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CA 2904743 A1 2014/09/25

(21) 2 904 743

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

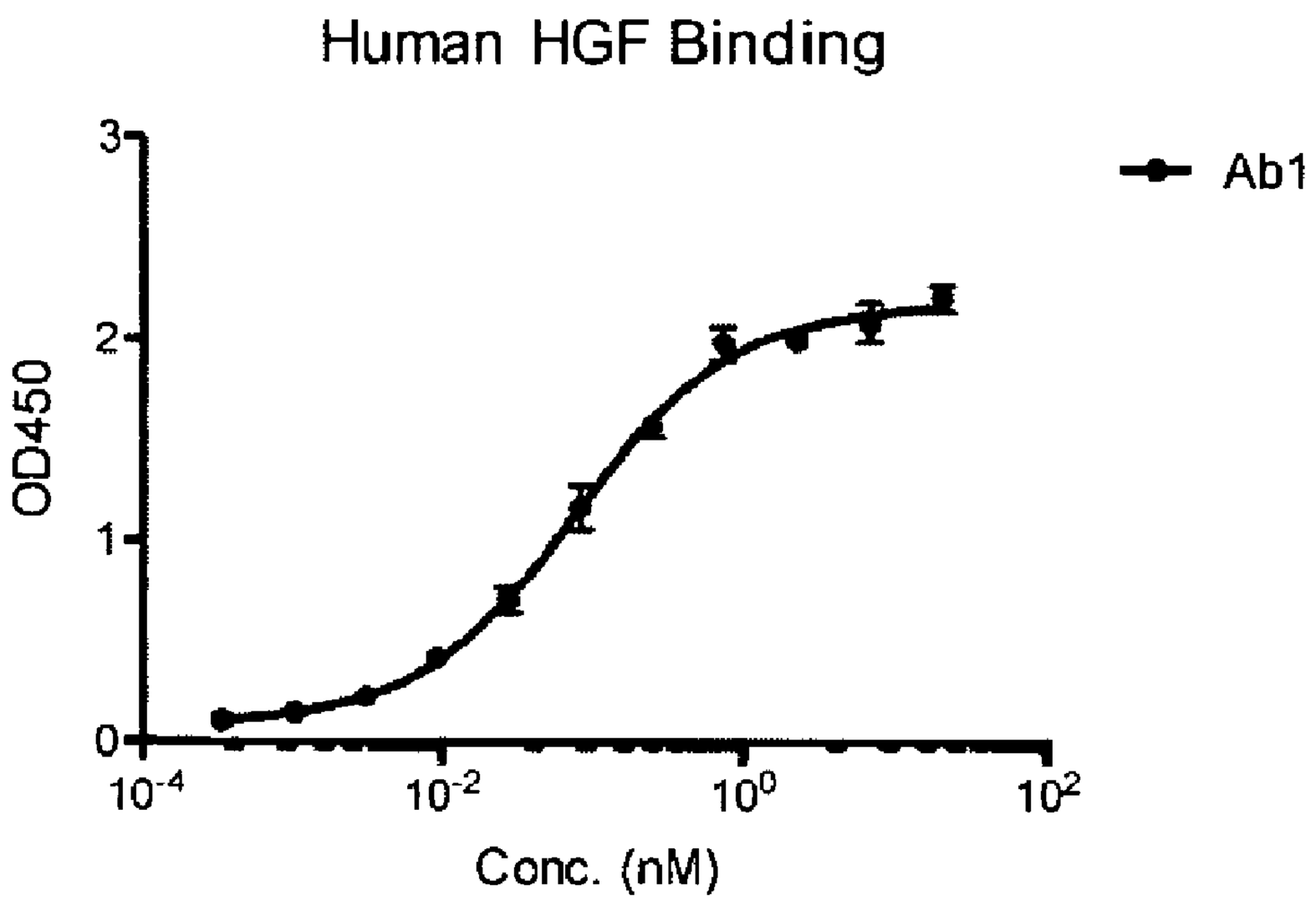
(86) Date de dépôt PCT/PCT Filing Date: 2014/03/14
(87) Date publication PCT/PCT Publication Date: 2014/09/25
(85) Entrée phase nationale/National Entry: 2015/09/08
(86) N° demande PCT/PCT Application No.: US 2014/029163
(87) N° publication PCT/PCT Publication No.: 2014/153117
(30) Priorités/Priorities: 2013/03/14 (US61/782,868); 2013/03/14 (US61/781,643)

(51) Cl.Int./Int.Cl. *C12N 15/13* (2006.01), *A61K 39/395* (2006.01), *A61K 47/48* (2006.01), *A61K 49/00* (2006.01), *C07K 16/22* (2006.01), *C07K 16/46* (2006.01), *C12N 1/15* (2006.01), *C12N 1/19* (2006.01), *C12N 15/63* (2006.01), *C12N 5/10* (2006.01)

(71) Demandeur/Applicant:
ALDER BIOPHARMACEUTICALS, INC., US

(72) Inventeurs/Inventors:
DUTZAR, BENJAMIN H., US;
ANDERSON, KATIE, US;
KOVACEVICH, BRIAN R., US;
FELDHAUS, ANDREW L., US; ...

(54) Titre : ANTICORPS DIRIGES CONTRE HGF ET COMPOSITIONS LES CONTENANT
(54) Title: ANTIBODIES TO HGF AND COMPOSITIONS CONTAINING




(57) Abrégé/Abstract:
The present invention is directed to antibodies and fragments thereof having binding specificity for HGF. Another embodiment of this invention relates to the antibodies described herein, and binding fragments thereof, comprising the sequences of the VH, VL and CDR polypeptides described herein, and the polynucleotides encoding them. The invention also contemplates conjugates of anti-HGF antibodies and binding fragments thereof conjugated to one or more functional or detectable moieties. The invention also contemplates methods of making said anti-HGF antibodies and binding fragments thereof. Embodiments of the invention also pertain to the use of anti-HGF antibodies, and binding fragments thereof, for the diagnosis, assessment and treatment of diseases and disorders associated with HGF.

(21) 2 904 743

(13) A1

(72) Inventeurs(suite)/Inventors(continued): LATHAM, JOHN A., US; GARCIA-MARTINEZ, LEON F., US

(74) Agent: BERESKIN & PARR LLP/S.E.N.C.R.L.,S.R.L.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 September 2014 (25.09.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/153117 A3

(51) International Patent Classification:
*C07K 16/22* (2006.01)

(21) International Application Number:
PCT/US2014/029163

(22) International Filing Date:
14 March 2014 (14.03.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/781,643 14 March 2013 (14.03.2013) US
61/782,868 14 March 2013 (14.03.2013) US

(71) Applicant: **ALDER BIOPHARMACEUTICALS, INC.** [US/US]; 11804 North Creek Parkway South, Bothell, Washington 98011 (US).

(72) Inventors: **DUTZAR, Benjamin, H.**; 3124A Franklin Avenue, E., Seattle, Washington 98102 (US). **ANDERSON, Katie**; 13235 86th Place, NE, Kirkland, Washington 98034 (US). **KOVACEVICH, Brian, R.**; 13916 233rd Street, SE, Snohomish, Washington 98296 (US). **FELDHAUS, Andrew, L.**; 6903 189th Place, SW, Lynnwood, Washington 98036 (US). **LATHAM, John, A.**; 2409 10th Avenue, NW, Seattle, Washington 98119 (US). **GARCIA-MARTINEZ, Leon, F.**; 4926 214th Street, SE, Woodinville, Washington 98072 (US).

(74) Agents: **TESKIN, Robin, L.** et al.; Leclair Ryan, P.C., Intellecutal Property Department, 2318 Mill Road, Suite 1100, Alexandria, Virginia 22314 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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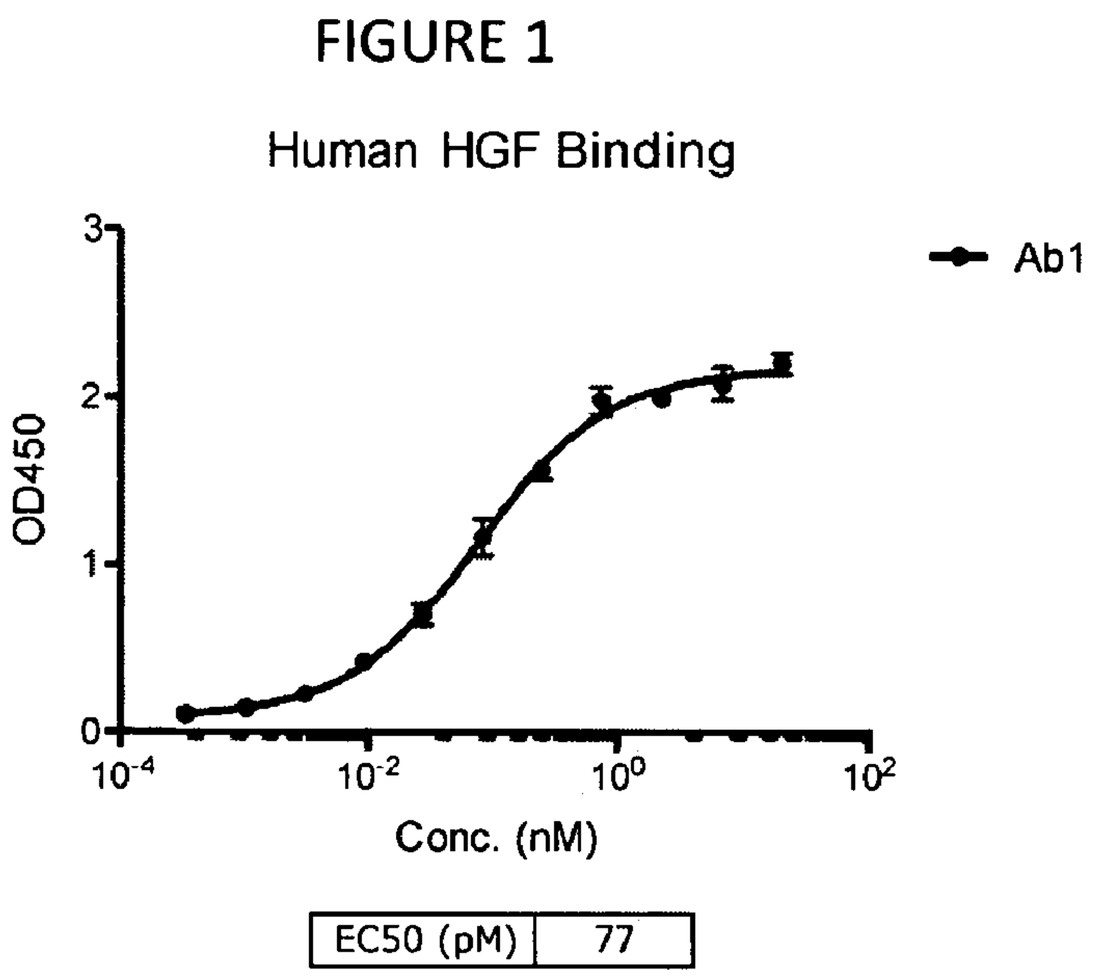
(54) Title: ANTIBODIES TO HGF AND COMPOSITIONS CONTAINING

FIGURE 1




| EC50 (pM) | 77 |
|---|---|

(57) Abstract: The present invention is directed to antibodies and fragments thereof having binding specificity for HGF. Another embodiment of this invention relates to the antibodies described herein, and binding fragments thereof, comprising the sequences of the VH, VL and CDR polypeptides described herein, and the polynucleotides encoding them. The invention also contemplates conjugates of anti-HGF antibodies and binding fragments thereof conjugated to one or more functional or detectable moieties. The invention also contemplates methods of making said anti-HGF antibodies and binding fragments thereof. Embodiments of the invention also pertain to the use of anti-HGF antibodies, and binding fragments thereof, for the diagnosis, assessment and treatment of diseases and disorders associated with HGF.

WO 2014/153117 A3

WO 2014/153117 A3

**(84) Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published**:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

**(88) Date of publication of the international search report**:
8 January 2015

**(15) Information about Correction**:

**Previous Correction**:
see Notice of 27 November 2014

# DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
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NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

# ANTIBODIES TO HGF AND COMPOSITIONS CONTAINING

**[0001]** This application claims priority to US Provisional Serial No. 61/782,868 and US Provisional Serial No. 61/781,643, both filed on March 14, 2013. The contents of both these applications are incorporated by reference in their entirety herein.

**[0002]** This application includes as part of its disclosure a biological sequence listing which is being concurrently submitted through EFS-Web. Said biological sequence listing is contained in a file named "43257o4013.txt" which was created on March 12, 2014 and has a size of 652,047 bytes, and is hereby incorporated by reference in its entirety.

## BACKGROUND OF THE INVENTION

### *Field of the Invention*

**[0003]** This invention pertains to antibodies and fragments thereof, preferably high affinity or avidity antibodies having binding specificity to Hepatocyte Growth Factor (hereinafter "HGF"). The invention also pertains to methods of screening for diseases and disorders associated with HGF, and methods of preventing or treating diseases and disorders associated with HGF by administering said antibodies or fragments thereof.

### *Description of Related Art*

**[0004]** Hepatocyte Growth Factor (HGF) (also known as scatter factor (SF) is produced as a single-chain inactive precursor that is cleaved by serine proteases into two chains that are linked by a disulfide bond. (Abounader, R., *et al.*, Neuro-Oncology, 7:436-451 (2005)) The gene encoding HGF is located on chromosome 7q21.1. The biologically active form of HGF is a heterodimer composed of a 69-kDa α-chain and a 34-kDa β-chain. The α-chain contains an N-terminal hairpin domain and 4 kringle domains, while the β-chain contains a serine protease-like domain having no enzymatic activity. *Id.*

**[0005]** Human Hepatocyte Growth Factor (HGF) is a multifunctional heterodimeric polypeptide produced by mesenchymal cells. HGF has been shown to stimulate angiogenesis, morphogenesis and motogenesis, as well as the growth and scattering of

various cell types (Bussolino et al., J. Cell. Biol. 119: 629, 1992; Zarnegar and Michalopoulos, J. Cell. Biol. 129:1177, 1995; Matsumoto et al, Ciba. Found. Symp. 212:198, 1997; Birchmeier and Gherardi, Trends Cell. Biol. 8:404, 1998; Xin et al., Am. J. pathol. 158:1111, 2001). The pleiotropic activities of HGF are mediated through its receptor, a transmembrane tyrosine kinase encoded by the proto-oncogene c-met. In addition to regulating a variety of normal cellular functions, HGF and its receptor c-met have been shown to be involved in the initiation, invasion and metastasis of tumors (Jeffers et al., J. Mol. Med. 74:505, 1996; Comoglio and Trusolino, J. Clin. Invest. 109:857, 2002). HGF/c-met are coexpressed, often over-expressed, on various human solid tumors including tumors derived from lung, colon, rectum, stomach, kidney, ovary, skin, multiple myeloma and thyroid tissue (Prat et al., Int. J. Cancer 49:323, 1991; Chan et al., Oncogene 2:593, 1988; Weidner et al., Am. J. Respir. Cell Mol. Biol, 8:229, 1993; Derksen et al., Blood 99:1405, 2002). HGF acts as an autocrine (Rong et al., Proc. Natl. Acad. Sci. USA 91:4731, 1994; Koochekpour et al., Cancer Res. 57:5391, 1997) and paracrine growth factor (Weidner et al., Am. J. Respir. Cell Mol. Biol. 8:229, 1993) and anti-apoptotic regulator (Gao et al., J. Biol. Chem. 276:47257, 2001) for these tumors.

