dosages and time courses of administration). Antibodies of the invention can be used to treat, inhibit, delay progression of, prevent/delay recurrence of, ameliorate, or prevent diseases, disorders or conditions associated with abnormal expression and/or activity of Globo series antigens (Globo H, SSEA-3, SSEA-4), including but not limited to cancer, muscular disorders, ubiquitin-pathway-related genetic disorders, immune/inflammatory disorders, neurological disorders, and other ubiquitin pathway-related disorders.

[00149] In certain embodiments, an immunoconjugate comprising an antibody of the invention conjugated with a cytotoxic agent is administered to the patient. In some embodiments, the immunoconjugate and/or antigen to which it is bound is/are internalized by cells expressing one or more proteins on their cell surface which are associated with Globo series antigens, resulting in increased therapeutic efficacy of the immunoconjugate in killing the target cell with which it is associated. In one embodiment, the cytotoxic agent targets or interferes with nucleic acid in the target cell. Examples of such cytotoxic agents include any of the chemotherapeutic agents noted herein (such as a maytansinoid or a calicheamicin), a radioactive isotope, or a ribonuclease or a DNA endonuclease.

[00150] Antibodies of the invention can be used either alone or in combination with other compositions in a therapy. For instance, an antibody of the invention may be co-administered with another antibody, and/or adjuvant/therapeutic agents (e.g., steroids). For instance, an antibody of the invention may be combined with an anti-inflammatory and/or antiseptic in a treatment scheme, e.g. in treating any of the diseases described herein, including cancer, muscular disorders, ubiquitin-pathway-related genetic disorders, immune/inflammatory disorders, neurological disorders, and other ubiquitin pathway-related disorders. Such

combined therapies noted above include combined administration (where the two or more agents are included in the same or separate formulations), and separate administration, in which case, administration of the antibody of the invention can occur prior to, and/or following, administration of the adjunct therapy or therapies.

[00151] An antibody of the invention (and adjunct therapeutic agent) can be administered by any suitable means, including parenteral, subcutaneous, intraperitoneal, intrapulmonary, and intranasal, and, if desired for local treatment, intralesional administration. Parenteral infusions include intramuscular, intravenous, intraarterial, intraperitoneal, or subcutaneous administration. In addition, the antibody is suitably administered by pulse infusion, particularly with declining doses of the antibody. Dosing can be by any suitable route, e.g. by injections, such as intravenous or subcutaneous injections, depending in part on whether the administration is brief or chronic.

Therapeutic Applications

[00152] Described herein are therapeutic methods that include administering to a subject in need of such treatment a therapeutically effective amount of a composition that includes one or more antibodies described herein.

[00153] In some embodiments, the subject (e.g., a human patient) in need of the treatment is diagnosed with, suspected of having, or at risk for cancer. Examples of the cancer include, but are not limited to, sarcoma, skin cancer, leukemia, lymphoma, brain cancer, lung cancer, breast cancer, oral cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, pancreas cancer, colon cancer, kidney cancer, cervix cancer, ovary cancer and prostate cancer. In some embodiments, the cancer is sarcoma, skin cancer, leukemia, lymphoma, brain cancer, lung cancer, breast cancer, ovarian cancer, prostate cancer, colon cancer, or pancreas cancer. In some preferred embodiments, the cancer is brain cancer or glioblastoma multiforme (GBM) cancer.

[00154] In preferred embodiments, the antibody is capable of targeting Globo series antigens-expressing cancer cells. In some embodiments, the antibody is capable of targeting Globo series antigens on cancer cells. In some embodiments, the antibody is capable of targeting Globo series antigens in cancers.

[00155] The treatment results in reduction of tumor size, elimination of malignant cells, prevention of metastasis, prevention of relapse, reduction or killing of disseminated cancer, prolongation of survival and/or prolongation of time to tumor cancer progression.

[00156] In some embodiments, the treatment further comprises administering an additional therapy to said subject prior to, during or subsequent to said administering of the antibodies. In some embodiments, the additional therapy is treatment with a chemotherapeutic agent. In some embodiments, the additional therapy is radiation therapy.

[00157] The methods of the invention are particularly advantageous in treating and preventing early stage tumors, thereby preventing progression to the more advanced stages resulting in a reduction in the morbidity and mortality associated with advanced cancer. The methods of the invention are also advantageous in preventing the recurrence of a tumor or the regrowth of a tumor, for example, a dormant tumor that persists after removal of the primary tumor, or in reducing or preventing the occurrence of a tumor.

[00158] In some embodiments, the methods as disclosed herein are useful for the treatment or prevention of a cancer, for example where a cancer is characterized by increased Globo H, SSEA-3 and/or SSEA-4 expression. In some embodiments the cancer comprises a cancer stem cell. In some embodiments, the cancer is a pre-cancer, and/or a malignant cancer and/or a therapy resistant cancer. In some embodiments, the cancer is a brain cancer.

[00159] The subject to be treated by the methods described herein can be a mammal, more preferably a human. Mammals include, but are not limited to, farm animals, sport animals, pets, primates, horses, dogs, cats, mice and rats. A human subject who needs the treatment may be a human patient having, at risk for, or suspected of having cancer, which include, but not limited to, sarcoma, skin cancer, leukemia, lymphoma, brain cancer, lung cancer, breast cancer, oral cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, pancreas cancer, colon cancer, kidney cancer, cervix cancer, ovary cancer and prostate cancer. A subject having cancer can be identified by routine medical examination.

[00160] "An effective amount" as used herein refers to the amount of each active agent required to confer therapeutic effect on the subject, either alone or in combination with one or more other active agents. Effective amounts vary, as recognized by those skilled in the art, depending on the particular condition being treated, the severity of the condition, the individual patient parameters including age, physical condition, size, gender and weight, the

duration of the treatment, the nature of concurrent therapy (if any), the specific route of administration and like factors within the knowledge and expertise of the health practitioner. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is generally preferred that a maximum dose of the individual components or combinations thereof be used, that is, the highest safe dose according to sound medical judgment. It will be understood by those of ordinary skill in the art, however, that a patient may insist upon a lower dose or tolerable dose for medical reasons, psychological reasons or for virtually any other reasons.

[00161] As used herein, the term “treating” refers to the application or administration of a composition including one or more active agents to a subject, who has cancer, a symptom of cancer, or a predisposition toward cancer, with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve, or affect cancer, the symptom of cancer, or the predisposition toward cancer.

[00162] "Development" or "progression" of cancer means initial manifestations and/or ensuing progression of cancer. Development of cancer can be detectable and assessed using standard clinical techniques as well known in the art. However, development also refers to progression that may be undetectable. For purpose of this disclosure, development or progression refers to the biological course of the symptoms. “Development” includes occurrence, recurrence, and onset. As used herein "onset" or “occurrence” of cancer includes initial onset and/or recurrence.

[00163] Conventional methods, known to those of ordinary skill in the art of medicine, can be used to administer the pharmaceutical composition to the subject, depending upon the type of disease to be treated or the site of the disease. This composition can also be administered via other conventional routes, e.g., administered orally, parenterally, by inhalation spray, topically, rectally, nasally, buccally, vaginally or via an implanted reservoir. The term “parenteral” as used herein includes subcutaneous, intracutaneous, intravenous, intramuscular, intraarticular, intraarterial, intrasynovial, intrasternal, intrathecal, intralesional, and intracranial injection or infusion techniques. In addition, it can be administered to the subject via injectable depot routes of administration such as using 1-, 3-, or 6-month depot injectable or biodegradable materials and methods.

[00164] Injectable compositions may contain various carriers such as vegetable oils, dimethylactamide, dimethyformamide, ethyl lactate, ethyl carbonate, isopropyl myristate, ethanol, and polyols (glycerol, propylene glycol, liquid polyethylene glycol, and the like). For intravenous injection, water soluble antibodies can be administered by the drip method, whereby a pharmaceutical formulation containing the antibody and a physiologically acceptable excipients is infused. Physiologically acceptable excipients may include, for example, 5% dextrose, 0.9% saline, Ringer's solution or other suitable excipients. Intramuscular preparations, e.g., a sterile formulation of a suitable soluble salt form of the antibody, can be dissolved and administered in a pharmaceutical excipient such as Water-for-Injection, 0.9% saline, or 5% glucose solution.

[00165] The exemplary therapeutic compositions (also referred to herein as pharmaceutical compositions) generally include a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" includes solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Supplementary active compounds can also be incorporated into the compositions. A pharmaceutical composition is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, e.g., intravenous, intradermal, subcutaneous, intramuscular, intra-arterial, oral (e.g., inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, phosphate buffered saline, tris-buffered saline, fixed oils, polyethylene glycols, glycerine, propylene glycol, or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates, or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH value can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes, or multiple dose vials made of glass or plastic.

[00166] Exemplary pharmaceutical compositions suitable for an injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous

administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL® (BASF, Parsippany, N.J.), or phosphate buffered saline (PBS). In all cases, the composition should be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, or sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[00167] Exemplary Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation include vacuum drying and freeze-drying, which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile- filtered solution thereof.

[00168] Exemplary oral compositions generally include an inert diluent or an edible carrier. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules, e.g., gelatin capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash. Pharmaceutically compatible binding agents, or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline

cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[00169] Furthermore, for oral administration, the exemplary formulations of the invention can take the form of, for example, tablets or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (e.g., pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (e.g., lactose, microcrystalline cellulose or calcium hydrogen phosphate); lubricants (e.g., magnesium stearate, talc or silica); disintegrants (e.g., potato starch or sodium starch glycolate); or wetting agents (e.g., sodium lauryl sulphate). The tablets can be coated by methods well known in the art. The compositions of the invention can be also introduced in microspheres or microcapsules, e.g., fabricated from poly-glycolic acid/lactic acid (PGLA) (see, U.S. Pat. Nos. 5,814,344; 5,100,669 and 4,849,222; PCT Publication Nos. WO 95/11010 and WO 93/07861). Liquid preparations for oral administration can take the form of, for example, solutions, syrups, emulsions or suspensions, or they can be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations can be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (e.g., sorbitol syrup, cellulose derivatives or hydrogenated edible fats); emulsifying agents (e.g., lecithin or acacia); non-aqueous vehicles (e.g., almond oil, oily esters, ethyl alcohol or fractionated vegetable oils); and preservatives (e.g., methyl or propyl-p-hydroxybenzoates or sorbic acid). The preparations can also contain buffer salts, flavoring, coloring and sweetening agents as appropriate. Preparations for oral administration can be suitably formulated to give controlled release of the active compound.

[00170] For administration by inhalation, or nasal administration the exemplary compounds/formulations can be delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

[00171] Systemic administration can also be transmucosal or transdermal. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives.

Transmucosal administration may be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art. The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

[00172] According to implementations, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to cell-specific antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Pat. No. 4,522,811, which is incorporated by reference herein.

[00173] It is advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

[00174] The pharmaceutical formulations of the invention can be delivered parenterally, i.e., by intravenous (i.v.), subcutaneous (s.c.), intraperitoneal (i.p.), intramuscular (i.m.), subdermal (s.d.), or intradermal (i.d.) administration, by direct injection, via, for example, bolus injection, continuous infusion, or gene gun (e.g., to administer a vector vaccine to a subject, such as naked DNA or RNA). Formulations for injection can be presented in unit dosage form, e.g., in ampoules or in multi-dose containers, with an added preservative. The compositions can take such forms as excipients, suspensions, solutions or emulsions in oily or aqueous vehicles, and can contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient can be in powder form for reconstitution with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

[00175] Dosage: Toxicity and therapeutic efficacy of such therapeutic compositions may be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD_{50}/ED_{50}. Therapeutic compositions which exhibit high therapeutic indices are preferred. While compounds that exhibit toxic side effects can be used, care should be taken to design a delivery system that targets such compounds to the site of affected location to minimize potential damage to uninfected cells and, thereby, reduce side effects.

[00176] Data obtained from cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage can vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the disclosure, the therapeutically effective dose can be estimated initially from cell culture assays. A dose can be formulated in animal models to achieve a circulating plasma concentration range that includes the IC_{50} (i.e., the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

[00177] In some embodiments, a therapeutically effective amount of a therapeutic composition (i.e., an effective dosage) may range from about 0.001 μg/kg to about 250 g/kg, 0.01 μg/kg to 10 g/kg, or 0.1 μg/kg to 1.0 g/kg or about or at least: 0.001, 0.002, 0.003, 0.004, 0.005, 0.006, 0.007, 0.008, 0.009; 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09;0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 125, 150, 175, 200, 225, or 250 grams or micrograms per kilogram of patient body weight, or any range between any of the numbers listed herein, or other ranges that would be apparent and understood by artisans without undue experimentation. The skilled artisan will appreciate that certain factors can influence the dosage and timing required to

effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health or age of the subject, and other diseases present.

[00178] In other embodiments, a therapeutically effective amount of Globo series moiety in the therapeutic composition (i.e., an effective dosage) may range from about 0.001 μg/kg to about 250 g/kg, 0.01 μg/kg to 10 g/kg, or 0.1 μg/kg to 1.0 g/kg or about or at least: 0.001, 0.002, 0.003, 0.004, 0.005, 0.006, 0.007, 0.008, 0.009; 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09;0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 125, 150, 175, 200, 225, or 250 grams or micrograms per kilogram of patient body weight, or any range between any of the numbers listed herein, or other ranges that would be apparent and understood by artisans without undue experimentation. The skilled artisan will appreciate that certain factors can influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health or age of the subject, and other diseases present. In one embodiment, the immunogenically effective amount of a pharmaceutically acceptable carrier comprising the vaccine ranges from about 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 0.55, 0.6, 0.65, 0.7, 0.75, 0.8, 0.85, 0.9, 0.95, 1.0, 1.25, 1.5, 1.75, 2.0, 2.25, 2.5, 2.75, 3.0, 3.25, 3.5, 3.75, 4.0, 4.25, 4.5, 4.75 to about 5.0 μg, or any range between any of the numbers listed herein.

[00179] In some embodiments, the therapeutic compositions of the invention are administered to a subject in need thereof (e.g., one having a cancer such as breast cancer) in a method that on average extends progression free survival or overall survival over a control placebo, e.g., a phosphate buffered saline placebo, by about or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50 days, weeks, months, or years.

[00180] Without further elaboration, it is believed that one skilled in the art can, based on the above description, utilize the present invention to its fullest extent. The following specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. All publications cited herein are incorporated by reference for the purposes or subject matter referenced herein.

EXAMPLES

Example 1: Clinical Sample Collection

[00181] In order to generate anti-Globo series antigens human monoclonal antibodies, B cells were isolated from peripheral blood of vaccinated patients. After administering Globo H-KLH vaccine (OBI-822/OBI-821) in a patient of recurrent ovarian cancer, blood samples were collected for the following analyzing procedure.

Example 2: Human Single B Cell Sorting and Cultivation

[00182] $IgD^-IgM^-IgA^-$ memory B cells were freshly isolated from human peripheral blood and plated into 384-well tissue culture plates at a density of one cell per well using fluorescence-activated cell sorter. The sorted B cells were stimulated to secrete IgG and incubated for several days. After incubation, B cell lysates and culture supernatants were collected separately.

Example 3: Amplification of Antibody Genes

[00183] In obtaining Globo H, SSEA-3 or SSEA-4 binding clones, genes encoding Ig VH, Ig Vκ or Ig Vλ are recovered from B cell lysates using RT-PCR and cloned into IgG expression vectors. Recombinant antibodies are expressed by transfection of mammalian cells and used to confirm the binding specificities or to implement other functional assays.

Example 4: Globo H, SSEA-3 and SSEA-4 Binding Assays

[00184] To screen for anti-Globo series antigen human antibodies, the culture supernatants containing secreted IgG were assayed for Globo H, SSEA-3 or SSEA-4 binding specificities using ELISA.

[00185] 1. Reagent/Buffer Preparation:

A. Globo H-ceramide, Globo H-lipid, SSEA-3-ceramide, SSEA-3-lipid, SSEA-4-ceramide and SSEA-4-lipid powder was dissolved in ethanol and storage at -20°C. 20 μg of antigen was added into 5 mL ethanol and mixed gently.