**[0006]** HGF is a 102 kDa protein with sequence and structural similarity to plasminogen and other enzymes of blood coagulation (Nakamura et al., Nature 342:440, 1989; Weidner et al., Am. J. Respir. Cell. Mol. Biol. 8:229, 1993, each of which is incorporated herein by reference). Human HGF is synthesized as a 728 amino acid precursor (preproHGF), which undergoes intracellular cleavage to an inactive, single chain form (proHGF) (Nakamura et al., Nature 342:440, 1989: Rosen et al., J. Cell. Biol. 127:1783, 1994). Upon extracellular secretion, proHGF is cleaved to yield the biologically active disulfide-linked heterodimeric molecule composed of an alpha-subunit and beta-subunit. (Nakamura et al., Nature 342:440, 1989; Naldini et al., EMBO J. 11:4825, 1992) The alpha-subunit contains 440 residues (69 kDa with glycosylation), consisting of the N-terminal hairpin domain and four kringle domains. The beta-subunit contains 234 residues (34 kDa) and has a serine protease-like domain, which lacks proteolytic activity. Cleavage of HGF is required for receptor activation, but not for receptor binding (Hartmann et al., Proc. Natl. Acad. Sci. USA 89:11574, 1992; Lokker et al., J. Biol. Chem. 288:17145, 1992). HGF contains 4 putative N-glycosylation sites, 1 in the alpha-subunit and 3 in the beta-subunit. HGF has 2 unique

cell specific binding sites: a high affinity (Kd=2 X $10^{-10}$ M) binding site for the c-met receptor and a low affinity (Kd=$10^{-9}$ M) binding site for heparin sulfate proteoglycans (HSPG), which are present on the cell surface and extracellular matrix (Naldinl et al., Oncogene 6:501, 1991; Bardelii et al., J. Biotechnol. 37:109, 1994; Sakata et al., J. Biol. Chem., 272:9457, 1997).

**[0007]** c-met is a member of the class IV protein tyrosine kinase receptor family. The full length c-met gene was cloned and identified as the c-met proto-oncogene (Cooper et al., Nature 311:29, 1984; Park et al., Proc. Natl. Acad. Sci. USA 84:6379, 1987). The c-met receptor is initially synthesized as a single chain, partially glycosylated precursor, $p170_{(MET)}$ (Park et al., Proc. Natl. Acad. Sci. USA 84:6379, 1987; Giordano et al., Nature 339:155, 1989; Giordano et al., Oncogene 4:1383, 1989; Bardelli et al., J. Biotechnol. 37:109, 1994). Upon further glycosylation, the protein is proteolytically cleaved into a heterodimeric 190 kDa mature protein (1385 amino acids), consisting of the 50 kDa alpha-subunit (residues 1-307) and the 145 kDa beta-subunit. The cytoplasmic tyrosine kinase domain of the beta-subunit is involved in signal transduction.

**[0008]** Several different approaches have been investigated to obtain HGF inhibitors or HGF antagonists. Such inhibitors include truncated HGF proteins such as NK1 (N terminal domain plus kringle domain 1: Lokker et al., J. Biol. Chem. 268:17145, 1993); NK2 (N terminal domain plus kringle domains 1 and 2: Chan et al., Science 254:1382, 1991); and NK4 (N-terminal domain plus four kringle domains), which was shown to partially inhibit the primary growth and metastasis of murine lung tumor LLC in a nude mouse model (Kuba et al., Cancer Res. 60:6737, 2000).

**[0009]** As another approach, Dodge (Master's Thesis, San Francisco State University, 1998) generated antagonist anti-c-met monoclonal antibodies (mAbs). One mAb, 5D5, exhibited strong antagonistic activity in ELISA, but induced a proliferative response of c-met-expressing BAF-3 cells, presumably due to dimerization of the membrane receptors. For this reason, a single domain form of the anti-c-met mAb 5D5 has been developed as an antagonist (Nguyen et al., Cancer Gene Ther, 10:840, 2003).

**[00010]** Cao et al., Proc. Natl. Acad. Sci. USA 98:7443, 2001, reported that the administration of a cocktail of three anti-HGF mAbs, which were selected based upon their ability to inhibit the scattering activity of HGF in vitro, were able to inhibit the growth of human tumors in the xenograft nude mouse model.

**[00011]** More recently, neutralizing (inhibitory) anti-HGF mAbs have been reported including L2G7 (Kim et al., Clin Cancer Res 12:1292, 2006, WO 2005/107800, and USP 7,220,410 HuL2G7 (WO 2007/115049, the human mAbs described in WO 2005/17107, and the HGF binding proteins described in WO 2007/143090 or WO 2007/143098. It has also been reported that the anti-HGF mAb L2G7, when administered systemically, can strongly inhibit growth or even induce regression of orthotopic (intracranial) glioma xenografts and prolong animal survival (Kim et al., op. cit and WO 2006/130773).

**[00012]** As disclosed herein, HGF promotes the growth and/or scattering of various cell types, and has been shown to be involved in the promotion of angiogenesis, the inhibition of cell growth, and the conversion from a mesenchymal to an epithelial phenotype. Also, both HGF and c-met are expressed in a wide variety of human tumors, and their expression levels is sometimes correlated with poor prognosis. Moreover HGF is believed to play a role in the development of a multitude of diseases and disorders, including but not limited to the development and metastasis of numerous cancers, and the development of macular degeneration. Due to the perceived involvement of HGF in a wide range of diseases and disorders, there remains a need in the art for HGF antagonists and compositions containing and methods useful for preventing or treating diseases associated with HGF, as well as methods of screening to identify patients having diseases or disorders associated with HGF. Particularly preferred are anti-HGF antagonists and compositions containing which effectively inhibit at least one HGF associated biological activity and which elicit minimal or no adverse reactions when administered to a patient. The present invention achieves this objective.

## BRIEF SUMMARY OF THE INVENTION

**[00013]** The present invention is directed to specific antibodies and fragments thereof having binding specificity for HGF, in particular antibodies having desired epitopic specificity, high affinity or avidity and/or functional properties. One embodiment of the invention encompasses chimeric or humanized antibodies and fragments thereof capable of binding to HGF and/or the HGF-HGFR complex. Another embodiment of this invention relates to the antibodies described herein, comprising the sequences of

the $V_H$, $V_L$ and CDR polypeptides described herein, and the polynucleotides encoding them. In more specific embodiments of the invention these antibodies will possess binding affinities (Kd's) less than 500 picomolar and/or $K_{off}$ values less than or equal to $10^{-4}$ $S^{-1}$.

**[00014]** More particularly, the invention provides rabbit antibodies and humanized and chimeric antibodies derived therefrom specific to HGF as well as antibody fragments specific to HGF which include e.g., Fab', $F(ab')_2$, Fv, scFv fragments, SMIPs (small molecule immunopharmaceuticals), camelbodies, nanobodies, monovalent antibodies such as MetMab like antibodies, and IgNAR which may be used in therapy and diagnostics.

**[00015]** Further, the invention provides nucleic acids and host cells containing that encode for and result in the expression of the subject anti-HGF antibodies, i.e., rabbit antibodies and antibody fragments and modified forms thereof including, by way of example, humanized and chimeric antibodies derived therefrom as well as antibody fragments which include e.g., Fab', $F(ab')_2$, Fv, scFv fragments, SMIPs (small molecule immunopharmaceuticals), camelbodies, nanobodies, monovalent antibodies such as MetMab like antibodies, and IgNAR.

**[00016]** Also the invention relates to expression systems for the manufacture of the inventive anti-HGF antibodies, including yeast, fungi, mammalian, and other cells useful for the manufacture of antibodies and antibody fragments.

**[00017]** Also, the invention relates to novel antibodies and antibody fragments that specifically bind to human HGF which compete with and/or specifically bind to the same or overlapping epitope(s) on HGF as any of the anti-HGF antibodies and antibody fragments exemplified herein.

**[00018]** Further, the invention provides anti-HGF antibodies and antibody fragments that partially or fully neutralize HGF, and which partially or completely inhibit one or more biological activities of HGF such as the ability of HGF to cause fibrosis or the scattering, proliferation, angiogenesis, or chemotaxis of cells.

**[00019]** The invention further pertains to the in vivo use of the subject anti-HGF antibodies and antibody fragments alone or in association with other active agents or drugs for blocking, inhibiting or neutralizing HGF or at least one activity of HGF and/or for inhibiting or blocking the HGF/HGF-R (c-met) interaction or inhibiting c-met activation.

**[00020]** The invention further specifically pertains to the in vivo use of the subject anti-HGF antibodies and antibody fragments alone or in association with other active agents or drugs.

**[00021]** The invention further specifically pertains to the, anti-HGF antibodies described herein, or fragments thereof, for ameliorating or reducing the symptoms of, or treating, or preventing, the following non-limiting listing of proliferative, non-proliferative diseases and disorders such as cancers, including ovarian cancer, breast cancer, lung cancer (small cell or non-small cell), colon and colorectal cancer, prostate cancer, pancreatic cancer, renal cancer, gastric cancer, liver cancer, bladder cancer, thyroid cancer, endometrial cancer, head-and-neck tumors, melanoma, sarcomas, leukemias; lymphomas; and brain tumors (e.g., glioblastomas), of children or adults; macular degeneration; Alzheimer's disease; and malarial infection. In a preferred embodiment, the disease is selected from a cancer or macular degeneration.

**[00022]** The invention further pertains to medicaments for the therapeutic and/or prophylactic treatment of different diseases such as a cancer, a tumor, a cell proliferative disorder, an immune (such as autoimmune) disorder and/or an angiogenesis-related disorder. In another embodiment, the invention provides use of a nucleic acid of the invention in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor, a cell proliferative disorder, an immune (such as autoimmune) disorder and/or an angiogenesis-related disorder.

**[00023]** The invention further pertains to the use of an expression vector of the invention in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor, a cell proliferative disorder, an immune (such as autoimmune) disorder and/or an angiogenesis-related disorder. In another embodiment of the invention, the invention provides use of an of a host cell of the invention in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor, a cell proliferative disorder, an immune (such as autoimmune) disorder and/or an angiogenesis-related disorder. In another embodiment of the invention, the invention provides the use of an article of manufacture of the invention in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor, a cell proliferative disorder, an immune (such as autoimmune) disorder and/or an angiogenesis-related

disorder. The invention further pertains to the use of a kit of the invention in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor, a cell proliferative disorder, an immune (such as autoimmune) disorder and/or an angiogenesis-related disorder.

**[00024]** The invention further specifically pertains to modulating disease states associated with dysregulation of the HGF/c-met signaling axis and thereby modulating at least one of cell proliferation, invasion, metastasis and angiogenesis.

**[00025]** Methods of the invention can be used to affect any pathological state associated with dysregulation of the HGF/c-met signaling which 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 malignant and benign tumors; non-leukemias and lymphoid malignancies; neuronal, glial, astrocytal, hypothalamic and other glandular, macrophagal, epithelial, stromal and blastocoelic disorders; and inflammatory, immunologic and other angiogenesis-related disorders. carcinoma, 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 and various types of head and neck cancer; disirders involving dysregulation of angiogenesis including both non-neoplastic and neoplastic conditions such as the cancers described herein and non-neoplastic disorders including but are not limited to undesired or aberrant hypertrophy, arthritis, rheumatoid arthritis (RA), psoriasis, psoriatic plaques, sarcoidosis, atherosclerosis, atherosclerotic plaques, diabetic and other proliferative retinopathies including retinopathy of prematurity, retrolental fibroplasia, neovascular glaucoma, age-related macular degeneration, diabetic macular edema, corneal neovascularization, corneal graft neovascularization, corneal graft rejection, retinal/choroidal neovascularization, neovascularization of the angle (rubeosis), ocular neovascular disease, vascular restenosis, arteriovenous malformations (AVM), meningioma, hemangioma, angiofibroma, thyroid hyperplasias

(including Grave's disease), corneal and other tissue transplantation, chronic inflammation, lung inflammation, acute lung injury/ARDS, sepsis, primary pulmonary hypertension, malignant pulmonary effusions, cerebral edema (e.g., associated with acute stroke/closed head injury/trauma), synovial inflammation, pannus formation in RA, myositis ossificans, hypertropic bone formation, osteoarthritis (OA), refractory ascites, polycystic ovarian disease, endometriosis, 3rd spacing of fluid diseases (pancreatitis, compartment syndrome, burns, bowel disease), uterine fibroids, premature labor, chronic inflammation such as IBD (Crohn's disease and ulcerative colitis), renal allograft rejection, inflammatory bowel disease, nephrotic syndrome, undesired or aberrant tissue mass growth (non-cancer), hemophilic joints, hypertrophic scars, inhibition of hair growth, Osler-Weber syndrome, pyogenic granuloma retrolental fibroplasias, scleroderma, trachoma, vascular adhesions, synovitis, dermatitis, preeclampsia, ascites, pericardial effusion (such as that associated with pericarditis), and pleural effusion.

**[00026]** In certain embodiments, a specific binding agent to HGF is used with one or more particular therapeutic agents to treat various cancers. In certain embodiments, a specific binding agent to HGF is used with one or more particular therapeutic agents to treat or prevent malaria. In certain embodiments, a specific binding agent to HGF is used with one or more particular therapeutic agents to treat or prevent proliferative diabetic retinopathy. In certain embodiments, in view of the condition and the desired level of treatment, two, three, or more agents may be administered. In certain embodiments, such agents may be provided together by inclusion in the same formulation. In certain embodiments, such agents and a specific binding agent to HGF may be provided together by inclusion in the same formulation. In certain embodiments, such agents may be formulated separately and provided together by inclusion in a treatment kit. In certain embodiments, such agents and a specific binding agent to HGF may be formulated separately and provided together by inclusion in a treatment kit. In certain embodiments, such agents may be provided separately.

**[00027]** The invention also contemplates conjugates of anti-HGF antibodies and binding fragments thereof conjugated to one or more functional or detectable moieties. The invention also contemplates methods of making said chimeric or humanized anti-HGF or anti-HGF/HGFR complex antibodies and binding fragments thereof. In one embodiment, binding fragments include, but are not limited to, Fab, Fab', F $(ab')_2$, Fv,

scFv fragments, SMIPs (small molecule immunopharmaceuticals), camelbodies, nanobodies, and IgNAR.

**[00028]** Embodiments of the invention pertain to the use of anti-HGF antibodies for the diagnosis, assessment and treatment of diseases and disorders associated with HGF or aberrant expression thereof. The invention also contemplates the use of fragments of anti-HGF antibodies for the diagnosis, assessment and treatment of diseases and disorders associated with HGF or aberrant expression thereof. Other embodiments of the invention relate to the production of anti-HGF antibodies in recombinant host cells, preferably diploid yeast such as diploid Pichia and other yeast strains.

## BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

**[00029]** Figure 1 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab1.

**[00030]** Figure 2 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab2.

**[00031]** Figure 3 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab3.

**[00032]** Figure 4 provides the human-HGF ELISA binding data obtained following the protocol in Example 7 infra for antibody Ab4.

**[00033]** Figure 5 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab5.

**[00034]** Figure 6 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab6.

**[00035]** Figure 7 provides the human-HGF ELISA binding data obtained following the protocol in infra for antibody Ab7.

**[00036]** Figure 8 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab8.

**[00037]** Figure 9 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab9.

**[00038]** Figure 10 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab10.

**[00039]** Figure 11 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab11.

**[00040]** Figure 12 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab12.

**[00041]** Figure 13 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab13.

**[00042]** Figure 14 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab14.

**[00043]** Figure 15 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab15.

**[00044]** Figure 16 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab16.

**[00045]** Figure 17 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab17.

**[00046]** Figure 18 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab18.

**[00047]** Figure 19 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab19.

**[00048]** Figure 20 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab20.

**[00049]** Figure 21 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab21.

**[00050]** Figure 22 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab23.

**[00051]** Figure 23 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab24.

**[00052]** Figure 24 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab25.

**[00053]** Figure 25 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab26.

**[00054]** Figure 26 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab27.

**[00055]** Figure 27 provides the human-HGF ELISA binding data obtained following the protocol in Example 8 infra for antibody Ab28.