B. Adding 50 μL of coating antigen (0.2 μg of antigen/well) into each well. Covering, labeling and incubating at room temperature for overnight.

C. Adding 100 μL/well of Blocking Buffer (Sigma, Cat#B6429) into each well and incubating at room temperature for 30 minutes.

[00186] 2. Addition of Culture Supernatants to Antigen-Coated Plate

A. After the blocking procedure, washing three times with 200 μL PBST Wash Buffer.

B. Transfering 50 μL of all diluted test samples to corresponding wells in the Antigen-Coated/Blocked Plate.

C. Incubating the plate at room temperature for 1 hour.

D. After incubating, washing three times with 200 μL PBST Wash Buffer.

[00187] 3. Addition of Secondary Antibody to Antigen-Coated Plate

A. Pipeting 25 μL of Secondary Antibody to 4975 μL of Blocking Buffer and mixing gently. (Goat anti-human IgG-AP for IgG antibody detection)

B. Adding 50 μL of Secondary Antibody Solution and incubating at room temperature for 45 minutes.

C. After incubating, washing four times with 200 μL Wash Buffer.

D. Adding 100 μL Substrate Solution (Sigma, Cat#P7998) and incubating for 20 minutes at 37°C.

E. Stop reaction by adding 50 μL of Stop Solution (Sigma, Cat#A5852), mixing well and then reading the absorbance at 405 nm on the ELISA Plate Reader.

[00188] 4. Data Analysis

A. The well that gives a reading above the cutoff value is defined as the potential Globo series antigen binding clone.

B. Cutoff value = X + 0.1. (X is the mean OD value of negative control).

C. Controls were treated the same as test samples. The differences are that the positive control has primary Abs known positive Ab (anti-Globo H, anti-SSEA-3, anti-SSEA-4 antibody or no IgG added as the primary antibody is negative control).

D. Data were analyzed statistically by Mann-Whitney test using GraphPad Prism 5 Software.

[00189] 5. Result

[00190] **Figure 1** indicated 20-2D, 31-2C and 4-22O had better binding affinity to Globo H. **Figure 2** indicated 20-2D, 31-2C and F-8C had better binding affinity to SSEA-3. Similarly, **Figure 3** indicated 20-2D, 31-2C and F-8C had better binding affinity to SSEA-4. Furthermore, the overall binding affinity of Globo series antiges (Globo H, SSEA-3 and SSEA-4) conjugated lipids were higher than conjugated ceramides. The following table showed the Kd value of human antibody clones binding to Globo series antigens (Globo H, SSEA-3 and SSEA-4).

Table 29. The exemplary kD value of human antibodies to Globo H-ceramide and Globo H-lipid

Human Antibody	**Globo H-ceramide**	**Globo H-Lipid**
20-2D	1.7E-08 M	2.7E-09 M
31-2C	1.7E-08 M	1.3E-09 M
4-22O	7.0E-08 M	3.6E-08 M
15-6J	6.6E-08 M	3.3E-09 M
23-12O	8.1E-08 M	2.7E-08 M
36-19H	9.9E-08 M	1E-09 M
15-20G	1.6E-07 M	1.8E-08 M
F-8C	6.1E-07 M	2.0E-09 M
21-6M	3.8E-07 M	5.8E-09 M

24-5D	4.6E-07 M	1.3E-08 M

Table 30. The exemplary kD value of human antibodies to SSEA-3-ceramide and SSEA-3-lipid

Human Antibody	**SSEA-3-ceramide**	**SSEA-3-Lipid**
20-2D	2.0E-08 M	2.4E-09 M
31-2C	1.6E-08 M	2.1E-09 M
4-22O	3.3E-08 M	9.2E-09 M
15-6J	8.8E-08 M	4.3E-09 M
23-12O	9.4E-08 M	2.7E-08 M
36-19H	>2.6E-07 M	3.2E-08 M
15-20G	2.6E-07 M	2.5E-08 M
F-8C	2.6E-08 M	2.1E-09 M
21-6M	>2.6E-07 M	3.7E-07 M
24-5D	>2.6E-07 M	1.2E-07 M

Table 31. The exemplary kD value of human antibodies to SSEA-4-ceramide and SSEA-4-lipid

Human Antibody	SSEA-4-ceramide	SSEA-4-Lipid
20-2D	5.2 E-08 M	3.6E-09 M
31-2C	2.2E-08 M	4.0E-09 M
4-22O	4.4E-08 M	3.1E-09 M
15-6J	7.0E-08 M	4.3E-09 M
23-12O	1.2E-07 M	1.1E-08 M
36-19H	>1.2E-07 M	1.6 E-08 M
15-20G	>1.2E-07 M	1.6E-07 M
F-8C	8.8E-08 M	2.9E-09 M
21-6M	>1.2E-07 M	>5.7E-07 M
24-5D	>1.2E-07 M	5.7E-07 M

[00191] Unless defined otherwise, all technical and scientific terms and any acronyms used herein have the same meanings as commonly understood by one of ordinary skill in the art in the field of this invention. Although any compositions, methods, kits, and means for communicating information similar or equivalent to those described herein can be used to practice this invention, the preferred compositions, methods, kits, and means for communicating information are described herein.

[00192] All references cited herein are incorporated herein by reference to the full extent allowed by law. The discussion of those references is intended merely to summarize the assertions made by their authors. No admission is made that any reference (or a portion of

any reference) is relevant prior art. Applicants reserve the right to challenge the accuracy and pertinence of any cited reference.

LISTING OF THE SEQUENCES

SEQ ID NO	DESCRIPTION	SEQUENCE
1	2-8M VH NUCLEOTIDE SEQUENCE	CAGCTGCAGTTGCAGGAGTCGGGCCCAGGACTGGT GAAGCCTGCGGAGACCCTGTCCCTCACCTGCTCTGT CTCCGGTGGCTACGTCACCATCAAGGATAATTATTG GGTCTGGTTCCGCCAGTCCCCAGGGAAGGAGCCGG AGTGGATTGGGAGTATGTCTTATAGTGGGAATGCCT ACTACAACCCGTCCCTCAAGAGTCGAGCCAGCATTT CCATAGACCGGTACAGGAACCAGTTCTCCCTGAGGT TGACTTCTGTGACCGCCGCAGACACGTCCATGTACT ACTGTGCGAGACGATCAGCAGCAGCTGGTGGGGGG AATGAATGGTTCGACCCCTGGGGCCAAGGAGCCCTT GTCACCGTCTCCTCA
2	2-8M VL NUCLEOTIDE SEQUENCE	CAGTCTGCTTTGACGCAGCCGCCCTCAGTGTCTGCG GCCCCAGGACGGAAGGTCGACATCTCCTGCTCTGGA AGCACCTTCAATATTGGGAACAATTATGTGTCGTGG TACCGGCAGTTCCCAGGAACAGCCCCCAAACTCCTC ATTTATGACAATGATAAGCGACCCTCAGGCATTCCT GACCGATTCTCTGGCTCCAGGTTCGGCACGTCAGCC ACCCTGGGCATCACCGGACTCCAGACTGACGACGA GGCCATTTATTACTGCGCAACATGGGATAACAGACT GGATGCTGTGGTTTTCGGCGGGGGGACCGAGTTGAT CGTCCTT
3	2-8M VH AMINO ACID SEQUENCE	QLQLQESGPGLVKPAETLSLTCSVSGGYVTIKDNYWV WFRQSPGKEPEWIGSMSYSGNAYYNPSLKSRASISIDR YRNQFSLRLTSVTAADTSMYYCARRSAAAGGGNEWF DPWGQGALVTVSS
4	2-8M VL AMINO ACID SEQUENCE	QSALTQPPSVSAAPGRKVDISCSGSTFNIGNNYVSWYR QFPGTAPKLLIYDNDKRPSGIPDRFSGSRFGTSATLGIT GLQTDDEAIYYCATWDNRLDAVVFGGGTELIVL
5	6-8N VH NUCLEOTIDE SEQUENCE	GAGGTGCACCTGGTGGAGTCTGGGGGAGGCCTGGT AAACCCGGGGGGGTCCCTTAGACTCTCCTGTTCAGC CTCTGGCTTCGCTTTCACTACCGCCTGGATGACCTGG GCCCGCCAGGCTCCAGGGAAGGGACTGGAATGGAT TGGCCTTATTAAAAGCACAAATGATGGTGGGTCTAT AGACTACGCTGCACCCGTGCAAGGCAGATTCACCAT CTCAAGAGATGATTCAAAGAACACGATTTACCTCCA AATGAGCAGCCTCAAAGCCGAGGACTCAGCCGTCT ACTATTGTGCCACAAACGATGTTGTTCGGCTTCGAG

		GGGTTACCCCCCCCATACTTCTGTGGGGCCAGGGGA CCCTGATCACCGTCTCCTCA
6	6-8N VL NUCLEOTIDE SEQUENCE	CAGCTTGTACTGACTCAATCGCCCTCAACCTCTGCCT CCCTGGGAGCCCCGGTCACACTCACCTGCACTCTGA GCAGTGGGCACCACAGCTACCCCGTCGCATGGCATC AGAAGCACCCAGAGAAGGGCCCTCGATACTTGATG AAGATTAACGGAGATGGCAGCCACACCAAGGGGGA CGGTATCCCTGATCGCTTCTCAGGCTCCAGCTCTGG GACTGGGCGCTATCTCACCATCTCCAGCCTCCAGTC TGAGGATGAGGCTGACTATTACTGTCAGACCTGGGC CACTGGATGGGTGTTCGGCGGAGGGACCAAACTGA CCGTCCTA
7	6-8N VH AMINO ACID SEQUENCE	EVHLVESGGGLVNPGGSLRLSCSASGFAFTTAWMTW ARQAPGKGLEWIGLIKSTNDGGSIDYAAPVQGRFTISR DDSKNTIYLQMSSLKAEDSAVYYCATNDVVRLRGVTP PILLWGQGTLITVSS
8	6-8N VL AMINO ACID SEQUENCE	QLVLTQSPSTSASLGAPVTLTCTLSSGHHSYPVAWHQ KHPEKGPRYLMKINGDGSHTKGDGIPDRFSGSSSGTGR YLTISSLQSEDEADYYCQTWATGWVFGGGTKLTVL
9	2-20G VH NUCLEOTIDE SEQUENCE	GAGTTGCAGTTGGTGGAGTCTGGGGGAAAGTTGGTA AATCCGGGGGGGTCCCTGAGACTCTCATGTGCAGCC TCTGGATTCACTTTCCCTAACGCCTGGTTTAACTGGG TCCGCCAGACTCCAGGGAGGGGGCTGGAGTGGGTT GCCCGTATTAAAAGTCATTCTGACGGTGGGACAGCC GACTACGCTGCACCCGTGAAAGGCAGATTCACCGTC TCAAGGGATGATTCAGAGAACATGGTGTTTCTGCAA ATGAACCGCCTGCGTGCCGAGGACACAGCCGTTTAT TATTGTACTACCTTGGAGATTTATCACCCTGTGGAC GTCTGGGGCCAGGGGACCACGGTCGCCGTCTCCTCA
10	2-20G VL NUCLEOTIDE SEQUENCE	GATGTTGTGCTGACTCAGTCTCCACTCTCCCTGTCCG TCACCCTTGGACAGCCGGCCTCCATCTCCTGCAGGT CCAGTCACAGCCTCCCAAGAGATGATGAATACTCCT ACCTGAATTGGTTTCAGCAGAGGCCAGGCCAGTCTC CAAGGCGCCTAATTTATAGGGTTTCTAAGCGGGACT CTGGGGTCCCAGACAGATTCAGCGGCAGTGGGTCA GACACTTATTTCACACTGACAATCAGCAGGGTGGAG GCTGAGGATGTTGGAGTTTATTACTGCATGCAAGGT ACATACTGGCCCGGGACGTTCGGCCAAGGGACGAA GTTGGAAATCGAGCGA
11	2-20G VH AMINO ACID SEQUENCE	ELQLVESGGKLVNPGGSLRLSCAASGFTFPNAWFNWV RQTPGRGLEWVARIKSHSDGGTADYAAPVKGRFTVSR DDSENMVFLQMNRLRAEDTAVYYCTTLEIYHPVDVW GQGTTVAVSS
12	2-20G VL AMINO ACID SEQUENCE	DVVLTQSPLSLSVTLGQPASISCRSSHSLPRDDEYSYLN WFQQRPGQSPRRLIYRVSKRDSGVPDRFSGSGSDTYFT LTISRVEAEDVGVYYCMQGTYWPGTFGQGTKLEIER

13	3-17I VH NUCLEOTIDE SEQUENCE	GAGGTGCACCTGGTGGAGTCTGGGGGAGGCCTCGT AAACCCGGGGGGGTCCCTTAGACTCTCCTGTACAGC CTCTGGATTCACTTTCATCACCGCCTGGATGACCTG GGCCCGCCAGGCTCCAGGGAGGGGGCTGGAGTGGA TTGGACTTATTAAAAGCGGAAATGATGGTGGGGCTA TAGAGTACGCTGCACCCGTGAAAGGCAGATTCACCA TCTCAAGAGATGATTCAAGGAATATGATTTATCTAC AAATGAATAATGTCAAAGCCGAGGACGCAGCCGTC TACTATTGTGCCACAAACGATGTTGCTTTGGTTTGG GGAGTTACCCCCCCCTTGCTTCTCTGGGGCCAGGGG ACCCGGGTCACCGTCTCTTCA
14	3-17I VL NUCLEOTIDE SEQUENCE	CAACTTGTGGTGACTCAATCGCCCTCTGCCTCTGCCT CCCTGGGAGGCTCGGTCAAGCTCACCTGCACTCTGA GCAGTGGGCACGGCAACTACCCCGTCGCATGGCATC AGCTCCACCCAGCGAAGGGCCCTCGATACTTGATGA AGCTTAATGCAGATGGCAGCCACATCAAGGGGGCC GGGATCACTGATCGCTTCTCAGGCTTCAGGTCTGGG GCTGAGCGCTACCTCACCATCTCCAGCCTCCAGTCT GAAGATGAGGCTGATTATTACTGTCAGACCTGGGCC CCTGGATGGGTGCTCGGCGGAGGGACCAAGCTGAC CGTCCTA
15	3-17I VH AMINO ACID SEQUENCE	EVHLVESGGGLVNPGGSLRLSCTASGFTFITAWMTWA RQAPGRGLEWIGLIKSGNDGGAIEYAAPVKGRFTISRD DSRNMIYLQMNNVKAEDAAVYYCATNDVALVWGVT PPLLLWGQGTRVTVSS
16	3-17I VL AMINO ACID SEQUENCE	QLVVTQSPSASASLGGSVKLTCTLSSGHGNYPVAWHQ LHPAKGPRYLMKLNADGSHIKGAGITDRFSGFRSGAE RYLTISSLQSEDEADYYCQTWAPGWVLGGGTKLTVL
17	B-21J VH NUCLEOTIDE SEQUENCE	CAGGTGCAACTGGTGGAGTGGGGGGGAGGCGTGGC CCAGCCTGGGACGTCCCTGAGGCTCACCTGTGATGC GTCTGGATTCAGCTTCAGACATTATGGCATGCACTG GGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGG TGGCAGTTATCTGGCATAATGGAAGAGACAGAGAG TATGCAGACTCCGTGAAGGGCCGCTTCACCATCTCC AGAGACAATTCCAAGTACACCCTGTCTTTACAAATG AACAGCCTGACAGTCGAAGACACGGCATTATATTAC TGCGGGAGAGATCGAGGTGAAGACGAGCCGATTGA CTTTTGGGGCCAGGGAACCCTGGTCACCGTCTCTTC A
18	B-21J VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAACCGTCTTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTCTCACCTGCACCTTGC GCAGTGGCCTCAGTGCTGGTCCCAAGTGGATATACT GGTACCAGCAGAGGGCAGGGAGTCCTCCCCAATTTC TCCTGACATACAAATCAGACTCAGAAGAGCGGCGG AGCTCTGGACTCCCCAGCCGCTTCTCTGGATCCAAG GATGGCTCGGCCAATGCAGGGATTTTACTCATCTCT GGGCTCCAATCTGAAGATGAGGCAGACTATTACTGT GCGATTTGGCACAGCAACGTTGTCTTTTTCGGCGCA GGGACCAGGTTGACCGTCCTG