**[00056]** Figure 28 provides the response of subcutaneous U-87MG glioma to treatment with a negative control antibody, or Ab10 or Ab12 (10 mg/kg/inj) following the protocol corresponding to Figure 28 and 29 in Example 10 *infra*.

**[00057]** Figure 29 provides the survival proportions curve of subcutaneous U-87MG glioma treated with either a negative control antibody, or Ab10 or Ab12 (10 mg/kg/inj) obtained following the protocol for Figure 28 and 29 in Example 10 *infra*.

**[00058]** Figure 30 provides the response of subcutaneous U-87MG glioma to treatment with increasing doses of Ab8 (10, 2.5 and 0.25 mg/kg/inj) or a negative control antibody (10 mg/kg/inj) obtained following the protocol corresponding to Figures 30 and 31 described in Example 10 infra.

**[00059]** Figure 31 provides the survival proportions curve of subcutaneous U-87MG glioma treated with either increasing doses of Ab8 (10, 2.5 and 0.25 mg/kg/inj) or a negative control antibody (10 mg/kg/inj) obtained following the experimental protocol corresponding to Figures 30 and 31 described in Example 10 *infra*.

**[00060]** Figure 32 provides the response of subcutaneous U-87MG glioma to treatment with increasing doses of Ab10 (10, 2.5 and 0.25 mg/kg/inj) or a negative control antibody (10 mg/kg/inj) obtained following the protocol corresponding to Figures 32 and 33 described in Example 10 *infra*.

**[00061]** Figure 33 provides the survival proportions curve of subcutaneous U-87MG glioma treated with either increasing doses of Ab10 (10, 2.5 and 0.25 mg/kg/inj) or a negative control antibody (10 mg/kg/inj) obtained following the protocol corresponding to Figures 32 and 33 in Example 10 *infra*.

**[00062]** Figure 34 provides the response of subcutaneous U-87MG glioma to treatment with increasing doses of Ab28 (30, 10, and 2.5 mg/kg/inj) or a negative control antibody (30 mg/kg/inj) obtained following the experimental protocol corresponding to Figures 34 and 35 described in Example 10 *infra*.

**[00063]** Figure 35 provides the survival proportions curve of subcutaneous U-87MG glioma treated with either increasing doses of Ab28 (30, 10, and 2.5 mg/kg/inj) or a negative control antibody (30 mg/kg/inj) obtained following the experimental protocol corresponding to Figures 34 and 35 described in Example 10 *infra*.

**[00064]** Figure 36 contains data from experiments showing the inhibition of human-HGF driven phosphorylation of Y1234/35, Y1003 and Y1349 of c-met by Ab8 using PC-3 cells (prostate adenocarcinoma) following the experimental protocol described in Example 11 *infra*.

**[00065]** Figures 37-50 respectively contain the results of experiments assaying the effect of different anti-HGF antibodies according to the invention (Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25 and Ab28) on human-HGF driven cell proliferation of 4mBr-5 cells (rhesus monkey bronchial epithelial cells) following the experimental protocol in Example 12 *infra*.

**[00066]** Figure 51 contains the results of experiments assaying the effect of an anti-HGF antibody (Ab8) according to the invention on human-HGF driven cell invasion of DBTRG cells (human glioblastoma) using Matrigel chambers following the experimental protocol described in Example 13 *infra*.

**[00067]** Figures 52A-52G provide the polypeptide sequences of the full-length heavy chain for antibodies Ab1-Ab21, and Ab23-28 aligned by their framework regions (FR), complementarity determining regions (CDRs), and constant regions.

**[00068]** Figures 53A-53D provide the polypeptide sequences of the full-length light chain for antibodies Ab1-Ab21 and Ab23-28 aligned by their framework regions (FR), complementarity determining regions (CDRs), and constant regions.

**[00069]** Figure 54A-54S provide the polynucleotide sequences encoding the full-length heavy chain for antibodies Ab1-Ab21 and Ab23-28 aligned by their framework regions (FR), complementarity determining regions (CDRs), and constant regions.

**[00070]** Figure 55A-55J provide the polynucleotide sequences encoding the full-length light chain for antibodies Ab1-Ab21 and Ab23-28 aligned by their framework regions (FR), complementarity determining regions (CDRs), and constant regions.

**[00071]** Figure 56 provides the polypeptide sequence coordinates for the variable region and complementarity determining regions (CDRs) of the heavy chain for antibodies Ab1-Ab21 and Ab23-28.

**[00072]** Figure 57 provides the polypeptide sequence coordinates for the constant region and framework regions (FR) of the heavy chain for antibodies Ab1-Ab21, and Ab23-28.

**[00073]** Figure 58 provides the polypeptide sequence coordinates for the variable region and complementarity determining regions (CDRs) of the light chain for antibodies Ab1-Ab21 and Ab23-28.

**[00074]** Figure 59 provides the polypeptide sequence coordinates for the constant region and framework regions (FR) of the light chain for antibodies Ab1-Ab21, and Ab23-28.

**[00075]** Figure 60 provides the polynucleotide sequence coordinates for the variable region and complementarity determining regions (CDRs) of the heavy chain for antibodies Ab1-Ab21 and Ab23-28.

**[00076]** Figure 61 provides the polynucleotide sequence coordinates for the constant region and framework regions (FR) of the heavy chain for antibodies Ab1-Ab21 and Ab23-28.

**[00077]** Figure 62 provides the polynucleotide sequence coordinates for the variable region and complementarity determining regions (CDRs) of the light chain for antibodies Ab1-Ab21 and Ab23-28.

**[00078]** Figure 63 provides the polynucleotide sequence coordinates for the constant region and framework regions (FR) of the light chain for antibodies Ab1-Ab21, and Ab23-28.

## DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

### *Definitions*

**[00079]** It is to be understood that this invention is not limited to the particular methodology, protocols, cell lines, animal species or genera, and reagents described, as such may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

**[00080]** As used herein the singular forms "a", "and", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a cell" includes a plurality of such cells and reference to "the protein" includes reference to one or more proteins and equivalents thereof known to those skilled in the art, and so forth. All technical and scientific terms used herein have the same meaning

as commonly understood to one of ordinary skill in the art to which this invention belongs unless clearly indicated otherwise.

**[00081]** Hepatocyte Growth Factor (HGF): As used herein, HGF encompasses not only the following preproprotein amino acid sequence available as NCBI Reference Sequence: NP_000592.3 (Homo sapiens HGF isoform 1 preproprotein):

**[00082]** MWVTKLLPALLLQHVLLHLLLLPIAIPYAEGQRKRRNTIHEFKKSAKT TLIKIDPALKIKTKKVNTADQCANRCTRNKGLPFTCKAFVFDKARKQCLWFPF NSMSSGVKKEFGHEFDLYENKDYIRNCIIGKGRSYKGTVSITKSGIKCQPWSSMI PHEHSFLPSSYRGKDLQENYCRNPRGEEGGPWCFTSNPEVRYEVCDIPQCSEVE CMTCNGESYRGLMDHTESGKICQRWDHQTPHRHKFLPERYPDKGFDDNYCRN PDGQPRPWCYTLDPHTRWEYCAIKTCADNTMNDTDVPLETTECIQGQGEGYR GTVNTIWNGIPCQRWDSQYPHEHDMTPENFKCKDLRENYCRNPDGSESPWCFT TDPNIRVGYCSQIPNCDMSHGQDCYRGNGKNYMGNLSQTRSGLTCSMWDKN MEDLHRHIFWEPDASKLNENYCRNPDDDAHGPWCYTGNPLIPWDYCPISRCEG DTTPTIVNLDHPVISCAKTKQLRVVNGIPTRTNIGWMVSLRYRNKHICGGSLIKE SWVLTARQCFPSRDLKDYEAWLGIHDVHGRGDEKCKQVLNVSQLVYGPEGSD LVLMKLARPAVLDDFVSTIDLPNYGCTIPEKTSCSVYGWGYTGLINYDGLLRV AHLYIMGNEKCSQHHRGKVTLNESEICAGAEKIGSGPCEGDYGGPLVCEQHKM RMVLGVIVPGRGCAIPNRPGIFVRVAYYAKWIHKIILTYKVPQS (SEQ ID NO: 1081), but also any pro-, mature, soluble, and/or membrane-bound forms of this HGF amino acid sequence, as well as mutants (mutiens), splice variants, isoforms, orthologs, homologues and variants of this sequence.

**[00083]** Hepatocyte Growth Factor Receptor (HGF-R): As used herein, the terms "HGF-R" and "c-met" refer to a cellular receptor for hepatocyte growth factor (HGF), which typically includes an extracellular domain, a transmembrane domain and an intracellular domain, as well as variants and fragments thereof which retain the ability to bind HGF, and includes the polypeptide molecule that comprises the full-length, native amino acid sequence. Human Hepatocyte Growth Factor (HGF) is a multifunctional heterodimeric polypeptide produced by mesenchymal cells. HGF has been shown to stimulate angiogenesis, morphogenesis and motogenesis, as well as the growth and scattering of various cell types (Bussolino et al., J. Cell. Biol. 119: 629, 1992; Zarnegar and Michalopoulos, J. Cell. Biol. 129:1177, 1995; Matsumoto et al., Ciba. Found. Symp. 212:198, 1997; Birchmeier and Gherardi, Trends Cell. Biol. 8:404,

1998; Xin et al. Am. J. Pathol. 158:1111, 2001). The pleiotropic activities of HGF are mediated through its receptor, a transmembrane tyrosine kinase encoded by the proto-oncogene c-met. In addition to regulating a variety of normal cellular functions, HGF and its receptor c-met have been shown to be involved in the initiation, invasion and metastasis of tumors (Jeffers et al., J. Mol. Med. 74:505, 1996; Comoglio and Trusolino, J. Clin. Invest. 109:857, 2002). HGF/c-met are coexpressed, often over-expressed, on various human solid tumors including tumors derived from lung, colon, rectum, stomach, kidney, ovary, skin, multiple myeloma and thyroid tissue (Prat et al., Int. J. Cancer 49:323, 1991; Chan et al., Oncogene 2:593, 1988; Weidner et al., Am. J. Respir. Cell. Mol. Biol. 8:229, 1993; Derksen et al., Blood 99:1405, 2002). HGF acts as an autocrine (Rong et al., Proc. Natl. Acad. Sci. USA 91:4731, 1994; Koochekpour et al., Cancer Res. 57:5391, 1997) and paracrine growth factor (Weidner et al., Am. J. Respir. Cell. Mol. Biol. 8:229, 1993) and anti-apoptotic regulator (Gao et al., J. Biol. Chem. 276:47257, 2001) for these tumors. HGF is a 102 kDa protein with sequence and structural similarity to plasminogen and other enzymes of blood coagulation (Nakamura et al., Nature 342:440, 1989; Weidner et al., Am. J. Respir. Cell. Mol. Biol. 8:229, 1993). Human HGF is synthesized as a 728 amino acid precursor (preproHGF), which undergoes intracellular cleavage to an inactive, single chain form (proHGF) (Nakamura et al., Nature 342:440, 1989; Rosen et al., J. Cell. Biol. 127:1783, 1994). Upon extracellular secretion, proHGF is cleaved to yield the biologically active disulfide-linked heterodimeric molecule composed of an a-subunit and n-subunit (Nakamura et al., Nature 342:440, 1989; Naldini et al., EMBO J. 11:4825, 1992). The alpha-subunit contains 440 residues (69 kDa with glycosylation), consisting of the N-terminal hairpin domain and four kringle domains. The beta-subunit contains 234 residues (34 kDa) and has a serine protease-like domain, which lacks proteolytic activity. HGF has two unique cell specific binding sites: a high affinity (Kd=2 X10-$^{10}$ M) binding site for the c-met receptor and a low affinity (Kd=$10^{-9}$ M) binding site for heparin sulfate proteoglycans (HSPG), which are present on the cell surface and extracellular matrix (Naldini et al., Oncogene 6:501, 1991; Bardelli et al., J. Biotechnol. 37:109, 1994; Sakata et al., J. Biol. Chem., 272:9457, 1997).

**[00084]** "C-met" or "HGF-R" is a member of the class IV protein tyrosine kinase receptor family. The full length c-met gene was cloned and identified as the c-met proto-oncogene (Cooper et al., Nature 311:29, 1984; Park et al., Proc. Natl. Acad. Sci.

USA 84:6379, 1987). NK2 (a protein encompassing the N-terminus and first two kringle domains of the alpha-subunit) is sufficient for binding to c-met and activation of the signal cascade for motility, however the full length protein is required for the mitogenic response (Weidner et al., Am. J. Respir. Cell. Mol. Biol. 8:229, 1993). HSPG binds to HGF by interacting with the N terminus of HGF. HGF/c-met have been reported to play important roles in several aspects of cancer development such as tumor initiation, invasion, metastasis, regulation of apoptosis and angiogenesis. Several different approaches have been investigated to obtain an effective antagonistic molecule: truncated HGF proteins such as NK1 (N terminal domain plus kringle domain 1; Lokker et al., J. Biol. Chem. 268:17145, 1993), NK2 (N terminal domain plus kringle domains 1 and 2; Chan et al., Science 254:1382, 1991) and NK4 (N-terminal domain plus four kringle domains; Kuba et al., Cancer Res. 60:6737, 2000), anti-c-met mAbs (Dodge, Master's Thesis, San Francisco State University, 1998) and anti-HGF mAbs (Cao et al., Proc. Natl. Acad. Sci. USA 98:7443, 2001).

**[00085]** The term "Neutralizing or Antagonizing Anti-HGF antibody or antibody fragment" or "HGF Antibody Antagonist" herein refers to a monoclonal antibody (mAb) that binds HGF (i.e., an anti-HGF mAb), wherein the binding partially or completely inhibits one or more biological activities of HGF (i.e., when the mAb is used as a single agent). Among the biological properties of HGF that a neutralizing antibody may inhibit are the ability of HGF to bind to its c-met receptor, to cause the scattering of certain cell lines such as Madin-Darby canine kidney (MDCK) cells; to stimulate proliferation of (i.e., be mitogenic for) certain cells including hepatocytes, Mv 1 Lu mink lung epithelial cells, and various human tumor cells; to cause scattering of specific cells, to stimulate angiogenesis, for example as measured by stimulation of human umbilical vascular endothelial cell (HUVEC) proliferation or tube formation or by induction of blood vessels when applied to the chick embryo chorioallantoic membrane (CAM), to promote cell invasion or metastasis, and to promote fibrosis.

**[00086]** A "blocking" antibody or an "antagonist" antibody preferably is one which inhibits or reduces biological activity of the antigen it binds (for e.g., activated HGF beta-chain or site/epitope on c-met to which activated HGF beta binds). Preferred blocking antibodies or antagonist antibodies substantially or completely inhibit the biological activity of the antigen.

**[00087]** An "agonist antibody", as used herein, is an antibody which mimics at least one of the functional activities of a polypeptide of interest (for e.g., an antibody could provide at least one of the c-met activating functions of activated HGF beta chain).

**[00088]** A "disorder" is any condition that would benefit from treatment with a substance/molecule or method 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 malignant and benign tumors; non-leukemias and lymphoid malignancies; neuronal, glial, astrocytal, hypothalamic and other glandular, macrophagal, epithelial, stromal and blastocoelic disorders; and inflammatory, immunologic and other angiogenesis-related disorders.