19	B-21J VH AMINO ACID SEQUENCE	QVQLVEWGGGVAQPGTSLRLTCDASGFSFRHYGMHW VRQAPGKGLEWVAVIWHNGRDREYADSVKGRFTISR DNSKYTLSLQMNSLTVEDTALYYCGRDRGEDEPIDFW GQGTLVTVSS
20	B-21J VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASLTCTLRSGLSAGPKWIYWY QQRAGSPPQFLLTYKSDSEERRSSGLPSRFSGSKDGSA NAGILLISGLQSEDEADYYCAIWHSNVVFFGAGTRLTV L
21	F-18D VH NUCLEOTIDE SEQUENCE	GAGGTGCGCCTGGTGGAGTCTGGGGGAGGCTTAAT AGAGCCGGGGGGGTCTCTTAGACTCTCATGTGAAGC CTCTGGATTCGTTTTCACTACCGCCTGGATGAATTGG GTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGT TGGCCGTATTAAGAGCAAAAATGAGGCTGAGACAA CAGACTACGCTGCACCCGTGAAAGGCAGATTCACCA TCTCAAGAGATGATTCAAAGGACACATTGTATCTGC AAATGAACAACCTGAAAACCGAAGACACAGCCGTC TATTATTGTACCACACTTGAGACGTATTACGAGTCC GACTTCTGGGGCCAGGGAGTCCTGGTCGCCGTCTCC TCA
22	F-18D VL NUCLEOTIDE SEQUENCE	GATGTTGTGATGACTCAGTCTCCACTCTCCCTGACC GTCACTCTTGGACAGCCGGCCTCCATCTCCTGCAGG TCTAGTCAAAGCCTCGCAGAGAGAGAAGAGGACAT CTTGTTAAACTGGTATCACCAGGGGCCAGGCCAATC TCCCAGGCGCCTAATTTATAGAGTTTCTAAGCGTGA GTCTGGGGTCCCAAATAAATTCAGCGGCAGTGTGTC AGGCACTGATTTCACCCTGAGAATCAGCAGGGTGGA GGCTGAGGATGTTGGGGTTTATTACTGCATGCAACG AACACACTGGCCTCAGACTTTTGGCCAGGGGACCAA GCTGGAGATCAGACGA
23	F-18D VH AMINO ACID SEQUENCE	EVRLVESGGGLIEPGGSLRLSCEASGFVFTTAWMNWV RQAPGKGLEWVGRIKSKNEAETTDYAAPVKGRFTISR DDSKDTLYLQMNNLKTEDTAVYYCTTLETYYESDFW GQGVLVAVSS
24	F-18D VL AMINO ACID SEQUENCE	DVVMTQSPLSLTVTLGQPASISCRSSQSLAEREEDILLN WYHQGPGQSPRRLIYRVSKRESGVPNKFSGSVSGTDFT LRISRVEAEDVGVYYCMQRTHWPQTFGQGTKLEIRR
25	J-5N VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGGAGTGGGGGGGAGGCGTGGT CCAGCCTGGGGGGTCCCTGAGACTTTGCTGTGCAGC GTCTGGATTCAGTTTAAGGAGTTTTGGCATGCACTG GGTCCGTCAGGCTCCAGGCAAGGGGCTGGAATGGG TGGCAGTTATTTGGCCCCGACGAAGTCAAATACAAT ATGCAGACTCCGTGAAGGGCCGAGTCACCATCTCCA GAGACGACTCTAGGAGTACGGTATGTCTGCAGATGA ACAGCCTGAGAGTCGAGGACACGGCTCTCTATCGCT GTGCGAGAGACCCCGGTGAGGACAATCCCATAGAT TACTGGGGCCAGGGAACCCTGGTCATCGTCTCCTCA

26	J-5N VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCTTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTCTCACCTGCACCTTCC TCAGCGGCATCAATGTTGGTCCCTACTGGATATACT GGTACCAGCAAAAGCCAGGGAGTCCTCCCCAGTTTC TCCTGAGGTACAAGTCAGACTCAGATAAGCACCAG GGCTCTGAAGTCCCCAGCCGCTTCTCTGGATCCAAA GATGCTTCGGCCAATGCAGGGATTTTACTCATCTCT GGGCTCCAGTCTGAAGATGAGGCTGACTATTACTGT ATGATCTGGCACGTCAGCGGTGTGATTTTCGGCGGA GGGACCAAGCTGACCGTCCTA
27	J-5N VH AMINO ACID SEQUENCE	QVQLVEWGGGVVQPGGSLRLCCAASGFSLRSFGMHW VRQAPGKGLEWVAVIWPRRSQIQYADSVKGRVTISRD DSRSTVCLQMNSLRVEDTALYRCARDPGEDNPIDYWG QGTLVIVSS
28	J-5N VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASLTCTFLSGINVGPYWIYWY QQKPGSPPQFLLRYKSDSDKHQGSEVPSRFSGSKDASA NAGILLISGLQSEDEADYYCMIWHVSGVIFGGGTKLTV L
29	J-8G VH NUCLEOTIDE SEQUENCE	CAGGTGCAACTGGTGGAGTGGGGGGGAGGCGTGGT CCAGCCTGGGACGTCCCTGAGACTCACCTGTGATGC GTCTGGATTCAGCTTCAGACATTATGGCATGCACTG GGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGG TGGCAGTTATCTGGCATAATGGAAGAGATAAAGACT ATGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCA GAGACAATTCCAAGTACACCCTGTCTTTACAAATGA ACAGCCTGACAGTCGAGGACACGGCATTATATTACT GTGGGAGAGATCGAGGTGAAGACGAGCCGATTGAC TTTTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA
30	J-8G VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAACCGTCTTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTCTCACCTGCACCTTGC GCAGTGGCCTCAATGTTGGTCCCTACTGGATATACT GGTACCAGCAGAAGGCAGGGAGTCCTCCCCAATTTC TCCTGAGATACAAATCAGACTCAGAAAAGCGGCGG AGCTCTGGAGTCCCCAGCCGCTTCTCTGGATCCAAA GATGCCTCGGCCAATGCAGGGATTTTACTCATCTCT GGGCTCCAGTCTGAAGATGAGGCTGACTATTATTGT GCGATTTGGCACAGCAATGCTGTCTTTTTCGGCGCA GGGACCAAGTTGACCGTCCTA
31	J-8G VH AMINO ACID SEQUENCE	QVQLVEWGGGVVQPGTSLRLTCDASGFSFRHYGMHW VRQAPGKGLEWVAVIWHNGRDKDYADSVKGRFTISR DNSKYTLSLQMNSLTVEDTALYYCGRDRGEDEPIDFW GQGTLVTVSS
32	J-8G VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASLTCTLRSGLNVGPYWIYW YQQKAGSPPQFLLRYKSDSEKRRSSGVPSRFSGSKDAS ANAGILLISGLQSEDEADYYCAIWHSNAVFFGAGTKLT VL
33	4-22O VH NUCLEOTIDE SEQUENCE	CAGGTGCAGATGGTGGAGTTTGGGGGAGGCATCTTC CAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCGCG TCTGGATTCCCCTTCAGGTACTATGGTTTCCACTGGG TCCGCCAGACTCCAGGCAAGGGGCTGGAGTGGCTG

		GCAGTTGTATGGCACAATGGAAGGGAGACATATTAT GAAGACTCCGTGAAGGGGCGATTCACCATCTCCAGA GACAATTACAAGAACACGCTGTATTTGCAAATGGAC AGCCTGAGAGTCGAGGACACGGCTGTCTATCACTGT GCGAGAGATCGTGGTAGCGACGAACCAATTGACTA CTGGGGCCAGGGAGTTTTGGTCACCGTCTCCTCA
34	4-22O VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTATCACCTGCACCTTAC GCAGTGACCTCACTGTTGGTCCCTACTGGATGTACT GGTACCAACAGAAGCCAGGGAGTCCTCCCCAATTTC TCCTGAGGTACAAGTCAGACTCCGAAAAGTATCAGG GCTCTGGAGTCCCCAGCCGCTTCTCTGGATCCAAAG ACGCTTCGGCCAATGCAGGGACTTTGCTCATCTCTG GACTCCAGTCTGAAGATGAGGCTGACTATTACTGTC AGACTTGGCACGCCAACACTGTGGTATTTGGCGGAG GGACCAAGCTGACCGTCCTA
35	4-22O VH AMINO ACID SEQUENCE	QVQMVEFGGGIFQPGGSLRLSCVASGFPFRYYGFHWV RQTPGKGLEWLAVVWHNGRETYYEDSVKGRFTISRD NYKNTLYLQMDSLRVEDTAVYHCARDRGSDEPIDYW GQGVLVTVSS
36	4-22O VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASITCTLRSDLTVGPYWMYW YQQKPGSPPQFLLRYKSDSEKYQGSGVPSRFSGSKDAS ANAGTLLISGLQSEDEADYYCQTWHANTVVFGGGTK LTVL
37	6-20C VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTCTTC CAGCCGGGGGGGTCCCTGAGACTCTCCTGTGCAGCG TCTGGATTCAGTTTCAGGAGATTTGGTATGCATTGG GTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGCT GGCAGTTGTTTGGCATGATGGAAGGGAGACACACT ATGGAGACTCCGTGAGGGGCCGATTCACCATCTCCA GAGACAACTCCATGCACATGGTGTTTTTGGACATGT ACAGCCTGAGGGTCGAGGACACGGCTCTATATCGCT GTGCGAGAGATCCTGGTCAGGACGAAGCCATTGACT ATTGGGGCCAGGGAGTCCTGGTCACCGTCTCGTCA
38	6-20C VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCTTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTCTCACCTGCACCTTAC ACAGTGGCCTCACTGTTGGTCCCTATTGGATATACT GGTTCCGGCAGAAGCCAGGGAGTCCCCCCCAGTTTC TCCTCAGGTACAAATCCGACTCAGAGGAGTACCGTG CCTCTGGAGTCCCCAGCCGCTTCTCTGGATCCAAAG ATGCTTCGGCCAACTCAGGCATTTTACTCATCTCTGG ACCACAGTCTGAAGACGAGGCTGACTATTACTGTAT GACTTGGCACACCAACAAGGTAGTCTTCGGCGGAG GGACCACACTGACCGTCCTA
39	6-20C VH AMINO ACID SEQUENCE	QVQLVESGGGVFQPGGSLRLSCAASGFSFRRFGMHWV RQAPGKGLEWLAVVWHDGRETHYGDSVRGRFTISRD NSMHMVFLDMYSLRVEDTALYRCARDPGQDEAIDYW GQGVLVTVSS

40	6-20C VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASLTCTLHSGLTVGPYWIYWF RQKPGSPPQFLLRYKSDSEEYRASGVPSRFSGSKDASA NSGILLISGPQSEDEADYYCMTWHTNKVVFGGGTTLT VL
41	12-14G VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCCAGGC TTCTGGATACACCTTCACCAACTATGGTGTCAACTG GGTGCGACAGGCCACTGGACAAGGGCTTGAGTGGA TGGGATGGATGAACACTAACAGTGGTGACACGGGT TATGCCCAGAAGTTCCAGGGCAGAGTCACCATGACC AGGGACACCTCCATAAACACAGCCTACATGGAGCT GAGCGGACTGACATCTGAGGACACGGCCGTCTATTA CTGTGCGCGAGCGTATTTTTTTGATTCGTGGAATAA GGGCAACTGGTTCGACCCCTGGGGCCAGGGAACCC CGGTCACCGTCTCCTCA
42	12-14G VL NUCLEOTIDE SEQUENCE	CAGTCTGTGCTGACTCAGGCACCCTCAGTGTCTGGG ACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTGGA GGCAGCTCCAACCTGGGAAGAAGTTATATATATTGG TACCAACAGTTCCCAGGAACGGCCCCCAGAGTCCTC ATTTATAAAAATAGTCAGCGGCCCTCAGGGGTCCCT GACCGATTCTCCGGCTCCAAGTCTGGCACCTCAGCC TCCCTGGCCATCAGTGGGCTCCGGTCCGAGGATGAG GCTCATTATTACTGTGCAGCATGGGATGACAGCCTG AGTGGGTCTTGGGTGTTCGGCGGAGGGACCAAGCTG ACCGTCCTA
43	12-14G VH AMINO ACID SEQUENCE	QVQLVQSGAEVKKPGASVKVSCQASGYTFTNYGVNW VRQATGQGLEWMGWMNTNSGDTGYAQKFQGRVTM TRDTSINTAYMELSGLTSEDTAVYYCARAYFFDSWNK GNWFDPWGQGTPVTVSS
44	12-14G VL AMINO ACID SEQUENCE	QSVLTQAPSVSGTPGQRVTISCSGGSSNLGRSYIYWYQ QFPGTAPRVLIYKNSQRPSGVPDRFSGSKSGTSASLAIS GLRSEDEAHYYCAAWDDSLSGSWVFGGGTKLTVL
45	15-6J VH NUCLEOTIDE SEQUENCE	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTTC GAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCGCG TCTGGATTCTCCTTCAGGCATTATGGTATGCACTGG GTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGCT GGCAGTTGTATGGCATGATGGAAGGGAGACACATT ATGGAGACTCCGTGAAGGGGCGATTCACCATCTCCA GAGACAATTACAAGAATACGCTGTTTTTGCAAATGG ACAGCCTGAGAGTCGAGGACACGGCTGTCTATCACT GTGCGAGAGATCGTGGTAGCGACGAACCTATTGACT ACTGGGGCCAGGGAGTTTTGGTCACCGTCTCCTCA
46	15-6J VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTATCACCTGCACCTTAC GCAGTGACGTCACTGTTAGTCCCTGGACATACTGGT ACCAACAGAAGCCAGGGAGTCCTCCCCGATTTCTCC TGAGATACAAATCAGACTCTGATAAGTATCAGGGCT CTGGAGTCCCCAGCCGCTTCTCTGGATCCAAAAATG CTTCGGCCAATGCAGCGATTTTACTCATCTCTGGGCT

		CCAGTCTGAAGATGAGGCTGACTATTACTGTCAGAC TTGGCACACCACCACTGTGGTATTTGGCGGAGGGAC CAAGCTGACCGTCCTA
47	15-6J VH AMINO ACID SEQUENCE	QVQLVEFGGGIFEPGGSLRLSCVASGFSFRHYGMHWV RQAPGKGLEWLAVVWHDGRETHYGDSVKGRFTISRD NYKNTLFLQMDSLRVEDTAVYHCARDRGSDEPIDYW GQGVLVTVSS
48	15-6J VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASITCTLRSDVTVSPWTYWYQ QKPGSPPRFLLRYKSDSDKYQGSGVPSRFSGSKNASAN AAILLISGLQSEDEADYYCQTWHTTTVVFGGGTKLTV L
49	18-11C VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG AGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCG TCTGGATACACTTTCACCAGCTTTGGTATCAACTGG GTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGAT GGGATGGATGAACTCCAACAGTGGTGATGCGGACT CTGCACAGAAGTTCCAGGGCAGACTCACTATGACCA CCGACACCTCCACAAGTACAGCCTACATGGAGCTGA GGAATCTGAGATCTGAGGACACGGCCGTATATTATT GCGCGAGAATGAATTTCCGTGGTTCGAAGTGGGAG GTGAACTGGTTCGACCCCTGGGGCCAGGGAACCCTG ATCACCGTCTCCTCA
50	18-11C VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTGGA AGCAGGTCCAACGTCGAAAGAAATTTTGTTTACTGG TACCAGCAACTCCCAGGAACGGCCCCCAAACTTCTC ATCTATATGAACAGTCAGCGGCCCTCAGGGGTCCCT GACCGATTCTCTGGCTCTCGTTCTGGCACCTCAGCCT CCCTGGCCATCACTGGGCTTCGGTCCGAGGATGAGG CTGACTATTATTGTGCAACTTGGGATGACAATCTGA GAGGCTGGGTGTTCGGCGGAGGGACCAAGGTGACC GTCCTA
51	18-11C VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKVSCKASGYTFTSFGINWV RQAPGQGLEWMGWMNSNSGDADSAQKFQGRLTMTT DTSTSTAYMELRNLRSEDTAVYYCARMNFRGSKWEV NWFDPWGQGTLITVSS
52	18-11C VL AMINO ACID SEQUENCE	QSVVTQPPSASGTPGQRVTISCSGSRSNVERNFVYWYQ QLPGTAPKLLIYMNSQRPSGVPDRFSGSRSGTSASLAIT GLRSEDEADYYCATWDDNLRGWVFGGGTKVTVL
53	20-2D VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG AGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCG TCTGGATACACCTTCACCAGGTTCGGCATCAACTGG GTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGAT GGGATGGATGAACTCCAACAGTGGTAATGCGGACT CTGCACAGAAGTTCCAGGGCAGACTCACTATGACCA CCGACACCTCCACAAGTACAGCCTACATGGAGCTGA GGAATCTAAGATCTGAGGACACGGCCGTATATTATT GCGCGAGAATGAATTACCGTGGTTCGAAGTGGGAA