**[00089]** 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.

**[00090]** "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.

**[00091]** 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, 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 and various types of head and neck cancer.

**[00092]** 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. Desirable effects of treatment include preventing occurrence or recurrence of disease, alleviation of

symptoms, diminishment of any direct or indirect pathological consequences of the disease, preventing metastasis, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. In some embodiments, antibodies of the invention are used to delay development of a disease or disorder.

**[00093]** An "effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic or prophylactic result. A "therapeutically effective amount" of a substance/molecule of the invention, agonist or antagonist may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the substance/molecule, agonist or antagonist 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, agonist or antagonist are outweighed by the therapeutically beneficial effects.

**[00094]** 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 will be less than the therapeutically effective amount.

**[00095]** The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes (e.g., $At^{211}$, $I^{131}$, $I^{125}$, $Y^{90}$, $Re^{186}$, $Re^{188}$, $Sm^{153}$, $Bi^{212}$, $P^{32}$ and radioactive isotopes of Lu), chemotherapeutic agents e.g. methotrexate, adriamicin, vinca alkaloids (vincristine, vinblastine, etoposide), doxorubicin, melphalan, mitomycin C, chlorambucil, daunorubicin or other intercalating agents, enzymes and fragments thereof such as nucleolytic enzymes, antibiotics, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, including fragments and/or variants thereof, and the various antitumor or anticancer agents disclosed below. Other cytotoxic agents are described below. A tumoricidal agent causes destruction of tumor cells.

**[00096]** A "chemotherapeutic agent" is a chemical compound useful in the treatment of a proliferative disease such as cancer. Examples of chemotherapeutic agents include alkylating agents such as thiotepa and CYTOXAN.®. cyclosphosphamide; alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa,

carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, trietylenephosphoramide, e and trimethylolomelamine; acetogenins (especially bullatacin and bullatacinone); a camptothecin (including the synthetic analogue topotecan); bryostatin; callystatin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogues); cryptophycins (particularly cryptophycin 1 and cryptophycin 8); dolastatin; duocarmycin (including the synthetic analogues, KW-2189 and CB1-TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimustine; antibiotics such as the enediyne antibiotics (e.g., calicheamicin, especially calicheamicin gamma1I and calicheamicin omegaI1 (see, e.g., Agnew, Chem Intl. Ed. Engl., 33: 183-186 (1994)); dynemicin, including dynemicin A; bisphosphonates, such as clodronate; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromophores), aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, ADRIAMYCIN®. doxorubicin (including morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine;

elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidanmol; nitraerine; pentostatin; phenamet; pirarubicin; losoxantrone; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK® polysaccharide complex (JHS Natural Products, Eugene, Oreg.); razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2"-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g., TAXOL® paclitaxel (Bristol-Myers Squibb Oncology, Princeton, N.J.), ABRAXANE.TM. Cremophor-free, albumin-engineered nanoparticle formulation of paclitaxel (American Pharmaceutical Partners, Schaumberg, Ill.), and TAXOTERE® doxetaxel (Rhone-Poulenc Rorer, Antony, France); chloranbucil; GEMZAR® gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitoxantrone; vincristine; NAVELBINE® vinorelbine; novantrone; teniposide; edatrexate; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoids such as retinoic acid; capecitabine; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

**[00097]** Also included in the definition of "chemotherapeutic agent" above are anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens and selective estrogen receptor modulators (SERMs), including, for example, tamoxifen (including NOLVADEX® tamoxifen), raloxifene, droloxifene, 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and FARESTON, toremifene; aromatase inhibitors that inhibit the enzyme aromatase, which regulates estrogen production in the adrenal glands, such as, for example, 4(5)-imidazoles, aminoglutethimide, MEGASE® megestrol acetate, AROMASIN® exemestane, formestanie, fadrozole, RIVISOR® vorozole, FEMARA® letrozole, and ARIMIDEX® anastrozole; and anti-androgens such as flutamide, nilutamide, bicalutamide, leuprolide, and goserelin; as well as troxacitabine (a 1,3-dioxolane nucleoside cytosine analog); antisense oligonucleotides, particularly those which inhibit expression of genes in signaling pathways implicated in abherant cell proliferation, such as, for example, PKC-

alpha, Ralf and H-Ras; ribozymes such as a VEGF expression inhibitor (e.g., ANGIOZYME® ribozyme) and a HER2 expression inhibitor; vaccines such as gene therapy vaccines, for example, ALLOVECTIN® vaccine, LEUVECTIN® vaccine, and VAXID® vaccine; PROLEUKIN® rIL-2; LURTOTECAN® topoisomerase 1 inhibitor; ABARELIX® rmRH; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

**[00098]** A "growth inhibitory agent" when used herein refers to a compound or composition which inhibits growth of a cell whose growth is dependent upon HGF/c-met activation either in vitro or in vivo. Thus, the growth inhibitory agent may be one which significantly reduces the percentage of HGF/c-met-dependent cells in S phase. Examples of growth inhibitory agents include agents that block cell cycle progression (at a place other than S phase), such as agents that induce G1 arrest and M-phase arrest. Classical M-phase blockers include the vincas (vincristine and vinblastine), taxanes, and topoisomerase II inhibitors such as doxorubicin, epirubicin, daunorubicin, etoposide, and bleomycin. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C. Further information can be found in The Molecular Basis of Cancer, Mendelsohn and Israel, eds., Chapter 1, entitled "Cell cycle regulation, oncogenes, and antineoplastic drugs" by Murakami et al. (WB Saunders: Philadelphia, 1995), especially p. 13. The taxanes (paclitaxel and docetaxel) are anticancer drugs both derived from the yew tree. Docetaxel (TAXOTERE®, Rhone-Poulenc Rorer), derived from the European yew, is a semisynthetic analogue of paclitaxel (TAXOL®, Bristol-Myers Squibb). Paclitaxel and docetaxel promote the assembly of microtubules from tubulin dimers and stabilize microtubules by preventing depolymerization, which results in the inhibition of mitosis in cells.

**[00099]** "Doxorubicin" is an anthracycline antibiotic. The full chemical name of doxorubicin is (8S-cis)-10-[(3-amino-2,3,6-trideoxy-alpha-L-lyxo-hexapyranosyl)oxy]-7,- 8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione.

**[000100]** The terms "cell proliferative disorder" and "proliferative disorder" herein refer to disorders that are associated with some degree of abnormal cell proliferation. In one embodiment, the cell proliferative disorder is cancer or a tumor. As noted

previously, a "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.

**[000101]** 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, 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 and various types of head and neck cancer.

**[000102]** The term “Dysregulation of angiogenesis” herein includes any condition wherein there is aberrant angiogenesis. This includes both non-neoplastic and neoplastic conditions. Neoplastics include but are not limited to cancers described above. Non-neoplastic disorders include but are not limited to undesired or aberrant hypertrophy, arthritis, rheumatoid arthritis (RA), psoriasis, psoriatic plaques, sarcoidosis, atherosclerosis, atherosclerotic plaques, diabetic and other proliferative retinopathies including retinopathy of prematurity, retrolental fibroplasia, neovascular glaucoma, age-related macular degeneration, diabetic macular edema, corneal neovascularization, corneal graft neovascularization, corneal graft rejection, retinal/choroidal neovascularization, neovascularization of the angle (rubeosis), ocular neovascular disease, vascular restenosis, arteriovenous malformations (AVM), meningioma, hemangioma, angiofibroma, thyroid hyperplasias (including Grave's disease), corneal and other tissue transplantation, chronic inflammation, lung inflammation, acute lung injury/ARDS, sepsis, primary pulmonary hypertension, malignant pulmonary effusions, cerebral edema (e.g., associated with acute stroke/closed head injury/trauma), synovial inflammation, pannus formation in RA, myositis ossificans, hypertropic bone formation, osteoarthritis (OA), refractory ascites, polycystic ovarian disease, endometriosis, 3rd spacing of fluid diseases (pancreatitis,

compartment syndrome, burns, bowel disease), uterine fibroids, premature labor, chronic inflammation such as IBD (Crohn's disease and ulcerative colitis), renal allograft rejection, inflammatory bowel disease, nephrotic syndrome, undesired or aberrant tissue mass growth (non-cancer), hemophilic joints, hypertrophic scars, inhibition of hair growth, Osler-Weber syndrome, pyogenic granuloma retrolental fibroplasias, scleroderma, trachoma, vascular adhesions, synovitis, dermatitis, preeclampsia, ascites, pericardial effusion (such as that associated with pericarditis), and pleural effusion.

**[000103]** The term "Recombinant cell" or "recombinant host cell" herein in general refers to any cell engineered to express one or more antibody polypeptides according to the invention. This includes by way of example bacterial, fungal, yeast, mammalian, invertebrate such as insect, plant and avian cells. Preferred host cells are yeast, fungi, especially filamentous fungi and mammalian cells. Yeast and filamentous fungi include, but are not limited to Pichia pastoris, Pichia finlandica, Pichia trehalophila, Pichia koclamae, Pichia membranaefaciens, Pichia minuta (Ogataea minuta, Pichia lindneri), Pichia opuntiae, Pichia thermotolerans, Pichia salictaria, Pichia guercuum, Pichia pijperi, Pichia stiptis, Pichia methanolica, Pichia sp., Saccharomyces cerevisiae, Saccharomyces sp., Hansenula polymorpha, Kluyveromyces sp., Kluyveromyces lactis, Candida albicans, Aspergillus nidulans, Aspergillus niger, Aspergillus oryzae, Trichoderma reesei, Chrysosporium lucknowense, Fusarium sp., Fusarium gramineum, Fusarium venenatum, Physcomitrella patens and Neurospora crassa. Pichia sp., any Saccharomyces sp., Hansenula polymorpha, any Kluyveromyces sp., Candida albicans, any Aspergillus sp., Trichoderma reesei, Chrysosporium lucknowense, any Fusarium sp. and Neurospora crassa.

**[000104]** Examples of invertebrate cells include insect cells such as Drosophila S2 and Spodoptera Sf9, as well as plant cells.

**[000105]** Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver

cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art. Preferred mammalian cells for antibody expression include CHO cells and COS cells. In an exemplary embodiment the recombinant host cells are haploidal or polyploidal yeast cells of the genus Pichia.

**[000106]** Mating competent yeast species: In the present invention this is intended to broadly encompass any diploid or tetraploid yeast which can be grown in culture. Such species of yeast may exist in a haploid, diploid, or other polyploid form. The cells of a given ploidy may, under appropriate conditions, proliferate for an indefinite number of generations in that form. Diploid cells can also sporulate to form haploid cells. Sequential mating can result in tetraploid strains through further mating or fusion of diploid strains. The present invention contemplates the use of haploid yeast, as well as diploid or other polyploid yeast cells produced, for example, by mating or spheroplast fusion.

**[000107]** Mating competent yeast include yeast which are a member of the *Saccharomycetaceae* family, which includes the genera *Arxiozyma*; *Ascobotryozyma*; *Citeromyces*; *Debaryomyces*; *Dekkera*; *Eremothecium; Issatchenkia*; *Kazachstania; Kluyveromyces*; *Kodamaea*; *Lodderomyces*; *Pachysolen*; Pichia; Saccharomyces; *Saturnispora*; Tetrapisispora; *Torulaspora*; *Williopsis;* and Zygosaccharomyces. Other types of yeast potentially useful in the invention include *Yarrowia*; *Rhodosporidium; Candida*; *Hansenula*; *Filobasium*; *Sporidiobolus*; *Bullera*; *Leucosporidium* and *Filobasidella.*

**[000108]** In a preferred embodiment of the invention, the mating competent yeast is a member of the genus Pichia. In a further preferred embodiment of the invention, the mating competent yeast of the genus Pichia is one of the following species: *Pichia pastoris, Pichia methanolica,* and *Hansenula polymorpha* (*Pichia angusta*). In a particularly preferred embodiment of the invention, the mating competent yeast of the genus *Pichia* is the species *Pichia pastoris*.

**[000109]** Haploid Yeast Cell: A cell having a single copy of each gene of its normal genomic (chromosomal) complement.

**[000110]** Polyploid Yeast Cell: A cell having more than one copy of its normal genomic (chromosomal) complement.

**[000111]** Diploid Yeast Cell: A cell having two copies (alleles) of essentially every gene of its normal genomic complement, typically formed by the process of fusion (mating) of two haploid cells.

**[000112]** Tetraploid Yeast Cell: A cell having four copies (alleles) of essentially every gene of its normal genomic complement, typically formed by the process of fusion (mating) of two haploid cells. Tetraploids may carry two, three, four or more different expression cassettes. Such tetraploids might be obtained in S. cerevisiae by selective mating homozygotic heterothallic a/a and alpha/alpha diploids and in Pichia by sequential mating of haploids to obtain auxotrophic diploids. For example, a [met his] haploid can be mated with [ade his] haploid to obtain diploid [his]; and a [met arg] haploid can be mated with [ade arg] haploid to obtain diploid [arg]; then the diploid [his] x diploid [arg] to obtain a tetraploid prototroph. It will be understood by those of skill in the art that reference to the benefits and uses of diploid cells may also apply to tetraploid cells.

**[000113]** Yeast Mating: The process by which two haploid yeast cells naturally fuse to form one diploid yeast cell.

**[000114]** Meiosis: The process by which a diploid yeast cell undergoes reductive division to form four haploid spore products. Each spore may then germinate and form a haploid vegetatively growing cell line.

**[000115]** Selectable Marker: A selectable marker is a gene or gene fragment that confers a growth phenotype (physical growth characteristic) on a cell receiving that gene as, for example through a transformation event. The selectable marker allows that cell to survive and grow in a selective growth medium under conditions in which cells that do not receive that selectable marker gene cannot grow. Selectable marker genes generally fall into several types, including positive selectable marker genes such as a gene that confers on a cell resistance to an antibiotic or other drug, temperature when two temperature sensitive ("ts") mutants are crossed or a ts mutant is transformed; negative selectable marker genes such as a biosynthetic gene that confers on a cell the ability to grow in a medium without a specific nutrient needed by all cells that do not have that biosynthetic gene, or a mutagenized biosynthetic gene that confers on a cell inability to grow by cells that do not have the wild type gene; and the like. Suitable markers include but are not limited to: ZEO; G418; LYS3; MET1; MET3a; ADE1; ADE3; URA3; and the like.

**[000116]** Expression Vector: These DNA vectors contain elements that facilitate manipulation for the expression of a foreign protein within the target host cell. Conveniently, manipulation of sequences and production of DNA for transformation is first performed in a bacterial host, e.g. E. coli, and usually vectors will include sequences to facilitate such manipulations, including a bacterial origin of replication and appropriate bacterial selection marker. Selection markers encode proteins necessary for the survival or growth of transformed host cells grown in a selective culture medium. Host cells not transformed with the vector containing the selection gene will not survive in the culture medium. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media. Exemplary vectors and methods for transformation of yeast are described, for example, in Burke, D., Dawson, D., & Stearns, T. (2000). Methods in yeast genetics: a Cold Spring Harbor Laboratory course manual. Plainview, N.Y.: Cold Spring Harbor Laboratory Press.

**[000117]** Expression vectors for use in the methods of the invention will further include a selectable auxotrophic or drug marker for identifying transformed cells such as yeast strains. A drug marker may further be used to amplify copy number of the vector in a host cell.

**[000118]** The polypeptide coding sequence of interest is operably linked to transcriptional and translational regulatory sequences that provide for expression of the polypeptide in yeast cells. These vector components may include, but are not limited to, one or more of the following: an enhancer element, a promoter, and a transcription termination sequence. Sequences for the secretion of the polypeptide may also be included, e.g. a signal sequence, and the like. An origin of replication is optional, as expression vectors are often integrated into the host, e.g., yeast genome. In one embodiment of the invention, the polypeptide of interest is operably linked, or fused, to sequences providing for optimized secretion of the polypeptide from yeast diploid cells.