		ATAAACTGGTTCGACCCCTGGGGCCAGGGAACCCTG ATCACCGTCTCCTCA
54	20-2D VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGGTCACCATTTCCTGTTCTGGT AGCAGGTCCAACGTCCAAAGAAATTTTGTTTACTGG TACCAGCAGCTCCCAGGAACGGCCCCCAAACTTCTC ATCTATATGAACAATAACCGCCCCTCAGGGGTCCCT GACCGATTCTCTGGCTCTCATTCTGGCACCTCAGCCT CCCTGGCCATCACTGGGCTTCGGTCCGAGGATGAGG CTGATTATTATTGTGCTACTTGGGATGACAATCTGA GAGGCTGGGTGTTCGGCGGAGGGACCAAGGTGACC GTCCTA
55	20-2D VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKVSCKASGYTFTRFGINWV RQAPGQGLEWMGWMNSNSGNADSAQKFQGRLTMTT DTSTSTAYMELRNLRSEDTAVYYCARMNYRGSKWEI NWFDPWGQGTLITVSS
56	20-2D VL AMINO ACID SEQUENCE	QSVVTQPPSASGTPGQRVTISCSGSRSNVQRNFVYWY QQLPGTAPKLLIYMNNNRPSGVPDRFSGSHSGTSASLA ITGLRSEDEADYYCATWDDNLRGWVFGGGTKVTVL
57	9-5L VH NUCLEOTIDE SEQUENCE	CAGGTGCACCTGGTGGAGTCTGGGGGAGACCTGGTC CAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCG TCTGGATTTACCCTCAAACGTTATGGCATTCACTGG GTCCGCCAGGCGCCAGGCAAGGGGCTGGAGTGGGT GGCAGTTACTTGGCATGATGGAAATATATACTATGC AGACTCCGTGAAGGGCCGACTCACCGTCTCCAGAGA CAGTTACAAGAACACGGTGGATCTACAAATGAACA GCCTGAAAGTCGAGGACACGGCTCTATATTACTGTG CGAGAGATGCCGGGCAAAATGCGCCCATTGACCTCT GGGGCCACGGAACCCTGGTCACCGTCTCCTCA
58	9-5L VL NUCLEOTIDE SEQUENCE	CAGGCTGTACTGACTCAGCCGTCTTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTCTCACCTGCACCTTAC CCAGTGGCATCAATGTTGCTACCCACTGGATATACT GGTACCAGCAGAAGCCTGGCAGTCCTCCCCAGTTTC TCCTGCGGTACAAATCAGACTCAGATATCCAACACG GCTCTGGAGTCCCCAGCCGCTTCTCTGGATCCAAAG ATGCTTCGGCCAATGCCGCGATTTTAGTCGTCTCTG GTCTCCAGTCTGAGGATGAGGCTGACTATTACTGTA TGATTTGGTATTCCACCGCCGTGGTTTTCGGCGGAG GGACCAAGCTGACCGTCCTG
59	9-5L VH AMINO ACID SEQUENCE	QVHLVESGGDLVQPGRSLRLSCAASGFTLKRYGIHWV RQAPGKGLEWVAVTWHDGNIYYADSVKGRLTVSRDS YKNTVDLQMNSLKVEDTALYYCARDAGQNAPIDLWG HGTLVTVSS
60	9-5L VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASLTCTLPSGINVATHWIYWY QQKPGSPPQFLLRYKSDSDIQHGSGVPSRFSGSKDASA NAAILVVSGLQSEDEADYYCMIWYSTAVVFGGGTKLT VL

61	15-20G VH NUCLEOTIDE SEQUENCE	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTTC CAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCGCG TCTGGATTCTCCTTCAGGTATTATGGTTTCCACTGGG TCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGCTG GCAGTTGTATGGCATGATGGAAGGGAGACACATTAT GGAGACTCCGTGAGGGGGCGATTCACCATCTCCAGA GACAATTACAAGAACACGGTGTTTTTGGAAATGGAC AGCCTGAGAGTCGAGGACACGGCTGTCTATCACTGT GCGAGAGATCGTGGTAGCGACGAACCTATTGACTAC TGGGGCCAGGGAGTTTTGGTCACCGTCTCCTCA
62	15-20G VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTATCACCTGCACCTTAC GCAGTGACCTCACTGTTAGTCCCTGGATATACTGGT ACCAACAGAAGCCAGGGAGTCCTCCCCGATTTCTCC TGAAATACAAATCAGACTCCAATAACTACCACGGCT CTGGAGTCCCCAGCCGCTTCTCTGGATCCAAAGATG CTTCGGCCAATGCAGCGATTTTACTCATCTCTGGACT CCAGTCTGAAGATGAGGCTGACTATTACTGTCAGAC TTGGCACACCACCACTGTGGTATTTGGCGGAGGGAC CAAGCTGACCGTCCTA
63	15-20G VH AMINO ACID SEQUENCE	QVQLVEFGGGIFQPGGSLRLSCVASGFSFRYYGFHWV RQAPGKGLEWLAVVWHDGRETHYGDSVRGRFTISRD NYKNTVFLEMDSLRVEDTAVYHCARDRGSDEPIDYW GQGVLVTVSS
64	15-20G VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASITCTLRSDLTVSPWIYWYQ QKPGSPPRFLLKYKSDSNNYHGSGVPSRFSGSKDASAN AAILLISGLQSEDEADYYCQTWHTTTVVFGGGTKLTV L
65	23-12O VH NUCLEOTIDE SEQUENCE	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTTC GAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCGCG TCTGGATTCTCCTTCAGGCATTATGGTATGCACTGG GTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGCT GGCAGTTGTATGGCATGATGGAAGGGAGACACATT ATGGAGACTCCGTGAAGGGGCGATTCACCATCTCCA GAGACAATTACAAGAATACGCTGTTTTTGCAAATGG ACAGCCTGAGAGTCGAGGACACGGCTGTCTATCACT GTGCGAGAGATCGTGGTAGCGACGAACCTATTGACT ACTGGGGCCAGGGAGTTTTGGTCACCGTCTCCTCA
66	23-12O VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTATCACCTGCACCTTAC GCAGTGACGTCACTGTTAGTCCCTGGACATACTGGT ACCAACAGAAGCCAGGGAGTCCTCCCCAATTTCTCC TGAGATACAAATCAGACTCTGATAAGTATCAGGGCT CTGGAGTCCCCAGCCGCTTCTCTGGATCCAAAAATG CTTCGGCCAATGCAGCGATTTTACTCATCTCTGGGCT CCAGTCTGAAGATGAGGCTGACTATTACTGTCAGAC TTGGCACACCAACAATGTGGTATTTGGCGGAGGGAC CAAGCTGACCGTCCTA

67	23-12O VH AMINO ACID SEQUENCE	QVQLVEFGGGIFEPGGSLRLSCVASGFSFRHYGMHWV RQAPGKGLEWLAVVWHDGRETHYGDSVKGRFTISRD NYKNTLFLQMDSLRVEDTAVYHCARDRGSDEPIDYW GQGVLVTVSS
68	23-12O VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASITCTLRSDVTVSPWTYWYQ QKPGSPPQFLLRYKSDSDKYQGSGVPSRFSGSKNASAN AAILLISGLQSEDEADYYCQTWHTNNVVFGGGTKLTV L
69	31-2C VH NUCLEOTIDE SEQUENCE	CAGGTGCAGTTGGTGGAGTTTGGGGGAGGCATTTTC CAGCCTGGGGGGTCCCTGAGACTCTCCTGTGTCGCG TCTGGATTCTCCTTCAGATATTATGGTTTCCACTGGG TCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGCTG GCAGTTGTATGGCATGATGGAAGGGAGACACATTAT GGAGACTCCGTGAAGGGGCGATTCACCATCTCCAGA GACAATTACAAGAACACGCTGTTTTTGCAAATGGAC AGCCTGAGAGTCGAGGACACGGCTGTCTATCACTGT GCGAGAGATCGTGGTAGCGACGAACCTATTGACTAC TGGGGCCAGGGAGTTTTGGTCACCGTCTCCTCA
70	31-2C VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCCTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTATCACCTGCACCTTAC GCAGTGGCCTCACTGTTAGTCCCTGGATATACTGGT ACCAACAGAAGCCAGGGAGTCCTCCCCAATTTCTCC TGAGATACAAATCAGACTCCGAAAACTACCGGGGC TCTGGAGTCCCCAGTCGCTTCTCTGGATCCAAAGAG GCTTCGGCCAATGCAGCGATTTTATTCATCTCTGGA CTCCAGTCTGAAGATGAGGCTGACTATTACTGTCAG ACTTGGCACACCAGCACAGTGGTATTTGGCGGAGGG ACCAAGCTGACCGTCCTA
71	31-2C VH AMINO ACID SEQUENCE	QVQLVEFGGGIFQPGGSLRLSCVASGFSFRYYGFHWV RQAPGKGLEWLAVVWHDGRETHYGDSVKGRFTISRD NYKNTLFLQMDSLRVEDTAVYHCARDRGSDEPIDYW GQGVLVTVSS
72	31-2C VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASITCTLRSGLTVSPWIYWYQ QKPGSPPQFLLRYKSDSENYRGSGVPSRFSGSKEASAN AAILFISGLQSEDEADYYCQTWHTSTVVFGGGTKLTVL
73	36-19H VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG AGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCG TCTGGATACATTTTCACCAACTTTGGCATCAACTGG GTGCGACAGGCCCCTGGTCAAGGGCTTGAGTGGATG GGATGGATGAACTCCAAGTATGGTAATGCGGACTCT GCACATAAGTTCCAGGACAGACTCACTATGACCACC GACACCTCCACAAGTACAGCCTACATGGAGCTGAG AAATCTGAGATCTGAGGACACGGCCGTATATTATTG CGCGAGAATGAATTACCGTGATTCGAAGTGGGACGT GAATTGGTTCGACCCCTGGGGCCAGGGAACCCTGAT CACCGTCTCCTCA

74	36-19H VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTGGA AGCAGGTCCAACGTCGAAAGAAATTTTGTTTACTGG TACCAGCAGCTCCCAGGAACGGCCCCCAAACTTCTC ATCTATATGAACAATCAGCGCCCCTCAGGGGTCCCT GACCGATTCTCTGGCTCTCGTTCTGGCACCTCAGCCT CCCTGGCCATCACTGGGCTTCGGTCCGAGGATGAGG CTGATTATTATTGTGCAGTTTGGGATGACAATCTCA GAGGCTGGGTGTTCGGCGGAGGGACCGAGGTGACC GTCCTA
75	36-19H VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKVSCKASGYIFTNFGINWV RQAPGQGLEWMGWMNSKYGNADSAHKFQDRLTMTT DTSTSTAYMELRNLRSEDTAVYYCARMNYRDSKWDV NWFDPWGQGTLITVSS
76	36-19H VL AMINO ACID SEQUENCE	QSVVTQPPSASGTPGQRVTISCSGSRSNVERNFVYWYQ QLPGTAPKLLIYMNNQRPSGVPDRFSGSRSGTSASLAIT GLRSEDEADYYCAVWDDNLRGWVFGGGTEVTVL
77	36-21L VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG AGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCG TCTGGATACACTTTCACCGGCTTTGGTATCAACTGG GTGCGACAGGCCCCAGGACAGGGGCTTGAGTGGAT GGGATGGATGAACTCCAACACTGGTGATGCGGACTC TGCACAGAAGTTCCAGGGCAGACTCACTATGACCAC CGACACCTCCACAAGTACAGCCCACATGGAGCTGAC GAATCTGGGATCTGAGGACACGGCCGTATACTATTG CGCGAGAATGAATTTCCTTGGTTCGAAGTGGGAGGT GAACTGGTTCGACCCCTGGGGCCAGGGAACCCTGAT CACCGTCTCCTCA
78	36-21L VL NUCLEOTIDE SEQUENCE	GATGTTGTGCTGACTCAGTCTCCACTCTCCCTGTCCG TCACCCTTGGACAGCCGGCCTCCATCTCCTGCAGGT CCAGTCACAGCCTCCCAAGAGATGATGAATACTCCT ACCTGAATTGGTTTCAGCAGAGGCCAGGCCAGTCTC CAAGGCGCCTAATTTATAGGGTTTCTAAGCGGGACT CTGGGGTCCCAGACAGATTCAGCGGCAGTGGGTCA GACACTTATTTCACACTGACAATCAGCAGGGTGGAG GCTGAGGATGTTGGAGTTTATTACTGCATGCAAGGT ACATACTGGCCCGGGACGTTCGGCCAAGGGACGAA GTTGGAAATCGAGCGA
79	36-21L VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKVSCKASGYTFTGFGINWV RQAPGQGLEWMGWMNSNTGDADSAQKFQGRLTMTT DTSTSTAHMELTNLGSEDTAVYYCARMNFLGSKWEV NWFDPWGQGTLITVSS
80	36-21L VL AMINO ACID SEQUENCE	DVVLTQSPLSLSVTLGQPASISCRSSHSLPRDDEYSYLN WFQQRPGQSPRRLIYRVSKRDSGVPDRFSGSGSDTYFT LTISRVEAEDVGVYYCMQGTYWPGTFGQGTKLEIER