**[000119]** Nucleic acids are "operably linked" when placed into a functional relationship with another nucleic acid sequence. For example, DNA for a signal sequence is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence. Generally,

"operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading frame. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites or alternatively via a PCR/recombination method familiar to those skilled in the art (GatewayR Technology; Invitrogen, Carlsbad California). If such sites do not exist, the synthetic oligonucleotide adapters or linkers are used in accordance with conventional practice.

**[000120]** Promoters are untranslated sequences located upstream (5') to the start codon of a structural gene (generally within about 100 to 1000 bp) that control the transcription and translation of particular nucleic acid sequences to which they are operably linked. Such promoters fall into several classes: inducible, constitutive, and repressible promoters (that increase levels of transcription in response to absence of a repressor). Inducible promoters may initiate increased levels of transcription from DNA under their control in response to some change in culture conditions, e.g., the presence or absence of a nutrient or a change in temperature.

**[000121]** The promoter fragment may also serve as the site for homologous recombination and integration of the expression vector into the same site in the host genome; alternatively a selectable marker is used as the site for homologous recombination.

**[000122]** Examples of suitable promoters useful in Pichia include the AOX1 and promoter (Cregg et al. (1989) Mol. Cell. Biol. 9:1316-1323); ICL1 promoter (Menendez et al. (2003) Yeast 20(13):1097-108); glyceraldehyde-3-phosphate dehydrogenase promoter (GAP) (Waterham et al. (1997) Gene 186(1):37-44); and FLD1 promoter (Shen et al. (1998) Gene 216(1):93-102). The GAP promoter is a strong constitutive promoter and the AOX and FLD1 promoters are inducible.

**[000123]** Other yeast promoters include ADH1, alcohol dehydrogenase II, GAL4, PHO3, PHO5, Pyk, and chimeric promoters derived therefrom. Additionally, non-yeast promoters may be used in the invention such as mammalian, insect, plant, reptile, amphibian, bacterial, fungal, viral, and avian promoters. Most typically the promoter will comprise a mammalian promoter (potentially endogenous to the expressed genes) or will comprise a yeast or viral promoter that provides for efficient transcription in yeast systems.

**[000124]** The polypeptides of interest may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, e.g. a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the polypeptide coding sequence that is inserted into the vector. The heterologous signal sequence selected preferably is one that is recognized and processed through one of the standard pathways available within the host cell. The *S. cerevisiae* alpha factor pre-pro signal has proven effective in the secretion of a variety of recombinant proteins from *P. pastoris*. Other yeast signal sequences include the alpha mating factor signal sequence, the invertase signal sequence, and signal sequences derived from other secreted yeast polypeptides. Additionally, these signal peptide sequences may be engineered to provide for enhanced secretion in diploid yeast expression systems. Other secretion signals of interest also include mammalian signal sequences, which may be heterologous to the protein being secreted, or may be a native sequence for the protein being secreted. Signal sequences include pre-peptide sequences, and in some instances may include propeptide sequences. Many such signal sequences are known in the art, including the signal sequences found on immunoglobulin chains, e.g., K28 preprotoxin sequence, PHA-E, FACE, human MCP-1, human serum albumin signal sequences, human Ig heavy chain, human Ig light chain, and the like. For example, see Hashimoto et. al. Protein Eng 11(2) 75 (1998); and Kobayashi et. al. Therapeutic Apheresis 2(4) 257 (1998).

**[000125]** Transcription may be increased by inserting a transcriptional activator sequence into the vector. These activators are cis-acting elements of DNA, usually about from 10 to 300 bp, which act on a promoter to increase its transcription. Transcriptional enhancers are relatively orientation and position independent, having been found 5' and 3' to the transcription unit, within an intron, as well as within the coding sequence itself. The enhancer may be spliced into the expression vector at a position 5' or 3' to the coding sequence, but is preferably located at a site 5' from the promoter.

**[000126]** Expression vectors used in eukaryotic host cells may also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from 3' to the translation termination codon, in untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain

nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA.

**[000127]** Construction of suitable vectors containing one or more of the above-listed components employs standard ligation techniques or PCR/recombination methods. Isolated plasmids or DNA fragments are cleaved, tailored, and re-ligated in the form desired to generate the plasmids required or via recombination methods. For analysis to confirm correct sequences in plasmids constructed, the ligation mixtures are used to transform host cells, and successful transformants selected by antibiotic resistance (e.g. ampicillin or Zeocin) where appropriate. Plasmids from the transformants are prepared, analyzed by restriction endonuclease digestion and/or sequenced.

**[000128]** As an alternative to restriction and ligation of fragments, recombination methods based on att sites and recombination enzymes may be used to insert DNA sequences into a vector. Such methods are described, for example, by Landy (1989) Ann.Rev.Biochem. 58:913-949; and are known to those of skill in the art. Such methods utilize intermolecular DNA recombination that is mediated by a mixture of lambda and *E.coli* –encoded recombination proteins. Recombination occurs between specific attachments (att) sites on the interacting DNA molecules. For a description of att sites see Weisberg and Landy (1983) Site-Specific Recombination in Phage Lambda, in Lambda II, Weisberg, ed.(Cold Spring Harbor, NY:Cold Spring Harbor Press), pp. 211-250. The DNA segments flanking the recombination sites are switched, such that after recombination, the att sites are hybrid sequences comprised of sequences donated by each parental vector. The recombination can occur between DNAs of any topology.

**[000129]** Att sites may be introduced into a sequence of interest by ligating the sequence of interest into an appropriate vector; generating a PCR product containing att B sites through the use of specific primers; generating a cDNA library cloned into an appropriate vector containing att sites; and the like.

**[000130]** Folding, as used herein, refers to the three-dimensional structure of polypeptides and proteins, where interactions between amino acid residues act to stabilize the structure. While non-covalent interactions are important in determining structure, usually the proteins of interest will have intra- and/or intermolecular covalent disulfide bonds formed by two cysteine residues. For naturally occurring proteins and polypeptides or derivatives and variants thereof, the proper folding is typically the

arrangement that results in optimal biological activity, and can conveniently be monitored by assays for activity, e.g. ligand binding, enzymatic activity, etc.

**[000131]** In some instances, for example where the desired product is of synthetic origin, assays based on biological activity will be less meaningful. The proper folding of such molecules may be determined on the basis of physical properties, energetic considerations, modeling studies, and the like.

**[000132]** The expression host may be further modified by the introduction of sequences encoding one or more enzymes that enhance folding and disulfide bond formation, i.e. foldases, chaperonins, etc. Such sequences may be constitutively or inducibly expressed in the yeast host cell, using vectors, markers, etc. as known in the art. Preferably the sequences, including transcriptional regulatory elements sufficient for the desired pattern of expression, are stably integrated in the yeast genome through a targeted methodology.

**[000133]** For example, the eukaryotic PDI is not only an efficient catalyst of protein cysteine oxidation and disulfide bond isomerization, but also exhibits chaperone activity. Co-expression of PDI can facilitate the production of active proteins having multiple disulfide bonds. Also of interest is the expression of BIP (immunoglobulin heavy chain binding protein); cyclophilin; and the like. In one embodiment of the invention, each of the haploid parental strains expresses a distinct folding enzyme, e.g. one strain may express BIP, and the other strain may express PDI or combinations thereof.

**[000134]** The terms "desired protein" or "desired antibody" are used interchangeably and refer generally to a parent antibody or fragment specific to a target, i.e., HGF or a chimeric or humanized antibody or a binding portion thereof derived therefrom or one containing the same CDRs or epitopic specificity as any of the anti-HGF antibodies or fragments described herein. The term “antibody” is intended to include any polypeptide chain-containing molecular structure with a specific shape that fits to and recognizes an epitope, where one or more non-covalent binding interactions stabilize the complex between the molecular structure and the epitope. The archetypal antibody molecule is the immunoglobulin, and all types of immunoglobulins, IgG, IgM, IgA, IgE, IgD, etc., from all sources, e.g. human, rodent, rabbit, cow, sheep, pig, dog, other mammals, chicken, other avians, etc., are considered to be “antibodies.” A preferred source for producing antibodies useful as starting material according to the invention is

rabbits. Numerous antibody coding sequences have been described; and others may be raised by methods well-known in the art. Examples thereof include chimeric antibodies, human antibodies and other non-human mammalian antibodies, humanized antibodies, single chain antibodies (such as scFvs), camelbodies, nanobodies, IgNAR (single-chain antibodies derived from sharks), small-modular immunopharmaceuticals (SMIPs), and antibody fragments such as Fabs, Fab', F(ab')2, monovalent antibody fragments such as MetMab like molecules, IgNars and the like. See Streltsov VA, et al., Structure of a shark IgNAR antibody variable domain and modeling of an early-developmental isotype, Protein Sci. 2005 Nov;14(11):2901-9. Epub 2005 Sep 30; Greenberg AS, et al., A new antigen receptor gene family that undergoes rearrangement and extensive somatic diversification in sharks, Nature. 1995 Mar 9;374(6518):168-73; Nuttall SD, et al., Isolation of the new antigen receptor from wobbegong sharks, and use as a scaffold for the display of protein loop libraries, Mol Immunol. 2001 Aug;38(4):313-26; Hamers-Casterman C, et al., Naturally occurring antibodies devoid of light chains, Nature. 1993 Jun 3;363(6428):446-8; Gill DS, et al., Biopharmaceutical drug discovery using novel protein scaffolds, Curr Opin Biotechnol. 2006 Dec;17(6):653-8. Epub 2006 Oct 19.

**[000135]** The present invention includes in particular includes monovalent antibody molecules that bind HGF, which are analogous to MetMab molecules. MetMab is a monovalent antibody specific to Met. (Met is a protein encoded by the nucleotide sequence set forth in Park et al., Proc. Natl. Acad. Sci. 84, 7479--(1987), or fragments thereof, as well as related polypeptides, which include, but are not limited to, allelic variants, splice variants, derivative variants, substitution variants, deletion variants, and/or insertion variants, fusion polypeptides, and interspecies homologs). The MetMab antibody, is a monovalent antibody known by different names including OA-5d5 (Genentech) and is also called One Armed 5d5, 5d5, MetMab, PRO143966, among others). Antibody OA-5d5, including its structure and properties, and methods for making and using it, are described in U.S. Publication No. 2007/0092520. In one embodiment, an anti-HGF antibody according to the invention may comprise a single Fab region linked to an Fc region. In such embodiment, an antibody of the invention may comprise light and heavy chain variable domains as described herein. In such an embodiment, the antibody is monovalent and may comprise an intact Fc region. In another such embodiment, the Fc region may comprise at least one protuberance (knob)

and at least one cavity (hole), wherein the presence of the protuberance and cavity enhances formation of a complex between an Fc polypeptide comprising the protuberance and an Fc polypeptide comprising the cavity, for example as described in WO 2005/063816. In one embodiment, the Fc region of an antibody of the invention may comprise a first and a second Fc polypeptide, wherein the first and second polypeptide each comprises one or more mutations with respect to wild type human Fc. In one embodiment, a cavity mutation is T366S, L368A and/or Y407V. In another embodiment, a protuberance mutation is T366W. In a specific embodiment, a monovalent antibody according to the subject invention may comprise a one-armed antibody synthesized as described in WO2005/063816. In such embodiment, the one-armed antibody may comprise Fc mutations constituting "knobs" and "holes" as described in WO2005/063816. For example, a hole mutation can be one or more of T366A, L368A and/or Y407V in an Fc polypeptide, and a cavity mutation can be T366W. The invention is also directed to an anti-human HGF monovalent agent that binds with the same HGF epitope and/or competes with an anti-HGF antibody for binding to HGF as an antibody or antibody fragment disclosed herein.

**[000136]** For example, antibodies or antigen binding fragments may be produced by genetic engineering. In this technique, as with other methods, antibody-producing cells are sensitized to the desired antigen or immunogen. The messenger RNA isolated from antibody producing cells is used as a template to make cDNA using PCR amplification. A library of vectors, each containing one heavy chain gene and one light chain gene retaining the initial antigen specificity, is produced by insertion of appropriate sections of the amplified immunoglobulin cDNA into the expression vectors. A combinatorial library is constructed by combining the heavy chain gene library with the light chain gene library. This results in a library of clones which co-express a heavy and light chain (resembling the Fab fragment or antigen binding fragment of an antibody molecule). The vectors that carry these genes are co-transfected into a host cell. When antibody gene synthesis is induced in the transfected host, the heavy and light chain proteins self-assemble to produce active antibodies that can be detected by screening with the antigen or immunogen.

**[000137]** Antibody coding sequences of interest include those encoded by native sequences, as well as nucleic acids that, by virtue of the degeneracy of the genetic code, are not identical in sequence to the disclosed nucleic acids, and variants thereof.

Variant polypeptides can include amino acid (aa) substitutions, additions or deletions. The amino acid substitutions can be conservative amino acid substitutions or substitutions to eliminate non-essential amino acids, such as to alter a glycosylation site, or to minimize misfolding by substitution or deletion of one or more cysteine residues that are not necessary for function. Variants can be designed so as to retain or have enhanced biological activity of a particular region of the protein (e.g., a functional domain, catalytic amino acid residues, etc). Variants also include fragments of the polypeptides disclosed herein, particularly biologically active fragments and/or fragments corresponding to functional domains. Techniques for in vitro mutagenesis of cloned genes are known. Also included in the subject invention are polypeptides that have been modified using ordinary molecular biological techniques so as to improve their resistance to proteolytic degradation or to optimize solubility properties or to render them more suitable as a therapeutic agent.

**[000138]** Chimeric antibodies may be made by recombinant means by combining the variable light and heavy chain regions ($V_L$ and $V_H$), obtained from antibody producing cells of one species with the constant light and heavy chain regions from another. Typically chimeric antibodies utilize rodent or rabbit variable regions and human constant regions, in order to produce an antibody with predominantly human domains. The production of such chimeric antibodies is well known in the art, and may be achieved by standard means (as described, e.g., in U.S. Patent No. 5,624,659, incorporated herein by reference in its entirety). It is further contemplated that the human constant regions of chimeric antibodies of the invention may be selected from IgG1, IgG2, IgG3, and IgG4 constant regions.

**[000139]** Humanized antibodies are engineered to contain even more human-like immunoglobulin domains, and incorporate only the complementarity-determining regions of the animal-derived antibody. This is accomplished by carefully examining the sequence of the hyper-variable loops of the variable regions of the monoclonal antibody, and fitting them to the structure of the human antibody chains. Although facially complex, the process is straightforward in practice. See, e.g., U.S. Patent No. 6,187,287, incorporated fully herein by reference.

**[000140]** In addition to entire immunoglobulins (or their recombinant counterparts), immunoglobulin fragments comprising the epitope binding site (e.g., Fab', F(ab')2, Fab, or other fragments) may be synthesized. "Fragment" or minimal immunoglobulins

may be designed utilizing recombinant immunoglobulin techniques. For instance "Fv" immunoglobulins for use in the present invention may be produced by synthesizing a fused variable light chain region and a variable heavy chain region. Combinations of antibodies are also of interest, e.g. diabodies, which comprise two distinct Fv specificities. In another embodiment of the invention, SMIPs (small molecule immunopharmaceuticals), camelbodies, nanobodies, and IgNAR are encompassed by immunoglobulin fragments.

**[000141]** Immunoglobulins and fragments thereof may be modified post-translationally, e.g. To add effector moieties such as chemical linkers, detectable moieties, such as fluorescent dyes, enzymes, toxins, substrates, bioluminescent materials, radioactive materials, chemiluminescent moieties and the like, or specific binding moieties, such as streptavidin, avidin, or biotin, and the like may be utilized in the methods and compositions of the present invention. Examples of additional effector molecules are provided infra.

**[000142]** A polynucleotide sequence "corresponds" to a polypeptide sequence if translation of the polynucleotide sequence in accordance with the genetic code yields the polypeptide sequence (i.e., the polynucleotide sequence "encodes" the polypeptide sequence), one polynucleotide sequence "corresponds" to another polynucleotide sequence if the two sequences encode the same polypeptide sequence.

**[000143]** A "heterologous" region or domain of a DNA construct is an identifiable segment of DNA within a larger DNA molecule that is not found in association with the larger molecule in nature. Thus, when the heterologous region encodes a mammalian gene, the gene will usually be flanked by DNA that does not flank the mammalian genomic DNA in the genome of the source organism. Another example of a heterologous region is a construct where the coding sequence itself is not found in nature (e.g., a cDNA where the genomic coding sequence contains introns, or synthetic sequences having codons different than the native gene). Allelic variations or naturally-occurring mutational events do not give rise to a heterologous region of DNA as defined herein.

**[000144]** A "coding sequence" is an in-frame sequence of codons that (in view of the genetic code) correspond to or encode a protein or peptide sequence. Two coding sequences correspond to each other if the sequences or their complementary sequences encode the same amino acid sequences. A coding sequence in association with

appropriate regulatory sequences may be transcribed and translated into a polypeptide. A polyadenylation signal and transcription termination sequence will usually be located 3' to the coding sequence. A "promoter sequence" is a DNA regulatory region capable of binding RNA polymerase in a cell and initiating transcription of a downstream (3' direction) coding sequence. Promoter sequences typically contain additional sites for binding of regulatory molecules (e.g., transcription factors) which affect the transcription of the coding sequence. A coding sequence is "under the control" of the promoter sequence or "operatively linked" to the promoter when RNA polymerase binds the promoter sequence in a cell and transcribes the coding sequence into mRNA, which is then in turn translated into the protein encoded by the coding sequence.

**[000145]** Vectors are used to introduce a foreign substance, such as DNA, RNA or protein, into an organism or host cell. Typical vectors include recombinant viruses (for polynucleotides) and liposomes (for polypeptides). A "DNA vector" is a replicon, such as plasmid, phage or cosmid, to which another polynucleotide segment may be attached so as to bring about the replication of the attached segment. An "expression vector" is a DNA vector which contains regulatory sequences which will direct polypeptide synthesis by an appropriate host cell. This usually means a promoter to bind RNA polymerase and initiate transcription of mRNA, as well as ribosome binding sites and initiation signals to direct translation of the mRNA into a polypeptide(s). Incorporation of a polynucleotide sequence into an expression vector at the proper site and in correct reading frame, followed by transformation of an appropriate host cell by the vector, enables the production of a polypeptide encoded by said polynucleotide sequence.

**[000146]** "Amplification" of polynucleotide sequences is the in vitro production of multiple copies of a particular nucleic acid sequence. The amplified sequence is usually in the form of DNA. A variety of techniques for carrying out such amplification are described in a review article by Van Brunt (1990, Bio/Technol., 8(4):291-294). Polymerase chain reaction or PCR is a prototype of nucleic acid amplification, and use of PCR herein should be considered exemplary of other suitable amplification techniques.

**[000147]** The general structure of antibodies in vertebrates now is well understood (Edelman, G. M., Ann. N.Y. Acad. Sci., 190: 5 (1971)). Antibodies consist of two identical light polypeptide chains of molecular weight approximately 23,000 Daltons (the "light chain"), and two identical heavy chains of molecular weight 53,000–70,000

(the "heavy chain"). The four chains are joined by disulfide bonds in a "Y" configuration wherein the light chains bracket the heavy chains starting at the mouth of the "Y" configuration. The "branch" portion of the "Y" configuration is designated the Fab region; the stem portion of the "Y" configuration is designated the FC region. The amino acid sequence orientation runs from the N-terminal end at the top of the "Y" configuration to the C-terminal end at the bottom of each chain. The N-terminal end possesses the variable region having specificity for the antigen that elicited it, and is approximately 100 amino acids in length, there being slight variations between light and heavy chain and from antibody to antibody.

**[000148]** The variable region is linked in each chain to a constant region that extends the remaining length of the chain and that within a particular class of antibody does not vary with the specificity of the antibody (i.e., the antigen eliciting it). There are five known major classes of constant regions that determine the class of the immunoglobulin molecule (IgG, IgM, IgA, IgD, and IgE corresponding to γ, μ, α, δ, and ε (gamma, mu, alpha, delta, or epsilon) heavy chain constant regions). The constant region or class determines subsequent effector function of the antibody, including activation of complement (Kabat, E. A., Structural Concepts in Immunology and Immunochemistry, 2nd Ed., p. 413-436, Holt, Rinehart, Winston (1976)), and other cellular responses (Andrews, D. W., et al., Clinical Immunobiology, pp 1-18, W. B. Sanders (1980); Kohl, S., et al., Immunology, 48: 187 (1983)); while the variable region determines the antigen with which it will react. Light chains are classified as either κ (kappa) or λ (lambda). Each heavy chain class can be prepared with either kappa or lambda light chain. The light and heavy chains are covalently bonded to each other, and the "tail" portions of the two heavy chains are bonded to each other by covalent disulfide linkages when the immunoglobulins are generated either by hybridomas or by B cells.

**[000149]** The expression "variable region" or "VR" refers to the domains within each pair of light and heavy chains in an antibody that are involved directly in binding the antibody to the antigen. Each heavy chain has at one end a variable domain (VH) followed by a number of constant domains. Each light chain has a variable domain (VL) at one end and a constant domain at its other end; the constant domain of the light chain is aligned with the first constant domain of the heavy chain, and the light chain variable domain is aligned with the variable domain of the heavy chain.

**[000150]** The expressions "complementarity determining region," "hypervariable region," or "CDR" refer to one or more of the hyper-variable or complementarity determining regions (CDRs) found in the variable regions of light or heavy chains of an antibody (See Kabat, E. A. et al., Sequences of Proteins of Immunological Interest, National Institutes of Health, Bethesda, Md., (1987)). These expressions include the hypervariable regions as defined by Kabat et al. ("Sequences of Proteins of Immunological Interest," Kabat E., et al., US Dept. of Health and Human Services, 1983) or the hypervariable loops in 3-dimensional structures of antibodies (Chothia and Lesk, J Mol. Biol. 196 901-917 (1987)). The CDRs in each chain are held in close proximity by framework regions and, with the CDRs from the other chain, contribute to the formation of the antigen binding site. Within the CDRs there are select amino acids that have been described as the selectivity determining regions (SDRs) which represent the critical contact residues used by the CDR in the antibody-antigen interaction (Kashmiri, S., Methods, 36:25-34 (2005)).

**[000151]** An "epitope" or "binding site" is an area or region on an antigen to which an antigen-binding peptide (such as an antibody) specifically binds. A protein epitope may comprise amino acid residues directly involved in the binding (also called immunodominant component of the epitope) and other amino acid residues, which are not directly involved in the binding, such as amino acid residues which are effectively blocked by the specifically antigen binding peptide (in other words, the amino acid residue is within the "footprint" of the specifically antigen binding peptide). The term epitope herein includes both types of amino acid binding sites in any particular region of HGF that specifically binds to an anti-HGF antibody. HGF may comprise a number of different epitopes, which may include, without limitation, (1) linear peptide antigenic determinants, (2) conformational antigenic determinants which consist of one or more non-contiguous amino acids located near each other in a mature HGF conformation; and (3) post-translational antigenic determinants which consist, either in whole or part, of molecular structures covalently attached to a HGF protein such as carbohydrate groups.

**[000152]** The phrase that a first antibody binds "substantially" or "at least partially" the same epitope as a second antibody means that the epitope binding site for the first antibody comprises at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more of the amino acid residues on the antigen that constitutes the epitope binding site of the

second antibody. Also, that a first antibody binds substantially or partially the same or overlapping epitope as a second antibody means that the first and second antibodies compete in binding to the antigen, as described above. Thus, the term "binds to substantially the same epitope or determinant as" a monoclonal antibody means that an antibody "competes" with the antibody.

**[000153]** The phrase "binds to the same or overlapping epitope or determinant as" an antibody of interest means that an antibody "competes" with said antibody of interest for at least one, or all residues on HGF to which said antibody of interest specifically binds. The identification of one or more antibodies that bind(s) to substantially or essentially the same epitope as the monoclonal antibodies described herein can be readily determined using any one of variety of immunological screening assays in which antibody competition can be assessed. A number of such assays are routinely practiced and well known in the art (see, e.g., U.S. Pat. No. 5,660,827, issued Aug. 26, 1997, which is specifically incorporated herein by reference). It will be understood that actually determining the epitope to which an antibody described herein binds is not in any way required to identify an antibody that binds to the same or substantially the same or overlapping epitope as the monoclonal antibody described herein.

**[000154]** For example, where the test antibodies to be examined are obtained from different source animals, or are even of a different Ig isotype, a simple competition assay may be employed in which the control antibody is mixed with the test antibody and then applied to a sample containing HGF. Protocols based upon ELISAs, radioimmunoassays, Western blotting, and the use of Surface plasmone resonance (with an instrument such as the Biacore) or biolayer interferometry (with an instrument such as the Octet) analysis are suitable for use in such simple competition studies.

**[000155]** In certain embodiments, one would pre-mix the control anti-HGF antibody with varying amounts of the test antibody (e.g., in ratios of about 1:1, 1:2, 1:10 or about 1:100) for a period of time prior to applying to the HGF antigen sample. In other embodiments, the control and varying amounts of test antibody can simply be added separately and admixed during exposure to the HGF antigen sample. As long as one can distinguish bound from free antibodies (e.g., by using separation or washing techniques to eliminate unbound antibodies) and control antibody from the test antibody (e.g., by using species specific or isotype specific secondary antibodies or by specifically labeling the control antibody with a detectable label) one will be able to

determine if the test antibody reduces the binding of the control antibody to the HGF antigens, indicating that the test antibody recognizes substantially the same epitope as the control ant-HGF antibody. The binding of the (labeled) control antibody in the presence of a completely irrelevant antibody (that does not bind HGF) can serve as the control high value. The control low value can be obtained by incubating the labeled control antibody with the same but unlabeled control antibody, where competition would occur and reduce binding of the labeled antibody. In a test assay, a significant reduction in labeled antibody reactivity in the presence of a test antibody is indicative of a test antibody that recognizes substantially the same epitope, i.e., one that competes with the labeled control antibody. For example, any test antibody that reduces the binding of the control antibody to HGF s by at least about 50%, such as at least about 60%, or more preferably at least about 70% (e.g., about 65-100%), at any ratio of :test antibody between about 1:1 or 1:10 and about 1:100 is considered to be an antibody that binds to substantially the same or overlapping epitope or determinant as the control antibody.

**[000156]** Preferably, such test antibody will reduce the binding of the control antibody to HGF antigen preferably at least about 50%, at least about 60%, at least about 80% or at least about 90% (e.g., about 95%) of the binding of 1 the control antibody observed in the absence of the test antibody.

**[000157]** Competition can also or alternatively be assessed by, for example, a flow cytometry test. In such a test, cells bearing HGF can be incubated first with a control antibody that binds HGF, and then with the test antibody labeled with a fluorochrome or biotin. The antibody is said to compete with control antibody if the binding obtained upon preincubation with saturating amount of control antibody is about 80%, preferably about 50%, about 40% or less (e.g., about 30%) of the binding (as measured by mean of fluorescence) obtained by the test antibody without preincubation with control antibody. Alternatively, an antibody is said to compete with the control antibody if the binding obtained with a labeled control antibody (by a fluorochrome or biotin) on cells preincubated with saturating amount of test antibody is about 80%, preferably about 50%, about 40%, or less (e.g., about 30%) of the binding obtained without preincubation with the test antibody.

**[000158]** A simple competition assay in which a test antibody is pre-adsorbed and applied at saturating concentration to a surface onto which HGF is immobilized also

may be advantageously employed. The surface in the simple competition assay is preferably a BIACORE chip (or other media suitable for surface plasmon resonance analysis). The binding of a control antibody that binds HGF to the HGF-coated surface is measured. This binding to the HGF-containing surface of the control antibody alone is compared with the binding of the control antibody in the presence of a test antibody. A significant reduction in binding to the HGF-containing surface by the control antibody in the presence of a test antibody indicates that the test antibody recognizes substantially the same epitope as the control antibody such that the test antibody "competes" with the control antibody. Any test antibody that reduces the binding of control antibody by at least about 20% or more, at least about 40%, at least about 50%, at least about 70%, or more, can be considered to be an antibody that binds to substantially the same epitope or determinant as the control antibody . Preferably, such test antibody will reduce the binding of the control antibody to HGF by at least about 50% (e.g., at least about 60%, at least about 70%, or more). It will be appreciated that the order of control and test antibodies can be reversed; i.e. The control antibody can be first bound to the surface and then the test antibody is brought into contact with the surface thereafter in a competition assay. Preferably, the antibody having higher affinity for HGF antigen is bound to the HGF-containing surface first, as it will be expected that the decrease in binding seen for the second antibody (assuming the antibodies are competing) will be of greater magnitude. Further examples of such assays are provided in e.g., Saunal and Regenmortel, (1995) J. Immunol. Methods 183: 33-41, the disclosure of which is incorporated herein by reference.

**[000159]** In addition, whether an antibody binds the same or overlapping epitope(s) on HGF as another antibody or the epitope bound by a test antibody may in particular be determined using a western-blot based assay. In this assay a library of peptides corresponding to the antigen bound by the antibody, herein HGF is made, which correspond to overlapping portions of the protein, typically 10-25, 10-20 or 10-15 amino acids long. These different overlapping amino acid peptides encompassing the HGF sequence are synthesized and covalently bound to a PepSpots nitrocellulose membrane (JPT Peptide technologies, Berlin, Germany). Blots are then prepared and probed according to the manufacturer's recommendations.

**[000160]** Essentially, the immunoblot assay then detects by fluorimetric means what peptides in the library bind to the test antibody and thereby can identify what residues

on the antigen, i.e., HGF, interact with the test antibody. (See an embodiment of this technique in US Patent No. 7,935,340, incorporated by reference herein).

**[000161]** The expressions "framework region" or "FR" refer to one or more of the framework regions within the variable regions of the light and heavy chains of an antibody (See Kabat, E. A. et al., Sequences of Proteins of Immunological Interest, National Institutes of Health, Bethesda, Md., (1987)). These expressions include those amino acid sequence regions interposed between the CDRs within the variable regions of the light and heavy chains of an antibody.

***Anti-HGF Antibodies and Binding Fragments Thereof***

Antibody Ab1

**[000162]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGFSLSAYAMSWVRQAPEKGLEWIAVIYVIG
ATDYASWAKGRFTISRTSTTVDLRIPSPTTEDTATYFCARVYDSVWNHFNLWG
PGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK (SEQ ID NO: 1).

**[000163]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGFSLSAYAMSWVRQAPEKGLEWIAVIYVIG
ATDYASWAKGRFTISRTSTTVDLRIPSPTTEDTATYFCARVYDSVWNHFNLWG
PGTLVTVSS (SEQ ID NO: 2).

**[000164]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab1 and which contain a constant heavy chain sequence comprising the sequence set

forth below:

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 10).

**[000165]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below:
AYDMTQTPASVEVAVGGTVTIKCQASQSISSWLAWYQQKPGQPPKLLIYQASK
LASGVPSRFKGSGSGTEFTLTISGVECADAATYYCQQAYSVSNVDNAFGGGTE
VVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN
RGEC (SEQ ID NO: 21).