81	41-18O VH NUCLEOTIDE SEQUENCE	GAGGTACAGCTGGTGGAGTCTGGGGGAGGCCTGGT CCAGCCTGGGGGGTCTCTGAGACTCTCCTGTGCAGC CTCTGGATTCACCTTTAATCACGATTGGATGACTTG GGTCCGCCAGGCTCCAGGGAAGGGTCTGGAGTGGG TGGCCAACATAATACAAGATGGAAGCGAAACATAC TATGTGGACTCTGTGAAGGGCCGATTCACCATCTCC AGAGACAATGCCAAGAATTTACTGTATCTGCAGATG AACAGCCTGAGAGTCGAGGACACGGCTGTGTATTTC TGTGGCCGGAGTATGGACGTCTGGGGCCAAGGGAC CACGGTCATCGTCTCCTCA
82	41-18O VL NUCLEOTIDE SEQUENCE	CAGTCTGTGCTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTGGA AGCAGCTCCAACATCGGAAGTAATACTGTGAACTGG TACCACCAGGTCCCAGGAACGGCCCCCAAACTCCTC ATCTATACTGATAATCAGCGGCCCTCAGGGGTCCCT GACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCC TCCCTGGCCATCAGTGGGCTCCAGTCTGAGGATGAA GGTGATTATTACTGTGCAGCGAGGGATGGCAGCCTG GATGTTTGGGTGTTCGGCGGAGGGACCAAAGTGACT GTCCTA
83	41-18O VH AMINO ACID SEQUENCE	EVQLVESGGGLVQPGGSLRLSCAASGFTFNHDWMTW VRQAPGKGLEWVANIIQDGSETYYVDSVKGRFTISRD NAKNLLYLQMNSLRVEDTAVYFCGRSMDVWGQGTT VIVSS
84	41-18O VL AMINO ACID SEQUENCE	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYH QVPGTAPKLLIYTDNQRPSGVPDRFSGSKSGTSASLAIS GLQSEDEGDYYCAARDGSLDVWVFGGGTKVTVL
85	5-14N VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG AGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCG TCTGGATACACTTTCACCAACTTTGGAATCAACTGG GTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGAT GGGATGGATGAACTCCAGAACTGGTGATGCGGACT CTGCACAGAACTTCCAGGGCAGGCTCACTATGACCA CCGACACCTCCAGAAGTATAGCCTACATGGAGCTGA CGCACCTGACCTCTGAGGACACGGCCGTATATTATT GCGCGAGAATGAATTTCCTTGGTTCGAGGTGGGAGG TGAACTGGTTCGACCCCTGGGGCCAGGGAACCCTGA TCACCGTCTCCTCA
86	5-14N VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGTGTCTGGG ACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTGGA AGCAGGTCCAACGTCGAAAGAAATTTTTTTTACTGG TATCAGCAATTCCCAGGAACGGCCCCCAAACTTCTC ATCTATATGAACAGTCAGCGGCCCGCAGGGGTCCCT GACCGATTCTCTGGCTCTCGTTCTGGCACCTCAGTTT CCCTGGCCATCACTGGGCTTCGGTCCGAGGATGAGG CTGACTATTATTGTGCAACTTGGGATGACAATCTGA GAGGCTGGGTGTTCGGCGGAGGGACCAAGGTGACC GTCCTA

87	5-14N VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKVSCKASGYTFTNFGINWV RQAPGQGLEWMGWMNSRTGDADSAQNFQGRLTMTT DTSRSIAYMELTHLTSEDTAVYYCARMNFLGSRWEVN WFDPWGQGTLITVSS
88	5-14N VL AMINO ACID SEQUENCE	QSVVTQPPSVSGTPGQRVTISCSGSRSNVERNFFYWYQ QFPGTAPKLLIYMNSQRPAGVPDRFSGSRSGTSVSLAIT GLRSEDEADYYCATWDDNLRGWVFGGGTKVTVL
89	11-19C VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG CGGCCTGGGGCCTCAGTGAAGATCTCCTGCAAGGCG TCTGGATACATTTTCACCAGCTTTGGTATCAACTGG GTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGAT GGGATGGATGAACTCCAACACTGGTGATGCGGACTC TCTACAGAAGTTCCAGGGCAGACTCACCATGACCAC CGACACCTCCACAAGCACAGCCTACATGGAATTGAG CAATCTGAGATCTGAAGACACGGCCGTATATTATTG CGCGAGAATGAATTTCCATGGTTCGAGGTGGGACGT GAACTGGTTCGACCCCTGGGGCCAGGGAACCCTGAT CACCGTCTCCTCA
90	11-19C VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGGTCATCATCTCCTGTTCTGGA AGCGGGTCCAACGTCGAAAGAAATTCTGTTTACTGG TACCAACAGTTCCCGGGAACGGCCCCCAAACTTCTC ATCTACATGAGCAATAGGCGCCCCTCAGGGGTCCCT GACCGATTCTTTGGCTCTCGTTCTGGCACCTCAGCCT CCCTGGCCATCACTGGGCTTCGGCCCGAGGATGAGG CTGATTATTATTGTGCAGTTTGGGATGACAGTCTGA GAGGCTGGGTATTCGGCGGAGGGACCAAGGTGACC GTCCTA
91	11-19C VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKISCKASGYIFTSFGINWVR QAPGQGLEWMGWMNSNTGDADSLQKFQGRLTMTTD TSTSTAYMELSNLRSEDTAVYYCARMNFHGSRWDVN WFDPWGQGTLITVSS
92	11-19C VL AMINO ACID SEQUENCE	QSVVTQPPSASGTPGQRVIISCSGSGSNVERNSVYWYQ QFPGTAPKLLIYMSNRRPSGVPDRFFGSRSGTSASLAIT GLRPEDEADYYCAVWDDSLRGWVFGGGTKVTVL
93	F-8C VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGCGGAGTCTGGGGGAGGCGTGGT CCAGCCTGGGGGGTCCCTGAGACTTTCCTGTGCAGC GTCTGGATTCAGTCTCAAGAGTTATGGCATTCACTG GGTCCGCCAGGCCCCAGGCAAGGGGCTGGAGTGGG TGGCAGTTATCTGGCCCCGACGAGATACACAGTATG CAGACTCCGTGAAGGGCCGAGTCACCATGTACAGA GACGACTATAGGAATACGGTCTATCTACAGATGAAC AGCCTGAGATTCGATGACGCGGCTCTGTATCGGTGT GCGAGAGATCGCGGTGAAGACAATCCCATA GATTTCTGGGGCCAGGGAACCCTGGTCACCGTCTCC TCA

94	F-8C VL NUCLEOTIDE SEQUENCE	CAGGCTGTGCTGACTCAGCCGTCTTCCCTCTCTGCAT CTCCTGGAGCATCAGCCAGTCTCACCTGCACCTTGC TCAGCGGCATCAATGTTGGTCCCTACTGGATATACT GGTATCAGCAGAAGGCAGGGAGTCCTCCCCAGTTTC TCCTCAGGTACAGGTCAGACTCAGATGAGGAGCAG GGCTCTGAGGTCCCCAGCCGCTTCTCTGGATCCAAA GATGCCTCGGCCAATGCAGGGATTTTGGTCATCTCT GGGCTCCAGTCTGAAGATGAAGCTGACTATTACTGT ATGATCTGGCACAGGACCGGTGTGATTTTCGGCGGA GGGACCAAGCTGACCGTCCTA
95	F-8C VH AMINO ACID SEQUENCE	QVQLAESGGGVVQPGGSLRLSCAASGFSLKSYGIHWV RQAPGKGLEWVAVIWPRRDTQYADSVKGRVTMYRD DYRNTVYLQMNSLRFDDAALYRCARDRGEDNPIDFW GQGTLVTVSS
96	F-8C VL AMINO ACID SEQUENCE	QAVLTQPSSLSASPGASASLTCTLLSGINVGPYWIYWY QQKAGSPPQFLLRYRSDSDEEQGSEVPSRFSGSKDASA NAGILVISGLQSEDEADYYCMIWHRTGVIFGGGTKLTV L
97	21-6M VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG AGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCG TCTGGATACATTTTCACCAGCTTTGGTATCAACTGG GTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGAT GGGATGGATGAACTCCAACACTGGTGATGCGGACTC TGTACAGAAGTTCCAGGGCAGACTCACCATGACCAC CGACCCCTCCACAAGTACAGCCTATATGGAACTGAG GAATCTGAGATCTGACGACACGGCCGTATATTATTG CGCGAGAATGAACTTCTTTGGTTCGCAGTGGGAAGT GAACTGGTTCGACCCCTGGGGCCAGGGAACCCTGAT CACCGTCTCCTCA
98	21-6M VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGATCACCATCTCCTGTTCTGGA AGCAGGTCCAACGTCGAAAGAAATTCTGTTTACTGG TACCAGCAGCTCCGAGGAACGGCCCCCAAACTTCTC ATCTATATGAGCAATCAGCGCCCCTCAGGGGTCCCT GACCGATTCTCTGGCTCTCGTTCTGGCACCTCAGCCT CCCTGGCCATCACTGGGCTTCGGTCCGAGGATGAGG CTGATTATTATTGTGCAGTTTGGGATGACAATCTCA GAGGCTGGGTGTTCGGCGGAGGGACCGAGGTGACC GTCCTA
99	21-6M VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKVSCKASGYIFTSFGINWVR QAPGQGLEWMGWMNSNTGDADSVQKFQGRLTMTTD PSTSTAYMELRNLRSDDTAVYYCARMNFFGSQWEVN WFDPWGQGTLITVSS
100	21-6M VL AMINO ACID SEQUENCE	QSVVTQPPSASGTPGQRITISCSGSRSNVERNSVYWYQ QLRGTAPKLLIYMSNQRPSGVPDRFSGSRSGTSASLAIT GLRSEDEADYYCAVWDDNLRGWVFGGGTEVTVL

101	22-14F VH NUCLEOTIDE SEQUENCE	CCAGGTGCACCTGGTGCAGTCTGGGGCTGAGATTAA GAGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGC GTCTGGATACACTTTCACCAGCTTTGGTATCAACTG GGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGA TGGGATGGATGAACTCCAACAGTGGTGATGCGGACT CTGCACAGAAGTTCCAGGGCAGACTCACTATGACCA CCGACACCTCCACAAGTACAGCCTACATGGAGCTGA GGAATCTGAGATCTGAGGACACGGCCGTATATTATT GCGCGAGAATGAATTTCCGTGGTTCGAAGTGGGAG GTGAACTGGTTCGACCCCTGGGGCCAGGGAACCCTG ATCACCGTCTCCTCA
102	22-14F VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTGGA AGCAGGTCCAACGTCGAAAGAAATTTTGTTTACTGG TACCAGCAACTCCCAGGAACGGCCCCCAAACTTCTC ATCTATATGAACAGTCAGCGGCCCTCAGGGGTCCCT GACCGATTCTCTGGCTCTCGTTCTGGCACCTCAGCCT CCCTGGCCATCACTGGGCTTCGGTCCGAGGATGAGG CTGACTATTATTGTGCAACTTGGGATGACAATCTGA GAGGCTGGGTGTTCGGCGGAGGGACCAAGGTGACC GTCCTA
103	22-14F VH AMINO ACID SEQUENCE	QVHLVQSGAEIKRPGASVKVSCKASGYTFTSFGINWV RQAPGQGLEWMGWMNSNSGDADSAQKFQGRLTMTT DTSTSTAYMELRNLRSEDTAVYYCARMNFRGSKWEV NWFDPWGQGTLITVSS
104	22-14F VL AMINO ACID SEQUENCE	QSVVTQPPSASGTPGQRVTISCSGSRSNVERNFVYWYQ QLPGTAPKLLIYMNSQRPSGVPDRFSGSRSGTSASLAIT GLRSEDEADYYCATWDDNLRGWVFGGGTKVTVL
105	24-5D VH NUCLEOTIDE SEQUENCE	CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGATTAAG AGGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCG TCTGGATACACCTTCACCAGATTTGGTATCAACTGG GTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGAT GGGATGGATGAACTCCAACACTGGTGATGCGGACTC TGCACAGAAGTTCCAGGGCAGACTCAGTATGACCAC CGACACCTCCACAAGTACAGCCTACATGGAGCTGAA GAGTCTGACATCTGACGACACGGCCGTATATTTTTG CGCGAGAATGAATTACTGGGGGTCGAAGTGGGACG TGAACTGGTTCGACCCCTGGGGCCAGGGAACCCTGA TCACCGTCTCCTCA
106	24-5D VL NUCLEOTIDE SEQUENCE	CAGTCTGTGGTGACTCAGCCACCCTCAGCGTCTGGG ACCCCCGGGCAGAGGGTCACCATCTCCTGTTCTGGA AGAAGGACCAACGTGGAAAGAAATTCTGTCTACTG GTACCAGCAGCTCCCAGGAACGGCCCCCAAACTTCT CATCTATATGAGCAATAAGCGCCCCTCAGGGGTCCC TGACCGATTCTCCGGCTCTCGTTCTGGCACCTCTGCC TCCCTGGCCATCACTGGGCTTCGGTCCGAGGATGAG GCTGATTATTATTGTGCAGTTTGGGATGACAATCTG AGAGGCTGGGTGTTCGGCGGAGGGACCAAGGTGAC CGTCCTA

107	24-5D VH AMINO ACID SEQUENCE	QVQLVQSGAEIKRPGASVKVSCKASGYTFTRFGINWV RQAPGQGLEWMGWMNSNTGDADSAQKFQGRLSMTT DTSTSTAYMELKSLTSDDTAVYFCARMNYWGSKWDV NWFDPWGQGTLITVSS
108	24-5D VL AMINO ACID SEQUENCE	QSVVTQPPSASGTPGQRVTISCSGRRTNVERNSVYWY QQLPGTAPKLLIYMSNKRPSGVPDRFSGSRSGTSASLAI TGLRSEDEADYYCAVWDDNLRGWVFGGGTKVTVL
109	15-6J CDRH1	GFSFRHYGMH
110	15-6J CDRH2	VVWHDGRETHYGDSV
111	15-6J CDRH3	DRGSDEPIDY
112	15-6J CDRL1	TLRSDVTVSPWTY
113	15-6J CDRL2	KSDSDKYQGS
114	15-6J CDRL3	QTWHTTTV
115	23-12O CDRH1	GFSFRHYGMH
116	23-12O CDRH2	VVWHDGRETHYGDSV
117	23-12O CDRH3	DRGSDEPIDY
118	23-12O CDRL1	TLRSDVTVSPWTY
119	23-12O CDRL2	KSDSDKYQGS
120	23-12O CDRL3	QTWHTSTV
121	31-2C CDRH1	GFSFRYYGFH
122	31-2C CDRH2	VVWHDGRETHYGDSV
123	31-2C CDRH3	DRGSDEPIDY
124	31-2C CDRL1	TLRSGLTVSPWIY
125	31-2C CDRL2	KSDSENYRGS
126	31-2C CDRL3	QTWHTSTV
127	15-20G CDRH1	GFSFRYYGFH
128	15-20G CDRH2	VVWHDGRETHYGDSV
129	15-20G CDRH3	DRGSDEPIDY
130	15-20G CDRL1	TLRSDLTVSPWIY

131	15-20G CDRL2	KSDSNNYHGS
132	15-20G CDRL3	QTWHTTTV
133	4-22O CDRH1	GFPFRYYGFH
134	4-22O CDRH2	VVWHNGRETYYEDSV
135	4-22O CDRH3	DRGSDEPIDY
136	4-22O CDRL1	TLRSDLTVGPYWMY
137	4-22O CDRL2	KSDSEKYQGS
138	4-22O CDRL3	QTWHANTV
139	6-20C CDRH1	GFSFRRFGMH
140	6-20C CDRH2	VVWHDGRETHYGDSV
141	6-20C CDRH3	DPGQDEAIDY
142	6-20C CDRL1	TLHSGLTVGPYWIY
143	6-20C CDRL2	KSDSEEYRAS
144	6-20C CDRL3	MTWHTNKV
145	J-5N CDRH1	GFSLRSFGMH
146	J-5N CDRH2	VIWPRRSQIQYADSV
147	J-5N CDRH3	DPGEDNPIDY
148	J-5N CDRL1	TFLSGINVGPYWIY
149	J-5N CDRL2	KSDSDKHQGS
150	J-5N CDRL3	MIWHVSGV
151	F-8C CDRH1	GFSLKSYGIH
152	F-8C CDRH2	VIWPRRDTQYADSV
153	F-8C CDRH3	DRGEDNPIDF
154	F-8C CDRL1	TLLSGINVGPYWIY
155	F-8C CDRL2	RSDSDEEQGS
156	F-8C CDRL3	MIWHRTGV

157	B-21J CDRH1	GFSFRHYGMH
158	B-21J CDRH2	VIWHNGRDREYADSV
159	B-21J CDRH3	DRGEDEPIDF
160	B-21J CDRL1	TLRSGLSAGPKWIY
161	B-21J CDRL2	KSDSEERRSS
162	B-21J CDRL3	AIWHSNVV
163	J-8G CDRH1	GFSFRHYGMH
164	J-8G CDRH2	VIWHNGRDKDYADSV
165	J-8G CDRH3	DRGEDEPIDF
166	J-8G CDRL1	TLRSGLNVGPYWIY
167	J-8G CDRL2	KSDSEKRRSS
168	J-8G CDRL3	AIWHSNAV
169	9-5L CDRH1	GFTLKRYGIH
170	9-5L CDRH2	VTWHDGNIYYADSV
171	9-5L CDRH3	DAGQNAPIDL
172	9-5L CDRL1	TLPSGINVATHWIY
172	9-5L CDRL2	KSDSDIQHGS
174	9-5L CDRL3	MIWYSTAV
175	2-20G CDRH1	GFTFPNAWFN
176	2-20G CDRH2	RIKSHSDGGTADYAAPV
177	2-20G CDRH3	LEIYHPVDV
178	2-20G CDRL1	RSSHSLPRDDEYSYLN
179	2-20G CDRL2	RVSKRDS
180	2-20G CDRL3	MQGTYWPGT
181	3-17I CDRH1	GFTFITAWMT
182	3-17I CDRH2	LIKSGNDGGAIEYAAPV