**[000166]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below:
AYDMTQTPASVEVAVGGTVTIKCQASQSISSWLAWYQQKPGQPPKLLIYQASK
LASGVPSRFKGSGSGTEFTLTISGVECADAATYYCQQAYSVSNVDNAFGGGTE
VVVKR (SEQ ID NO: 22).

**[000167]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab1 which contain a constant light chain sequence comprising the sequence set forth below:
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO: 30).

**[000168]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 4; SEQ ID NO: 6; and SEQ ID NO: 8 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1 or which contain the variable

heavy chain sequence of SEQ ID NO: 2, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 24; SEQ ID NO: 26; and SEQ ID NO: 28 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 21 or which contain the variable light chain sequence of SEQ ID NO: 22, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000169]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 3; SEQ ID NO: 5; SEQ ID NO: 7; and SEQ ID NO: 9 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 1 or the variable heavy chain sequence of SEQ ID NO: 2, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 23; SEQ ID NO: 25; SEQ ID NO: 27; and SEQ ID NO: 29 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 21 or the variable light chain sequence of SEQ ID NO: 22, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000170]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000171]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 1 or SEQ ID NO: 2 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 21 or SEQ ID NO: 22 or polypeptides that are at least 90% or 95% identical thereto.

**[000172]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 4; SEQ ID NO: 6; and SEQ ID NO: 8 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1 or the variable heavy chain sequence of SEQ ID NO: 2 or sequences that are at least 90% or 95% identical thereto.

**[000173]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 24; SEQ ID NO: 26; and SEQ ID NO: 28 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 21 or the variable light chain sequence of SEQ ID NO: 22 or sequences that are at least 90% or 95% identical thereto.

**[000174]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 3; SEQ ID NO: 5; SEQ ID NO: 7; and SEQ ID NO: 9 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 1 or the variable heavy chain sequence of SEQ ID NO: 2 or sequences that are at least 90% or 95% identical thereto.

**[000175]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 23; SEQ ID NO: 25; SEQ ID NO: 27; and SEQ ID NO: 29 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 21 or the variable light chain sequence of SEQ ID NO: 22 or sequences that are at least 90% or 95% identical thereto.

**[000176]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 2; the variable light chain region of SEQ ID NO: 22; the complementarity-determining regions (SEQ ID NO: 4;

SEQ ID NO: 6; and SEQ ID NO: 8) of the variable heavy chain region of SEQ ID NO: 2; and the complementarity-determining regions (SEQ ID NO: 24; SEQ ID NO: 26; and SEQ ID NO: 28) of the variable light chain region of SEQ ID NO: 22 or sequences that are at least 90% or 95% identical thereto.

**[000177]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 2; the variable light chain region of SEQ ID NO: 22; the framework regions (SEQ ID NO: 3; SEQ ID NO: 5; SEQ ID NO: 7; and SEQ ID NO: 9) of the variable heavy chain region of SEQ ID NO: 2; and the framework regions (SEQ ID NO: 23; SEQ ID NO: 25; SEQ ID NO: 27; and SEQ ID NO: 29) of the variable light chain region of SEQ ID NO: 22.

**[000178]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab1, comprising, or alternatively consisting of, SEQ ID NO: 1 and SEQ ID NO: 21, or an antibody or antibody fragment comprising the CDRs of Ab1 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab1 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab1 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab1.

**[000179]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab1, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 2 and the variable light chain sequence of SEQ ID NO: 22 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 2 and/or SEQ ID NO: 22 which retain the binding specificity for HGF.

**[000180]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab1. In another embodiment of the invention, anti-HGF antibodies such as Ab1 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid

yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000181]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab1 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab2

**[000182]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSAYAMSWVRQAPGKGLEWVAVIY
VIGATDYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSVWN
HFNLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV
SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 41).

**[000183]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSAYAMSWVRQAPGKGLEWVAVIY
VIGATDYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSVWN
HFNLWGQGTLVTVSS (SEQ ID NO: 42).

**[000184]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab2 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT

CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK (SEQ ID NO: 50).

**[000185]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DIQMTQSPSTLSASVGDRVTITCQASQSISSWLAWYQQKPGKAPKLLIYQASKL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVSNVDNAFGGGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C (SEQ ID NO: 61).

**[000186]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DIQMTQSPSTLSASVGDRVTITCQASQSISSWLAWYQQKPGKAPKLLIYQASKL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVSNVDNAFGGGTKVE IKR (SEQ ID NO: 62).

**[000187]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab2 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 70).

**[000188]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 44; SEQ ID NO: 46; and SEQ ID NO: 48 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 41 or which contain the variable heavy chain sequence of SEQ ID NO: 42, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 64; SEQ ID NO: 66; and SEQ ID NO: 68 which correspond to the complementarity-determining regions (CDRs, or

hypervariable regions) of the light chain sequence of SEQ ID NO: 61 or which contain the variable light chain sequence of SEQ ID NO: 62, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000189]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 43; SEQ ID NO: 45; SEQ ID NO: 47; and SEQ ID NO: 49 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 41 or the variable heavy chain sequence of SEQ ID NO: 42, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 63; SEQ ID NO: 65; SEQ ID NO: 67; and SEQ ID NO: 69 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 61 or the variable light chain sequence of SEQ ID NO: 62, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000190]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000191]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 41 or SEQ ID NO: 42 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 61 or SEQ ID NO: 62 or polypeptides that are at least 90% or 95% identical thereto.

**[000192]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 44; SEQ ID NO: 46; and SEQ ID NO: 48 which correspond to the complementarity-determining regions (CDRs, or

hypervariable regions) of the heavy chain sequence of SEQ ID NO: 41 or the variable heavy chain sequence of SEQ ID NO: 42 or sequences that are at least 90% or 95% identical thereto.

**[000193]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 64; SEQ ID NO: 66; and SEQ ID NO: 68 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 61 or the variable light chain sequence of SEQ ID NO: 62 or sequences that are at least 90% or 95% identical thereto.

**[000194]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 43; SEQ ID NO: 45; SEQ ID NO: 47; and SEQ ID NO: 49 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 41 or the variable heavy chain sequence of SEQ ID NO: 42 or sequences that are at least 90% or 95% identical thereto.

**[000195]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 63; SEQ ID NO: 65; SEQ ID NO: 67; and SEQ ID NO: 69 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 61 or the variable light chain sequence of SEQ ID NO: 62 or sequences that are at least 90% or 95% identical thereto.

**[000196]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 42; the variable light chain region of SEQ ID NO: 62; the complementarity-determining regions (SEQ ID NO: 44; SEQ ID NO: 46; and SEQ ID NO: 48) of the variable heavy chain region of SEQ ID NO: 42; and the complementarity-determining regions (SEQ ID NO: 64; SEQ ID NO:

66; and SEQ ID NO: 68) of the variable light chain region of SEQ ID NO: 62 or sequences that are at least 90% or 95% identical thereto.

**[000197]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 42; the variable light chain region of SEQ ID NO: 62; the framework regions (SEQ ID NO: 43; SEQ ID NO: 45; SEQ ID NO: 47; and SEQ ID NO: 49) of the variable heavy chain region of SEQ ID NO: 42; and the framework regions (SEQ ID NO: 63; SEQ ID NO: 65; SEQ ID NO: 67; and SEQ ID NO: 69) of the variable light chain region of SEQ ID NO: 62.

**[000198]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab2, comprising, or alternatively consisting of, SEQ ID NO: 41 and SEQ ID NO: 61, or an antibody or antibody fragment comprising the CDRs of Ab2 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab2 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab2 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab2.

**[000199]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab2, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 42 and the variable light chain sequence of SEQ ID NO: 62 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 42 and/or SEQ ID NO: 62 which retain the binding specificity for HGF.

**[000200]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab2. In another embodiment of the invention, anti-HGF antibodies such as Ab2 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000201]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab2 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab3

**[000202]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGLTISSYYMSWVRQAPGKGLEWIGTINPGA
NTYFASWAKGRFTISRTSTTVDLKITSPTTEDTATYFCAREGDSNDWGVFDLW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG
ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV
EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED
PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK (SEQ ID NO: 81).

**[000203]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGLTISSYYMSWVRQAPGKGLEWIGTINPGA
NTYFASWAKGRFTISRTSTTVDLKITSPTTEDTATYFCAREGDSNDWGVFDLW
GQGTLVTVSS (SEQ ID NO: 82).

**[000204]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab3 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA

PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK (SEQ ID NO: 90).

**[000205]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEIAVGGTVTIRCQASEDIESYLAWYQQKPGQPPKLLIYRASDL ASGVSSRFKGSGSGTDYTLTISGVECDDAATYYCQQGYTIDNVDNTFGGGTEV VVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC (SEQ ID NO: 101).

**[000206]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEIAVGGTVTIRCQASEDIESYLAWYQQKPGQPPKLLIYRASDL ASGVSSRFKGSGSGTDYTLTISGVECDDAATYYCQQGYTIDNVDNTFGGGTEV VVKR (SEQ ID NO: 102).

**[000207]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab3 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 110).

**[000208]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 84; SEQ ID NO: 86; and SEQ ID NO: 88 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 81 or which contain the variable heavy chain sequence of SEQ ID NO: 82, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 104; SEQ ID NO: 106; and SEQ ID NO: 108 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 101 or which contain the variable light chain sequence of SEQ ID NO: 102, or antibodies or fragments

containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000209]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 83; SEQ ID NO: 85; SEQ ID NO: 87; and SEQ ID NO: 89 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 81 or the variable heavy chain sequence of SEQ ID NO: 82, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 103; SEQ ID NO: 105; SEQ ID NO: 107; and SEQ ID NO: 109 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 101 or the variable light chain sequence of SEQ ID NO: 102, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000210]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000211]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 81 or SEQ ID NO: 82 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 101 or SEQ ID NO: 102 or polypeptides that are at least 90% or 95% identical thereto.

**[000212]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 84; SEQ ID NO: 86; and SEQ ID NO: 88 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 81 or the variable

heavy chain sequence of SEQ ID NO: 82 or sequences that are at least 90% or 95% identical thereto.

**[000213]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 104; SEQ ID NO: 106; and SEQ ID NO: 108 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 101 or the variable light chain sequence of SEQ ID NO: 102 or sequences that are at least 90% or 95% identical thereto.

**[000214]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 83; SEQ ID NO: 85; SEQ ID NO: 87; and SEQ ID NO: 89 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 81 or the variable heavy chain sequence of SEQ ID NO: 82 or sequences that are at least 90% or 95% identical thereto.

**[000215]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 103; SEQ ID NO: 105; SEQ ID NO: 107; and SEQ ID NO: 109 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 101 or the variable light chain sequence of SEQ ID NO: 102 or sequences that are at least 90% or 95% identical thereto.

**[000216]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 82; the variable light chain region of SEQ ID NO: 102; the complementarity-determining regions (SEQ ID NO: 84; SEQ ID NO: 86; and SEQ ID NO: 88) of the variable heavy chain region of SEQ ID NO: 82; and the complementarity-determining regions (SEQ ID NO: 104; SEQ ID NO: 106; and SEQ ID NO: 108) of the variable light chain region of SEQ ID NO: 102 or sequences that are at least 90% or 95% identical thereto.

**[000217]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 82; the variable light chain region of SEQ ID NO: 102; the framework regions (SEQ ID NO: 83; SEQ ID NO: 85; SEQ ID NO: 87; and SEQ ID NO: 89) of the variable heavy chain region of SEQ ID NO: 82; and the framework regions (SEQ ID NO: 103; SEQ ID NO: 105; SEQ ID NO: 107; and SEQ ID NO: 109) of the variable light chain region of SEQ ID NO: 102.

**[000218]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab3, comprising, or alternatively consisting of, SEQ ID NO: 81 and SEQ ID NO: 101, or an antibody or antibody fragment comprising the CDRs of Ab3 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab3 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab3 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab3.

**[000219]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab3, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 82 and the variable light chain sequence of SEQ ID NO: 102 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 82 and/or SEQ ID NO: 102 which retain the binding specificity for HGF.

**[000220]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab3. In another embodiment of the invention, anti-HGF antibodies such as Ab3 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable *Pichia* species include, but are not limited to, Pichia pastoris.

**[000221]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF,

including the heavy and/or light chains of Ab3 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab4

**[000222]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVQPGTPLTLSCTASGLTISSYYMSWVRQAPGKGLEWVGTINPGA
NTYFASSAKGRFTISRSSTTLDLKMTSPTAEDTATYYCAREGDSNDWGVFDLW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG
ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV
EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED
PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK (SEQ ID NO: 121).

**[000223]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVQPGTPLTLSCTASGLTISSYYMSWVRQAPGKGLEWVGTINPGA
NTYFASSAKGRFTISRSSTTLDLKMTSPTAEDTATYYCAREGDSNDWGVFDLW
GQGTLVTVSS (SEQ ID NO: 122).

**[000224]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab4 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN

GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK (SEQ ID NO: 130).

**[000225]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQSPASVEAAVGGTVTIRCQASEDIESYLAWYQQKPGQPPKLLIYRASD LASGVSSRFKGSGSGTDYTLTISGLEPEDAATYYCQQGYTIDNVDNTFGGGTKV EIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC (SEQ ID NO: 141).

**[000226]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQSPASVEAAVGGTVTIRCQASEDIESYLAWYQQKPGQPPKLLIYRASD LASGVSSRFKGSGSGTDYTLTISGLEPEDAATYYCQQGYTIDNVDNTFGGGTKV EIKR (SEQ ID NO: 142).

**[000227]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab4 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 150).

**[000228]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 124; SEQ ID NO: 126; and SEQ ID NO: 128 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 121 or which contain the variable heavy chain sequence of SEQ ID NO: 122, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 144; SEQ ID NO: 146; and SEQ ID NO: 148 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 141 or which contain the variable light chain sequence of SEQ ID NO: 142, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%,

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97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000229]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 123; SEQ ID NO: 125; SEQ ID NO: 127; and SEQ ID NO: 129 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 121 or the variable heavy chain sequence of SEQ ID NO: 122, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 143; SEQ ID NO: 145; SEQ ID NO: 147; and SEQ ID NO: 149 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 141 or the variable light chain sequence of SEQ ID NO: 142, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000230]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000231]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 121 or SEQ ID NO: 122 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 141 or SEQ ID NO: 142 or polypeptides that are at least 90% or 95% identical thereto.

**[000232]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 124; SEQ ID NO: 126; and SEQ ID NO: 128 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 121 or the variable heavy chain sequence of SEQ ID NO: 122 or sequences that are at least 90% or 95% identical thereto.

**[000233]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 144; SEQ ID NO: 146; and SEQ ID NO: 148 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 141 or the variable light chain sequence of SEQ ID NO: 142 or sequences that are at least 90% or 95% identical thereto.

**[000234]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 123; SEQ ID NO: 125; SEQ ID NO: 127; and SEQ ID NO: 129 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 121 or the variable heavy chain sequence of SEQ ID NO: 122 or sequences that are at least 90% or 95% identical thereto.

**[000235]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 143; SEQ ID NO: 145; SEQ ID NO: 147; and SEQ ID NO: 149 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 141 or the variable light chain sequence of SEQ ID NO: 142 or sequences that are at least 90% or 95% identical thereto.

**[000236]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 122; the variable light chain region of SEQ ID NO: 142; the complementarity-determining regions (SEQ ID NO: 124; SEQ ID NO: 126; and SEQ ID NO: 128) of the variable heavy chain region of SEQ ID NO: 122; and the complementarity-determining regions (SEQ ID NO: 144; SEQ ID NO: 146; and SEQ ID NO: 148) of the variable light chain region of SEQ ID NO: 142 or sequences that are at least 90% or 95% identical thereto.