183	3-17I CDRH3	NDVALVWGVTPPLLL
184	3-17I CDRL1	TLSSGHGNYPVA
185	3-17I CDRL2	NADGSHIKGA
186	3-17I CDRL3	QTWAPGW
187	F-18D CDRH1	GFVFTTAWMN
188	F-18D CDRH2	RIKSKNEAETTDYAAPV
189	F-18D CDRH3	LETYYESDF
190	F-18D CDRL1	RSSQSLAEREEDILLN
191	F-18D CDRL2	RVSKRES
192	F-18D CDRL3	MQRTHWPQT
193	41-18O CDRH1	GFTFNHDWMT
194	41-18O CDRH2	NIIODGSETYYVDSV
195	41-18O CDRH3	GRVSMDV
196	41-18O CDRL1	SGSSSNIGSNTVN
197	41-18O CDRL2	TDNQRPS
198	41-18O CDRL3	AARDGSLDVW
199	18-11C CDRH1	GYTFTSFGIN
200	18-11C CDRH2	WMNSNSGDADSAQKF
201	18-11C CDRH3	MNFRGSKWEVNWFDP
202	18-11C CDRL1	SGSRSNVERNFVY
203	18-11C CDRL2	MNSQRPS
204	18-11C CDRL3	ATWDDNLRGW
205	22-14F CDRH1	GYTFTSFGIN
206	22-14F CDRH2	WMNSNSGDADSAQKF
207	22-14F CDRH3	MNFRGSKWEVNWFDP
208	22-14F CDRL1	SGSRSNVERNFVY

209	22-14F CDRL2	MNSQRPS
210	22-14F CDRL3	ATWDDNLRGW
211	20-2D CDRH1	GYTFTRFGIN
212	20-2D CDRH2	WMNSNSGNADSAQKF
213	20-2D CDRH3	MNYRGSKWEINWFDP
214	20-2D CDRL1	SGSRSNVQRNFVY
215	20-2D CDRL2	MNNNRPS
216	20-2D CDRL3	ATWDDNLRGW
217	36-21L CDRH1	GYTFTGFGIN
218	36-21L CDRH2	WMNSNTGDADSAQKF
219	36-21L CDRH3	MNFLGSKWEVNWFDP
220	36-21L CDRL1	RSSHSLPRDDEYSYLN
221	36-21L CDRL2	RVSKRDS
222	36-21L CDRL3	MQGTYWPGT
223	36-19H CDRH1	GYIFTNFGIN
224	36-19H CDRH2	WMNSKYGNADSAHKF
225	36-19H CDRH3	MNYRDSKWDVNWFDP
226	36-19H CDRL1	SGSRSNVERNFVY
227	36-19H CDRL2	MNNQRPS
228	36-19H CDRL3	AVWDDNLRGW
229	21-6M CDRH1	GYIFTSFGIN
230	21-6M CDRH2	WMNSNTGDADSVQKF
231	21-6M CDRH3	MNFFGSQWEVNWFDP
232	21-6M CDRL1	SGSRSNVERNSVY
233	21-6M CDRL2	MSNQRPS
234	21-6M CDRL3	AVWDDNLRGW

235	24-5D CDRH1	GYTFTRFGIN
236	24-5D CDRH2	WMNSNTGDADSAQKF
237	24-5D CDRH3	MNYWGSKWDVNWFDP
238	24-5D CDRL1	SGRRTNVERNSVY
239	24-5D CDRL2	MSNKRPS
240	24-5D CDRL3	AVWDDNLRGW
241	12-14G CDRH1	GYTFTNYGVN
242	12-14G CDRH2	WMNTNSGDTGYAQKF
243	12-14G CDRH3	AYFFDSWNKGNWFDP
244	12-14G CDRL1	SGGSSNLGRSYIY
245	12-14G CDRL2	KNSQRPS
246	12-14G CDRL3	AAWDDSLSGSW
247	2-8M CDRH1	GGYVTIKDNYWV
248	2-8M CDRH2	SMSYSGNAYYNPSL
249	2-8M CDRH3	RSAAAGGGNEWFDP
250	2-8M CDRL1	SGSTFNIGNNYVS
251	2-8M CDRL2	DNDKRPS
252	2-8M CDRL3	ATWDNRLDAV
253	6-8N CDRH1	GFAFTTAWMT
254	6-8N CDRH2	LIKSTNDGGSIDYAAPV
255	6-8N CDRH3	NDVVRLRGVTPPILL
256	6-8N CDRL1	TLSSGHHSYPVA
257	6-8N CDRL2	NGDGSHTKGDG
258	6-8N CDRL3	QTWATGW
259	5-14N CDRH1	GYIFTNFGIN
260	5-14N CDRH2	WMNSRTGDADSAQNF

261	5-14N CDRH3	MNFLGSRWEVNWFDP
262	5-14N CDRL1	SGSRSNVERNFFY
263	5-14N CDRL2	MNSQRPAG
264	5-14N CDRL3	ATWDDNLRGW
265	11-19C CDRH1	GYIFTSFGIN
266	11-19C CDRH2	WMNSNTGDADSLQKF
267	11-19C CDRH3	MNFHGSRWDVNWFDP
268	11-19C CDRL1	SGSGSNVERNSVY
269	11-19C CDRL2	MSNRPRSG
270	11-19C CDRL3	AVWDDSLRGW

What is claimed is:

1. An antibody, or an antigen-binding fragment thereof capable of targeting the Globo-Series carbohydrate antigen, comprising:

a. three heavy chain CDRs, having about 90% to about 100% identity to amino acid sequences selected from SEQ ID NOs: 109, 110, and 111; SEQ ID NOs: 115, 116, and 117; SEQ ID NOs: 121, 122, and 123; SEQ ID NOs: 127, 128, and 129; SEQ ID NOs: 133, 134, and 135; SEQ ID NOs: 139, 140, and 141; SEQ ID NOs: 145, 146, and 147; SEQ ID NOs: 151, 152, and 153; SEQ ID NOs: 157, 158, and 159; SEQ ID NOs: 163, 164, and 165; SEQ ID NOs: 169, 170, and 171; SEQ ID NOs: 175, 176 and 177; SEQ ID NOs: 181, 182, and 183; SEQ ID NOs: 187, 188, and 189; SEQ ID NOs: 193, 194, and 195; SEQ ID NOs: 199, 200, and 201; SEQ ID NOs: 205, 206, and 207; SEQ ID NOs: 211, 212, and 213; SEQ ID NOs: 217, 218, and 219; SEQ ID NOs: 223, 224, and 225; SEQ ID NOs: 229, 230, and 231; SEQ ID NOs: 235, 236, and 237; SEQ ID NOs: 241, 242, and 243; SEQ ID NOs: 247, 248, and 249; SEQ ID NOs: 253, 254 and 255; SEQ ID NOs: 259, 260, and 261; SEQ ID NOs: 265, 266, and 267; or conservatively modified amino acid substitutions; and/or

b. three light chain CDRs, having about 90% to about 100% identity to amino acid sequences selected from SEQ ID NOs: 112, 113, and 114; SEQ ID NOs: 118, 119, and 120; SEQ ID NOs: 124, 125, and 126; SEQ ID NOs: 130, 131, and 132; SEQ ID NOs: 136, 137, and 138; SEQ ID NOs: 142, 143, and 144; SEQ ID NOs: 148, 149, and 150; SEQ ID NOs: 154, 155, and 156; SEQ ID NOs: 160, 161, and 162; SEQ ID NOs: 166, 167, and 168; SEQ ID NOs: 172, 173, and 174; SEQ ID NOs: 178, 179, and 180; SEQ ID NOs: 184, 185, and 186; SEQ ID NOs: 190, 191, and 192; SEQ ID NOs: 196, 197, and 198; SEQ ID NOs: 202, 203, and 204; SEQ ID NOs: 208, 209, and 210; SEQ ID NOs: 214, 215, and 216; SEQ ID NOs: 220, 221, and 222; SEQ ID NOs: 226, 227, and 228; SEQ ID NOs: 232, 233, and 234; SEQ ID NOs: 238, 239, and 240; SEQ ID NOs: 244, 245, and 246; SEQ ID NOs: 250, 251, and 252; SEQ ID NOs: 256, 257, and 258; SEQ ID NOs: 262, 263, and 264; SEQ ID NOs: 268, 269, and 270; or conservatively modified amino acid substitutions.

2. An antibody, or an antigen-binding fragment thereof capable of targeting the Globo-Series carbohydrate antigen, comprising:

a. the heavy chain variable domain, having about 80% to about 100% identity to amino acid sequences selected from SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 11, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 23, SEQ ID NO: 27, SEQ ID NO: 31, SEQ ID NO: 35, SEQ ID NO: 39, SEQ ID NO: 43, SEQ ID NO: 47, SEQ ID NO: 51, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 63, SEQ ID NO: 67, SEQ ID NO: 71, SEQ ID NO: 75, SEQ ID NO: 79, SEQ ID NO: 83, SEQ ID NO: 87, SEQ ID NO: 91, SEQ ID NO: 95, SEQ ID NO: 99, SEQ ID NO: 103, SEQ ID NO: 107; or conservatively modified amino acid substitutions; and/or

b. the light chain variable domain, having about 80% to about 100% identity to amino acid sequences selected from SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 12, SEQ ID NO: 16, SEQ ID NO: 20, SEQ ID NO: 24, SEQ ID NO: 28, SEQ ID NO: 32, SEQ ID NO: 36, SEQ ID NO: 40, SEQ ID NO: 44, SEQ ID NO: 48, SEQ ID NO: 52, SEQ ID NO: 56, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 76, SEQ ID NO: 80, SEQ ID NO: 84, SEQ ID NO: 88, SEQ ID NO: 92, SEQ ID NO: 96, SEQ ID NO: 100, SEQ ID NO: 104, SEQ ID NO: 108 or conservatively modified amino acid substitutions.

3. The antibody or antigen-binding fragment thereof of any one of claims 1-2, wherein the variable domain is capable of binding one or more Globo series antigens.

4. The antibody or antigen-binding portion thereof of claim 3, wherein the Globo series antigen is SSEA-4 (Neu5Acα2→ 3Galβ1→ 3GalNAcβ1→ 3Galα1→ 4Galβ1→ 4Glcβ1).

5. The antibody or antigen-binding portion thereof of claim 3, wherein the Globo series antigen is SSEA-3 (2Galβ1→ 3GalNAcβ1→ 3Galα1→ 4Galβ1→ 4Glcβ1).

6. The antibody or antigen-binding portion thereof of claim 3, wherein the Globo series antigen is Globo H (Fucα1→2 Galβ1→3 GalNAcβ1→3 Galα1→4 Galβ1→4 Glc).

7. The antibody, or an antigen-binding portion thereof of any one of claims 1-2, wherein the antibody is a human antibody.

8. The antibody of claim 7, wherein the antibody is an IgG or IgM.

9. The antibody or antigen-binding portion thereof of claims 1-2, wherein the antibody or antigen-binding portion thereof is selected from: (a) a whole immunoglobulin molecule; (b) an scFv; (c) a Fab fragment; (d) an $F(ab')_2$; or (e) a disulfide linked Fv.

10. A pharmaceutical composition, comprising:

an antibody or an antigen-binding fragment thereof of any one of claims 1-2; and at least one pharmaceutically acceptable carrier.

11. The pharmaceutical composition of claim 10, further comprising at least one additional therapeutic agent.

12. A method for inhibiting the proliferation of cancer cells, comprising the administering of an effective amount of a pharmaceutical composition according to claim 10 to a subject in need thereof, wherein the proliferation of cancer cells is inhibited.

13. The method of claim 12, wherein the subject is human.

14. A method of treating cancer in a subject, the method comprising administering to the subject in need thereof an effective amount of the antibody or an antigen-binding fragment thereof of any one of claims 1-2.

15. The method of claim 14, wherein the cancer is selected from the group consisting of sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervix cancer, endometrial cancer, ovarian cancer, testical cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer.

16. The method of claim 14, wherein the subject is human.

17. A method for cancer diagnosis in a subject, comprising:

a. Applying one or more antibodies of any one of claims 1-2 that detect expression of a panel of markers to a cell or sample obtained from the subject;

b. Assaying the binding of the one or more antibodies to the cell or the sample; and

c. Comparing the binding with a normal control to determine the presence of the cancer in the subject.

18. The method of claim 17, wherein the markers consisting of Globo-H, SSEA-3 or SSEA-4.

19. The method of claim 17, wherein the cancer is selected from the group consisting of sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervix cancer, endometrial cancer, ovarian cancer, testical cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer.

20. The method of claim 17, wherein the cell is cancer stem cell.

21. The method of claim 17, wherein the sample consists serum, blood, plasma, cells, cell medium, saliva, urine, lymph node fluid, tumor biopsy or tissue culture.

22. The method of claim 17, wherein the subject is human.

23. A method of imaging a subject comprising:

a. Administering an effective amount of an antibody or an antigen-binding fragment thereof of any one of claims 1-2, wherein the antibody or an antigen-binding fragment is conjugated to an imaging agent; and

b. Detecting the imaging agent in the subject.

24. The method of claim 23, wherein the imaging agent is a fluorophore, a dye, an MRI contrast agent or a radionuclide.

25. The method of claim 23, wherein the subject has a cancer, the method further defined

as a method of detecting a cancer metastasis.

26. The method of claim 23, wherein the subject is human.

27. A method of isolating an antibody, or an antigen-binding fragment in a subject, comprising:

a. Administering to the subject a therapeutically effective dose of Globo series antigens vaccine and a pharmaceutically acceptable carrier:

b. Collecting a sample from the subject;

c. Isolating B cells from the sample; and

d. Cultivating and screening the B cells which bind to the Globo series antigens.

28. The method of claim 27, wherein the Globo series antigens comprising Globo-H, SSEA-3 or SSEA-4.

29. The method of claim 27, wherein the subject is human.

30. The method of claim 27, wherein the sample consists serum, blood, plasma, cells, cell medium, lymph node fluid, tumor biopsy or tissue culture.

31. An antibody-drug conjugate (ADC) comprising a drug conjugated to an antibody or an antigen-binding fragment that binds Globo series antigens, wherein VH selected from SEQ ID No: 3, SEQ ID No: 7, SEQ ID No: 11, SEQ ID No: 15, SEQ ID No: 19, SEQ ID No: 23, SEQ ID No: 27, SEQ ID No: 31, SEQ ID No: 35, SEQ ID No: 39, SEQ ID No: 43, SEQ ID No: 47, SEQ ID No: 51, SEQ ID No: 55, , SEQ ID No: 59, SEQ ID No: 63, SEQ ID No: 67, SEQ ID No: 71, SEQ ID No: 75, SEQ ID No: 79, SEQ ID No: 83, SEQ ID No: 87, SEQ ID No: 91, SEQ ID No: 95, SEQ ID No: 99, SEQ ID No: 103, or SEQ ID No: 107 and VL selected from SEQ ID No: 4, SEQ ID No: 8, SEQ ID No: 12, SEQ ID No: 16, SEQ ID No: 20, SEQ ID No: 24, SEQ ID No: 28, SEQ ID No: 32, SEQ ID No: 36, SEQ ID No: 40, SEQ ID No: 44, SEQ ID No: 48, SEQ ID No: 52, SEQ ID No: 56, SEQ ID No: 60, SEQ ID No: 64, SEQ ID No: 68, SEQ ID No: 72, SEQ ID No: 76, SEQ ID No: 80, SEQ ID No: 84, SEQ ID No: 88, SEQ ID No: 92, SEQ ID No: 96, SEQ ID No: 100, SEQ ID No: 104, or SEQ ID No: 108.;
and

wherein the drug is covalently conjugated to the antibody or the antigen-binding fragment by a linker.

32. The ADC of claim 31, wherein the Globo series antigens comprising Globo-H, SSEA-3 or SSEA-4.

33. The ADC of claim 31, wherein the linker comprising a *p*-nitrophenyl linker, a 4-(4-N-maleimidomethyl) cyclohexane-1-carboxyl hydrazide (MMCCH) linker, a maleimidocaproyl (MC) linker or a maleimidomethyl cyclohexane-1-carboxylate (MCC) linker.

34. The ADC of claim 31, wherein the drug is a chemical compound or a biological agent.

35. The ADC of claim 31, wherein the drug is an anti-proliferative agent.

36. The ADC of claim 35, wherein the anti-proliferative agent is selected from cyclophosphamide, opiate, granulocyte colony-stimulating factor (GCSF), estrogen inhibitors (tamoxifen or Fareston), aromatase inhibitors (Arimidex, Aromasin or Femara), pituitary downregulators (Zoladex or Lupron), Novaldex (tamoxifen selective estrogen-receptor modulator), Evista (rolaxifene), Faslodex (estrogen receptor down-regulator), anticoagulant (Refludan), enzyme (Elitek), Hematopoietic growth factor, anti-neoplastic Agent (antimetabolites, miscellaneous cytotoxic agents, vinca alkaloid, Epipodophyllotoxins, Alkylating agents, Taxanes, Antitumor antibiotics, Camptothecins, Nitrosoureas), HER1/EGFR tyrosine kinase inhibitor (Tarceva), VEGF protein inhibitor (Avastin), HER-2/ErbB2 inhibitor (Tyverb/Tykerb), Interferon, Interleukin, Monoclonal antibody, or Glucocorticoid steroid.

37. The ADC of claim 35, wherein the anti-proliferative agent is selected from erlotinib (TARCEVA); docetaxel (TAXOTERE); gemcitabine (GEMZAR); cisplatin; carboplatin; paclitaxel (TAXOL); trastuzumab (HERCEPTIN); temozolomide (TEMODAL); tamoxifen (NOLVADEX, ISTUBAL, VALODEX); doxorubicin (ADRIAMYCIN); oxaliplatin (ELOXATIN); bortezomib (VELCADE); sutent (SUNITINIB); letrozole (FEMARA); imatinib mesylate (GLEEVEC); MEK inhibitor (Exelixis); fulvestrant (FASLODEX); leucovorin (folinic acid); rapamycin (RAPAMUNE); lapatinib (TYKERB); lonafarnib (SARASAR); sorafenib (NEXAVAR); gefitinib (IRESSA); irinotecan (CAMPTOSAR); tipifarnib (ZARNESTRA); ABRAXANE (Cremophor-free); paclitaxel; vandetanib

(ZACTIMA); chloranmbucil; temsirolimus (TORISEL); pazopanib; canfosfamide (TELCYTA); thiotepa; cyclosphosphamide (CYTOXAN, NEOSAR); 5-fluorouracil (5-FU); vinorelbine (NAVELBINE); novantrone; teniposide; edatrexate; daunomycin; aminopterin; capecitabine (XELODA); ibandronate; topoisomerase inhibitor RFS 2000; -difluoromethylornithine (DMFO); tamoxifen (NOLVADEX); raloxifene; droloxifene, 4-hydroxytamoxifen; trioxifene; keoxifene; onapristone; FARESTON (toremifine citrate); 4(5)-imidazoles; aminoglutethimide; MEGASE (megestrol acetate); AROMASIN (exemestane); formestanie; fadrozole; RIVISOR® (vorozole); FEMARA (letrozole); ARIMIDEX (anastrozole); flutamide; nilutamide; bicalutamide; leuprolide; goserelin; troxacitabine (α-1,3-dioxolane nucleoside cytosine analog); lipid kinase inhibitor; oblimersen (GENASENSE); ANGIOZYME; ALLOVECTIN; LEUVECTIN; VAXID; PROLEUKIN; LURTOTECAN; ABARELIX; bevacizumab (AVASTIN); alemtuzumab (Campath); bevacizumab (AVASTIN); cetuximab (ERBITUX); panitumumab (VECTIBIX); rituximab (RITUXAN); pertuzumab (OMNITARG); trastuzumab (HERCEPTIN); tositumomab (Bexxar, Corixia); gemtuzumab; or ozogamicin (MYLOTARG).

38. A method of treating cancer in a subject, the method comprising administering to the subject in need thereof an effective amount of the ADC of claim 31.

39. The method of claim 38, wherein the cancer is selected from the group consisting of sarcoma, skin cancer, leukemia, lymphoma, brain cancer, glioblastoma, lung cancer, breast cancer, oral cancer, head-and-neck cancer, nasopharyngeal cancer, esophagus cancer, stomach cancer, liver cancer, bile duct cancer, gallbladder cancer, bladder cancer, pancreatic cancer, intestinal cancer, colorectal cancer, kidney cancer, cervix cancer, endometrial cancer, ovarian cancer, testical cancer, buccal cancer, oropharyngeal cancer, laryngeal cancer and prostate cancer.

40. The method of claim 38, wherein the subject is human.

FIG. 1A

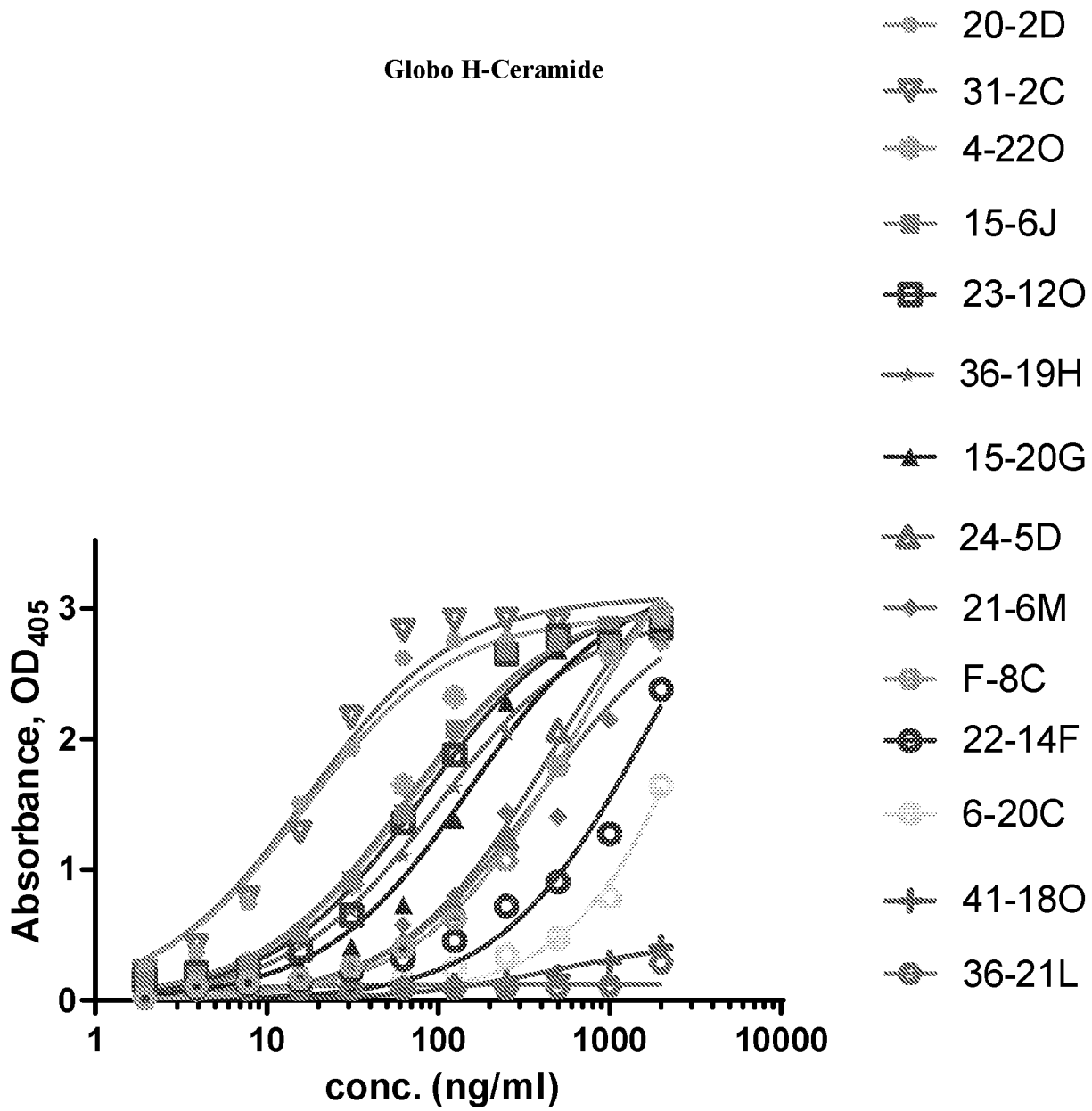

Globo H-Ceramide
20-2D
31-2C
4-22O
15-6J
23-12O
36-19H
15-20G
24-5D
21-6M
F-8C
22-14F
6-20C
41-18O
36-21L
Absorbance, OD405
0
1
2
3
1
10
100
1000
10000
conc. (ng/ml)

FIG. 1B

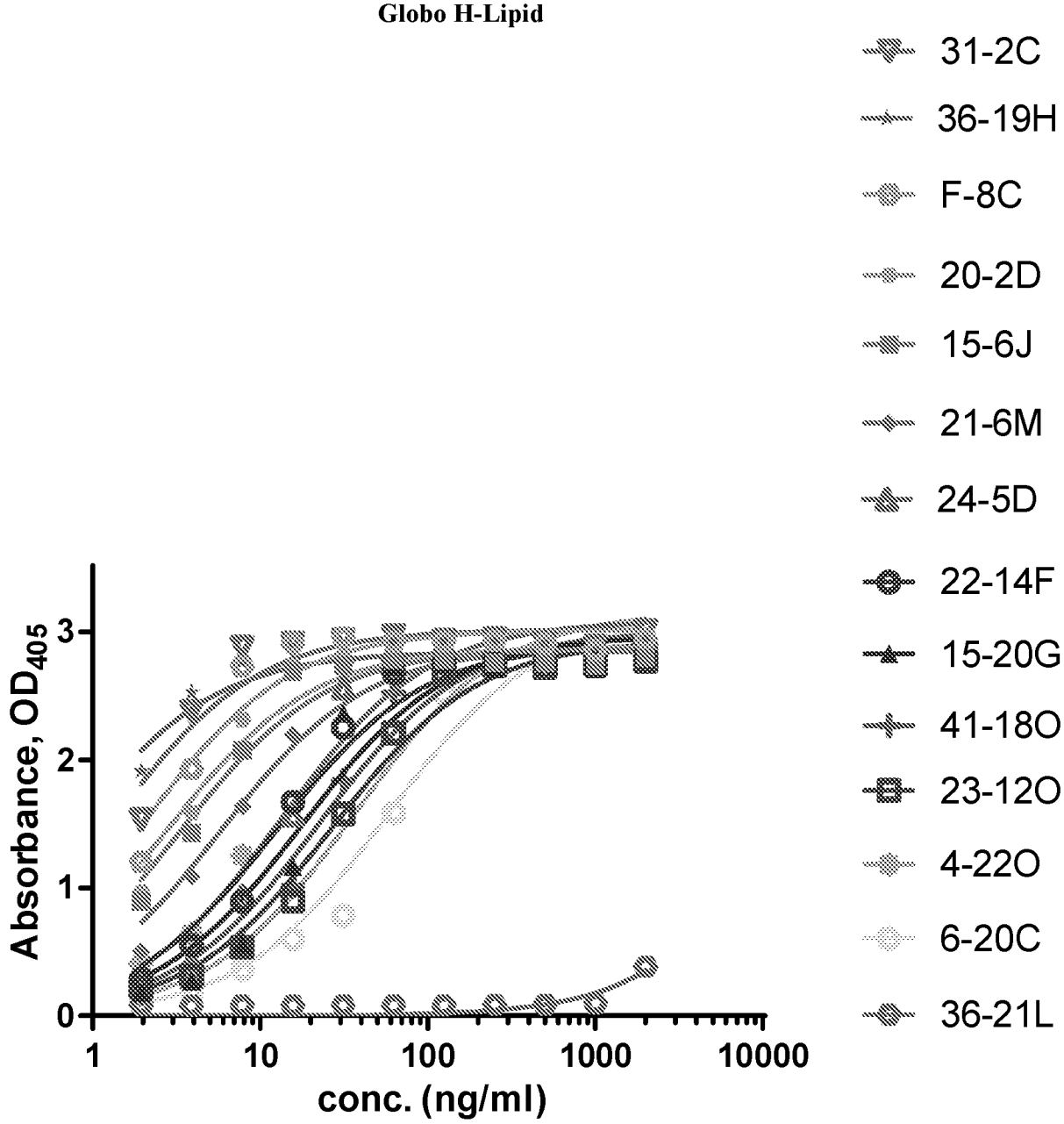

Globo H-Lipid
31-2C
36-19H
F-8C
20-2D
15-6J
21-6M
24-5D
22-14F
15-20G
41-18O
23-12O
4-22O
6-20C
36-21L
Absorbance, OD405
0
1
2
3
1
10
100
1000
10000
conc. (ng/ml)

FIG. 2A

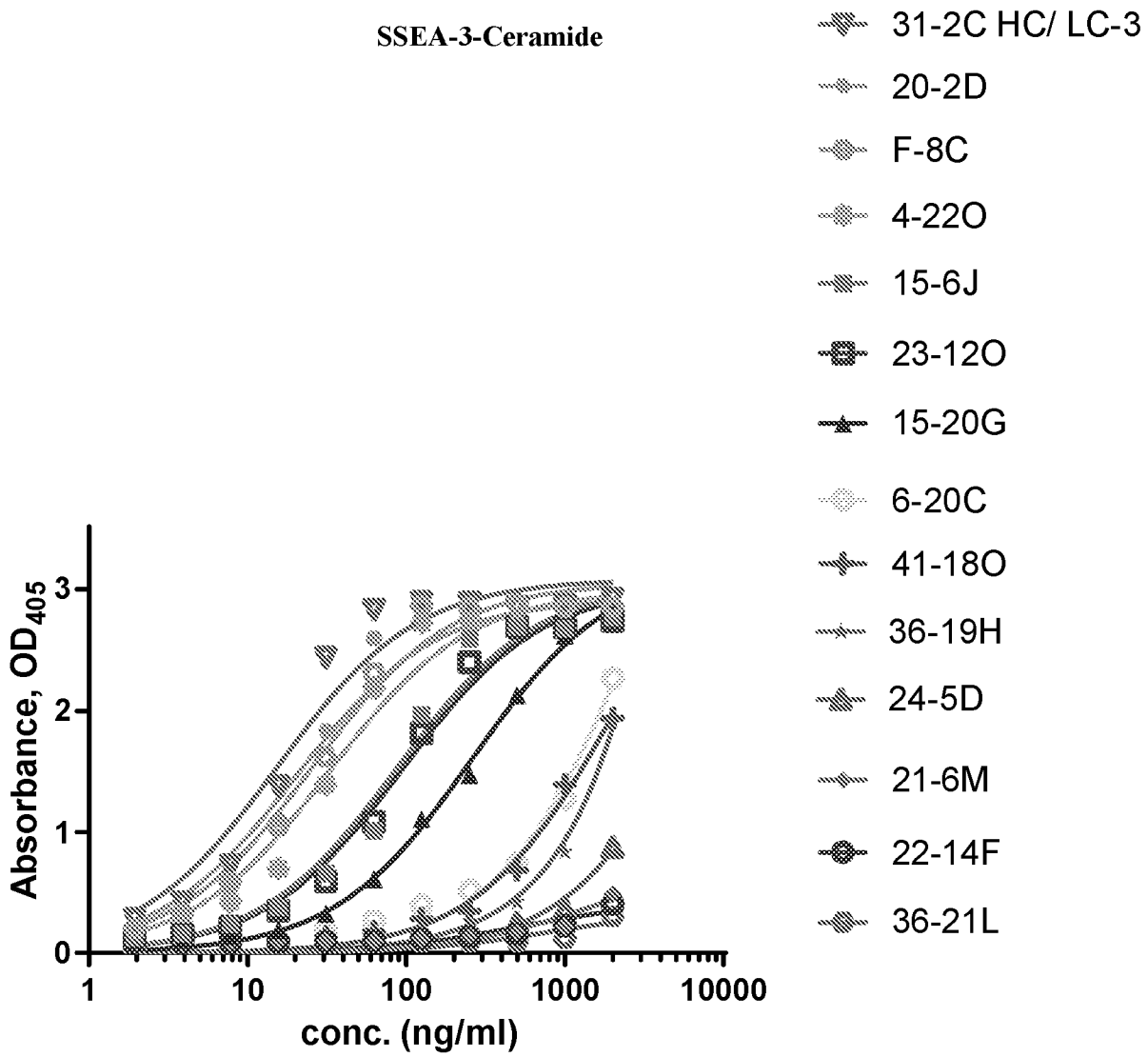

SSEA-3-Ceramide
31-2C HC/ LC-3
20-2D
F-8C
4-22O
15-6J
23-12O
15-20G
6-20C
41-18O
36-19H
24-5D
21-6M
22-14F
36-21L
Absorbance, OD405
0
1
2
3
1
10
100
1000
10000
conc. (ng/ml)

FIG. 2B

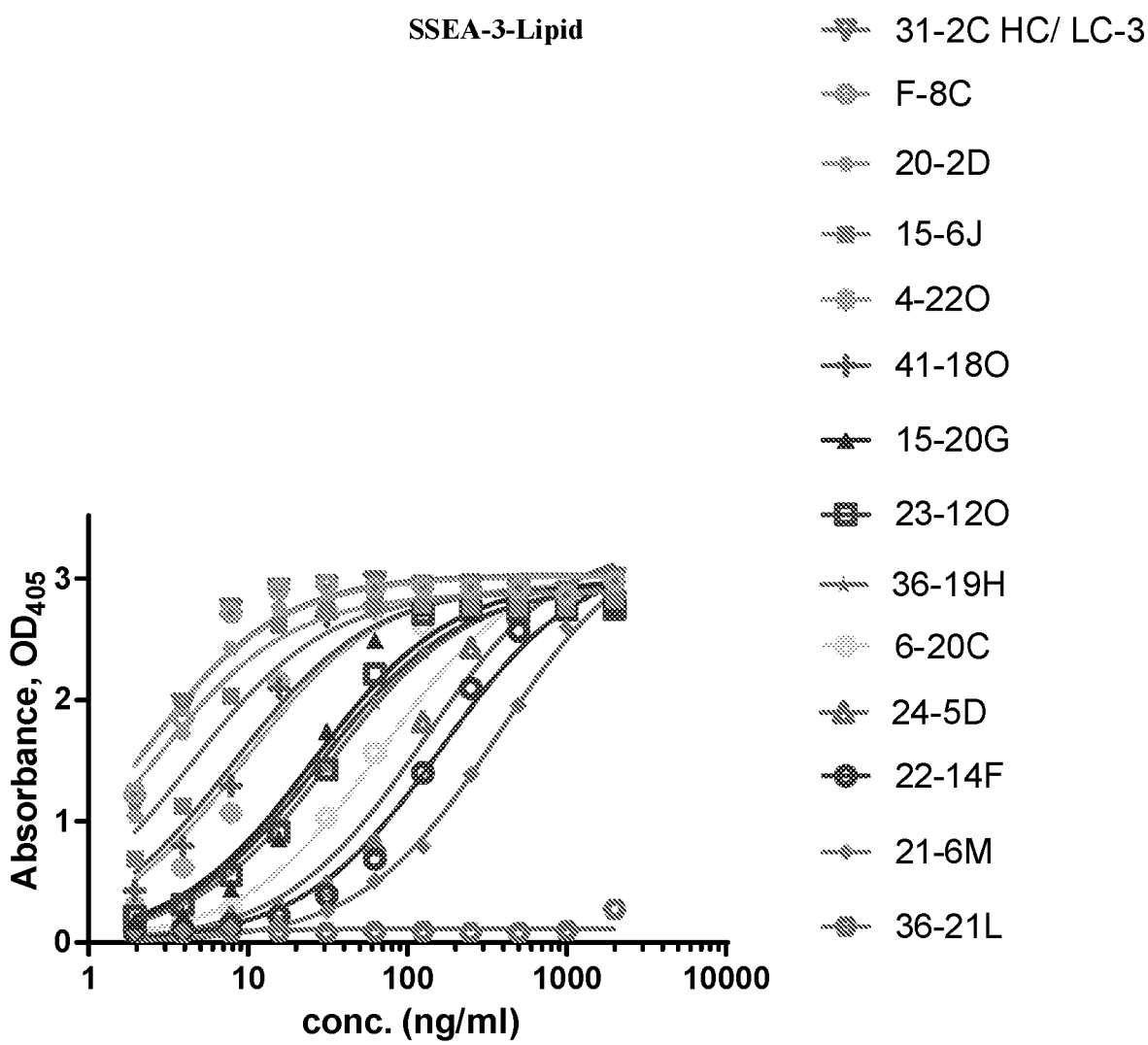

SSEA-3-Lipid
31-2C HC/ LC-3
F-8C
20-2D
15-6J
4-22O
41-18O
15-20G
23-12O
36-19H
6-20C
24-5D
22-14F
21-6M
36-21L
Absorbance, OD405
0
1
2
3
1
10
100
1000
10000
conc. (ng/ml)

FIG. 3A

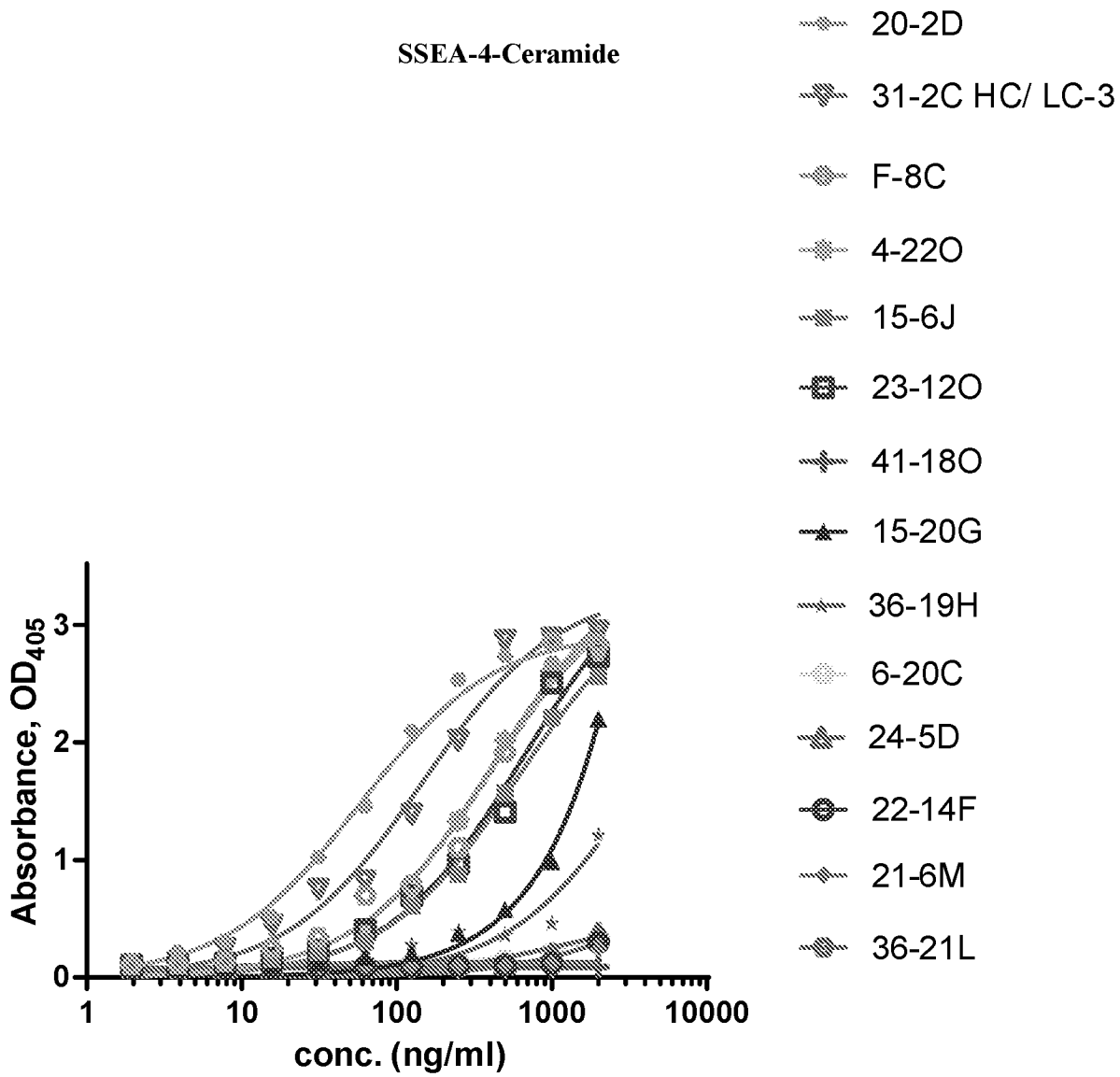
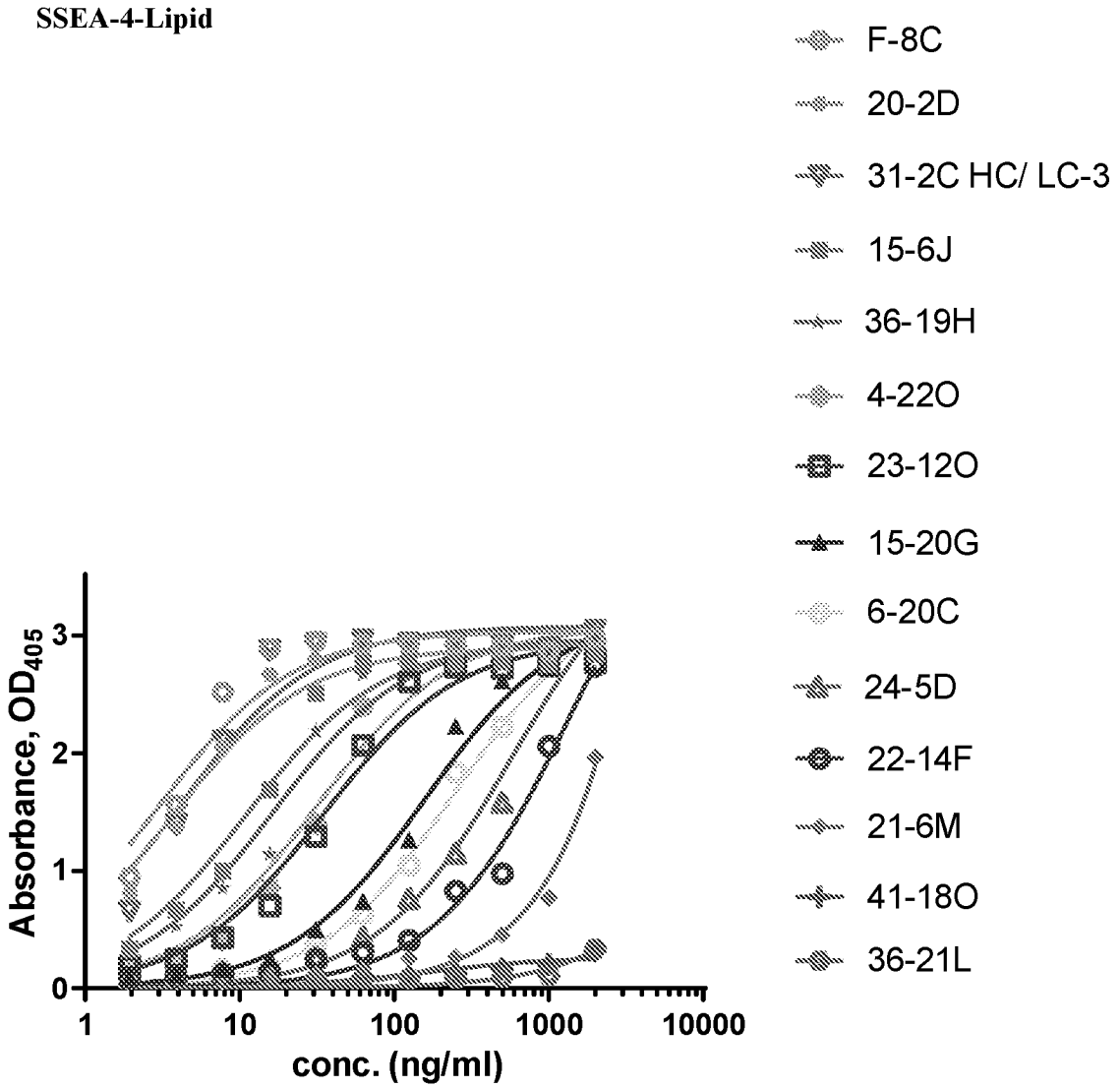

SSEA-4-Ceramide
20-2D
31-2C HC/ LC-3
F-8C
4-22O
15-6J
23-12O
41-18O
15-20G
36-19H
6-20C
24-5D
22-14F
21-6M
36-21L
Absorbance, OD405
0
1
2
3
1
10
100
1000
10000
conc. (ng/ml)

FIG. 3B


SSEA-4-Lipid
F-8C
20-2D
31-2C HC/ LC-3
15-6J
36-19H
4-22O
23-12O
15-20G
6-20C
24-5D
22-14F
21-6M
41-18O
36-21L
Absorbance, OD405
0
1
2
3
1
10
100
1000
10000
conc. (ng/ml)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/044713

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 12-16,23-30,38-40
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 12-16, 23-30 and 38-40 pertain to methods for treatment of the human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required under PCT Article 17(2)(a)(i) and Rule 39.1(iv), to search.

2. ☒ Claims Nos.: 1-26,31-40
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
A sequence listing in the form of an Annex C/ST.25 text file was not furnished to this Authority. Therefore a meaningful opinion on claims 1-26 and 31-40 was not established.

3. ☒ Claims Nos.: 9
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required addtional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

C07K 16/44(2006.01)i, A61K 49/16(2006.01)i, G01N 33/574(2006.01)i, A61K 39/00(2006.01)n

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K 16/44; A61K 39/395; A61K 31/7105; A61K 39/00; C07K 14/705; C07K 16/30; A61K 49/16; G01N 33/574

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: antibody, Globo H, SSEA-3, SSEA-4, B cell, screening

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2016-0102151 A1 (ACADEMIA SINICA) 14 April 2016 See paragraphs [0175], [0176], [0178], [0181], [0182], [0185], [0227], [0228].	27-30
X	US 2009-0317411 A1 (WONG, CHI-HUEY et al.) 24 December 2009 See paragraph [0023]; and claims 14-16.	27-30
A	WO 2016-026742 A1 (MILTENYI BIOTEC GMBH) 25 February 2016 See abstract; and claim 1.	27-30
A	WO 2015-143123 A2 (MACKAY MEMORIAL HOSPITAL OF TAIWAN PRESBYTERIAN CHURCH AND MACKAY MEMORIAL SOCIAL WORK FOUNDATION et al.) 24 September 2015 See abstract; and claim 1.	27-30
A	DANISHEFSKY, SAMUEL J. et al., `Development of Globo-H cancer vaccine`, Accounts of Chemical Research, 10 February 2015, vol. 48, pp. 643-652 See pages 643, 650.	27-30

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 November 2017 (28.11.2017)	**28 November 2017 (28.11.2017)**

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2017/044713

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International application No.

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