**[000237]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention,

fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 122; the variable light chain region of SEQ ID NO: 142; the framework regions (SEQ ID NO: 123; SEQ ID NO: 125; SEQ ID NO: 127; and SEQ ID NO: 129) of the variable heavy chain region of SEQ ID NO: 122; and the framework regions (SEQ ID NO: 143; SEQ ID NO: 145; SEQ ID NO: 147; and SEQ ID NO: 149) of the variable light chain region of SEQ ID NO: 142.

**[000238]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab4, comprising, or alternatively consisting of, SEQ ID NO: 121 and SEQ ID NO: 141, or an antibody or antibody fragment comprising the CDRs of Ab4 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab4 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab4 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab4.

**[000239]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab4, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 122 and the variable light chain sequence of SEQ ID NO: 142 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 122 and/or SEQ ID NO: 142 which retain the binding specificity for HGF.

**[000240]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab4. In another embodiment of the invention, anti-HGF antibodies such as Ab4 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000241]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab4 as well as fragments, variants,

combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab5

**[000242]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGTPLTLTCTVSGFSLNNYAVGWVRQAPGKGLEWIGIIYLSG
NTDYANWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARKFDTGYDIWGPGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF
NWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE
WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK (SEQ ID NO: 161).

**[000243]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGTPLTLTCTVSGFSLNNYAVGWVRQAPGKGLEWIGIIYLSG
NTDYANWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARKFDTGYDIWGPGTL
VTVSS (SEQ ID NO: 162).

**[000244]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab5 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 170).

**[000245]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASMEVAVGGTVTIKCQASQSISTYLAWYQQKPGQPPKLLIYDASD LASGVSSRFKGSGSGTQFTLTISGVECDDAATYYCQQDWSDSNVDNAFGGGTE VVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC (SEQ ID NO: 181).

**[000246]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASMEVAVGGTVTIKCQASQSISTYLAWYQQKPGQPPKLLIYDASD LASGVSSRFKGSGSGTQFTLTISGVECDDAATYYCQQDWSDSNVDNAFGGGTE VVVKR (SEQ ID NO: 182).

**[000247]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab5 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 190).

**[000248]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 164; SEQ ID NO: 166; and SEQ ID NO: 168 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 161 or which contain the variable heavy chain sequence of SEQ ID NO: 162, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 184; SEQ ID NO: 186; and SEQ ID NO: 188 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 181 or which contain the variable light chain sequence of SEQ ID NO: 182, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000249]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 163; SEQ ID NO: 165; SEQ ID NO: 167; and SEQ ID NO: 169 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 161 or the variable heavy chain sequence of SEQ ID NO: 162, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 183; SEQ ID NO: 185; SEQ ID NO: 187; and SEQ ID NO: 189 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 181 or the variable light chain sequence of SEQ ID NO: 182, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000250]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000251]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 161 or SEQ ID NO: 162 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 181 or SEQ ID NO: 182 or polypeptides that are at least 90% or 95% identical thereto.

**[000252]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 164; SEQ ID NO: 166; and SEQ ID NO: 168 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 161 or the variable heavy chain sequence of SEQ ID NO: 162 or sequences that are at least 90% or 95% identical thereto.

**[000253]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 184; SEQ ID NO: 186; and SEQ ID NO: 188 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 181 or the variable light chain sequence of SEQ ID NO: 182 or sequences that are at least 90% or 95% identical thereto.

**[000254]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 163; SEQ ID NO: 165; SEQ ID NO: 167; and SEQ ID NO: 169 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 161 or the variable heavy chain sequence of SEQ ID NO: 162 or sequences that are at least 90% or 95% identical thereto.

**[000255]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 183; SEQ ID NO: 185; SEQ ID NO: 187; and SEQ ID NO: 189 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 181 or the variable light chain sequence of SEQ ID NO: 182 or sequences that are at least 90% or 95% identical thereto.

**[000256]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 162; the variable light chain region of SEQ ID NO: 182; the complementarity-determining regions (SEQ ID NO: 164; SEQ ID NO: 166; and SEQ ID NO: 168) of the variable heavy chain region of SEQ ID NO: 162; and the complementarity-determining regions (SEQ ID NO: 184; SEQ ID NO: 186; and SEQ ID NO: 188) of the variable light chain region of SEQ ID NO: 182 or sequences that are at least 90% or 95% identical thereto.

**[000257]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 162; the variable light chain region of SEQ ID NO: 182; the framework regions (SEQ ID NO: 163; SEQ ID NO: 165; SEQ ID NO: 167; and SEQ ID NO: 169) of the variable heavy chain region of SEQ ID NO: 162; and the framework regions (SEQ ID NO: 183; SEQ ID NO: 185; SEQ ID NO: 187; and SEQ ID NO: 189) of the variable light chain region of SEQ ID NO: 182.

**[000258]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab5, comprising, or alternatively consisting of, SEQ ID NO: 161 and SEQ ID NO: 181, or an antibody or antibody fragment comprising the CDRs of Ab5 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab5 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab5 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab5.

**[000259]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab5, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 162 and the variable light chain sequence of SEQ ID NO: 182 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 162 and/or SEQ ID NO: 182 which retain the binding specificity for HGF.

**[000260]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab5. In another embodiment of the invention, anti-HGF antibodies such as Ab5 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia* pastoris.

**[000261]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab5 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab6

**[000262]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVMPGTPLTLTCTVSGFSLSSNAISWVRQAPEKGLEWIGVIYVIG
VTDYASWAQGRFTISKTSTTVDLKIPSPTTEDTATYFCARVYDSGWNHFNLWG
PGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK (SEQ ID NO: 201).

**[000263]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVMPGTPLTLTCTVSGFSLSSNAISWVRQAPEKGLEWIGVIYVIG
VTDYASWAQGRFTISKTSTTVDLKIPSPTTEDTATYFCARVYDSGWNHFNLWG
PGTLVTVSS (SEQ ID NO: 202).

**[000264]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab6 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 210).

**[000265]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: ADIVMTQTPSSVEAAVGGTVTIKCQASENIYRLLAWYQQKPGQRPKLLIYSAST LASGVPSRFKGSGSGTQFTLTISDLECADAATYYCQNYYYSSRSSYDTYNVFGG GTEVVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTK SFNRGEC (SEQ ID NO: 221).

**[000266]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: ADIVMTQTPSSVEAAVGGTVTIKCQASENIYRLLAWYQQKPGQRPKLLIYSAST LASGVPSRFKGSGSGTQFTLTISDLECADAATYYCQNYYYSSRSSYDTYNVFGG GTEVVVKR (SEQ ID NO: 222).

**[000267]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab6 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 230).

**[000268]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 204; SEQ ID NO: 206; and SEQ ID NO: 208 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 201 or which contain the variable heavy chain sequence of SEQ ID NO: 202, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 224; SEQ ID NO: 226; and SEQ ID NO: 228 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 221 or which contain the variable light chain sequence of SEQ ID NO: 222, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000269]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 203; SEQ ID NO: 205; SEQ ID NO: 207; and SEQ ID NO: 209 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 201 or the variable heavy chain sequence of SEQ ID NO: 202, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 223; SEQ ID NO: 225; SEQ ID NO: 227; and SEQ ID NO: 229 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 221 or the variable light chain sequence of SEQ ID NO: 222, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000270]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000271]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 201 or SEQ ID NO: 202 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 221 or SEQ ID NO: 222 or polypeptides that are at least 90% or 95% identical thereto.

**[000272]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 204; SEQ ID NO: 206; and SEQ ID NO: 208 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 201 or the variable heavy chain sequence of SEQ ID NO: 202 or sequences that are at least 90% or 95% identical thereto.

**[000273]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 224; SEQ ID NO: 226; and SEQ ID NO: 228 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 221 or the variable light chain sequence of SEQ ID NO: 222 or sequences that are at least 90% or 95% identical thereto.

**[000274]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 203; SEQ ID NO: 205; SEQ ID NO: 207; and SEQ ID NO: 209 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 201 or the variable heavy chain sequence of SEQ ID NO: 202 or sequences that are at least 90% or 95% identical thereto.

**[000275]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 223; SEQ ID NO: 225; SEQ ID NO: 227; and SEQ ID NO: 229 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 221 or the variable light chain sequence of SEQ ID NO: 222 or sequences that are at least 90% or 95% identical thereto.

**[000276]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 202; the variable light chain region of SEQ ID NO: 222; the complementarity-determining regions (SEQ ID NO: 204; SEQ ID NO: 206; and SEQ ID NO: 208) of the variable heavy chain region of SEQ ID NO: 202; and the complementarity-determining regions (SEQ ID NO: 224; SEQ ID NO: 226; and SEQ ID NO: 228) of the variable light chain region of SEQ ID NO: 222 or sequences that are at least 90% or 95% identical thereto.

**[000277]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 202; the variable light chain region of SEQ ID NO: 222; the framework regions (SEQ ID NO: 203; SEQ ID NO: 205; SEQ ID NO: 207; and SEQ ID NO: 209) of the variable heavy chain region of SEQ ID NO: 202; and the framework regions (SEQ ID NO: 223; SEQ ID NO: 225; SEQ ID NO: 227; and SEQ ID NO: 229) of the variable light chain region of SEQ ID NO: 222.

**[000278]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab6, comprising, or alternatively consisting of, SEQ ID NO: 201 and SEQ ID NO: 221, or an antibody or antibody fragment comprising the CDRs of Ab6 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab6 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab6 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab6.

**[000279]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab6, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 202 and the variable light chain sequence of SEQ ID NO: 222 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 202 and/or SEQ ID NO: 222 which retain the binding specificity for HGF.

**[000280]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab6. In another embodiment of the invention, anti-HGF antibodies such as Ab6 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000281]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab6 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab7

**[000282]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVMPGTPLTLTCTVSGFSLSSNAISWVRQAPEKGLEWIGVIYVIG
VTDYASWAQGRFTISKTSTTVDLKIPSPTTEDTATYFCARVYDSGWNHFNLWG
PGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK (SEQ ID NO: 241).

**[000283]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVMPGTPLTLTCTVSGFSLSSNAISWVRQAPEKGLEWIGVIYVIG
VTDYASWAQGRFTISKTSTTVDLKIPSPTTEDTATYFCARVYDSGWNHFNLWG
PGTLVTVSS (SEQ ID NO: 242).

**[000284]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab7 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 250).

**[000285]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASQSISSWLAWYQQKPGQPPKLLIYEASK LASGVPSRFSGSGSGTQFTLTISGVECADAATYYCQQAYSVANVDNAFGGGTE VVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC (SEQ ID NO: 261).

**[000286]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASQSISSWLAWYQQKPGQPPKLLIYEASK LASGVPSRFSGSGSGTQFTLTISGVECADAATYYCQQAYSVANVDNAFGGGTE VVVKR (SEQ ID NO: 262).

**[000287]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab7 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 270).

**[000288]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 244; SEQ ID NO: 246; and SEQ ID NO: 248 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 241 or which contain the variable heavy chain sequence of SEQ ID NO: 242, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 264; SEQ ID NO: 266; and SEQ ID NO: 268 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 261 or which contain the variable light chain sequence of SEQ ID NO: 262, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000289]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 243; SEQ ID NO: 245; SEQ ID NO: 247; and SEQ ID NO: 249 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 241 or the variable heavy chain sequence of SEQ ID NO: 242, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 263; SEQ ID NO: 265; SEQ ID NO: 267; and SEQ ID NO: 269 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 261 or the variable light chain sequence of SEQ ID NO: 262, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000290]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000291]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 241 or SEQ ID NO: 242 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 261 or SEQ ID NO: 262 or polypeptides that are at least 90% or 95% identical thereto.

**[000292]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 244; SEQ ID NO: 246; and SEQ ID NO: 248 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 241 or the variable heavy chain sequence of SEQ ID NO: 242 or sequences that are at least 90% or 95% identical thereto.

**[000293]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 264; SEQ ID NO: 266; and SEQ ID NO: 268 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 261 or the variable light chain sequence of SEQ ID NO: 262 or sequences that are at least 90% or 95% identical thereto.

**[000294]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 243; SEQ ID NO: 245; SEQ ID NO: 247; and SEQ ID NO: 249 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 241 or the variable heavy chain sequence of SEQ ID NO: 242 or sequences that are at least 90% or 95% identical thereto.

**[000295]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 263; SEQ ID NO: 265; SEQ ID NO: 267; and SEQ ID NO: 269 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 261 or the variable light chain sequence of SEQ ID NO: 262 or sequences that are at least 90% or 95% identical thereto.

**[000296]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 242; the variable light chain region of SEQ ID NO: 262; the complementarity-determining regions (SEQ ID NO: 244; SEQ ID NO: 246; and SEQ ID NO: 248) of the variable heavy chain region of SEQ ID NO: 242; and the complementarity-determining regions (SEQ ID NO: 264; SEQ ID NO: 266; and SEQ ID NO: 268) of the variable light chain region of SEQ ID NO: 262 or sequences that are at least 90% or 95% identical thereto.

**[000297]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 242; the variable light chain region of SEQ ID NO: 262; the framework regions (SEQ ID NO: 243; SEQ ID NO: 245; SEQ ID NO: 247; and SEQ ID NO: 249) of the variable heavy chain region of SEQ ID NO: 242; and the framework regions (SEQ ID NO: 263; SEQ ID NO: 265; SEQ ID NO: 267; and SEQ ID NO: 269) of the variable light chain region of SEQ ID NO: 262.

**[000298]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab7, comprising, or alternatively consisting of, SEQ ID NO: 241 and SEQ ID NO: 261, or an antibody or antibody fragment comprising the CDRs of Ab7 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab7 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab7 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab7.

**[000299]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab7, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 242 and the variable light chain sequence of SEQ ID NO: 262 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 242 and/or SEQ ID NO: 262 which retain the binding specificity for HGF.

**[000300]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab7. In another embodiment of the invention, anti-HGF antibodies such as Ab7 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000301]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab7 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

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light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab8

**[000302]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNAISWVRQAPGKGLEWVGVIYV
IGVTDYASSAQGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSGWNH
FNLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 281).

**[000303]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNAISWVRQAPGKGLEWVGVIYV
IGVTDYASSAQGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSGWNH
FNLWGQGTLVTVSS (SEQ ID NO: 282).

**[000304]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab8 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 290).

**[000305]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DIQMTQSPSTLSASVGDRVTITCQASQSISSWLAWYQQKPGKAPKLLIYEASKL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVANVDNAFGGGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C (SEQ ID NO: 301).

**[000306]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DIQMTQSPSTLSASVGDRVTITCQASQSISSWLAWYQQKPGKAPKLLIYEASKL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVANVDNAFGGGTKVE IKR (SEQ ID NO: 302).

**[000307]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab8 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 310).

**[000308]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 284; SEQ ID NO: 286; and SEQ ID NO: 288 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 281 or which contain the variable heavy chain sequence of SEQ ID NO: 282, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 304; SEQ ID NO: 306; and SEQ ID NO: 308 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 301 or which contain the variable light chain sequence of SEQ ID NO: 302, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000309]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 283; SEQ ID NO: 285; SEQ ID NO: 287; and SEQ ID NO: 289 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 281 or the variable heavy chain sequence of SEQ ID NO: 282, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 303; SEQ ID NO: 305; SEQ ID NO: 307; and SEQ ID NO: 309 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 301 or the variable light chain sequence of SEQ ID NO: 302, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000310]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000311]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 281 or SEQ ID NO: 282 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 301 or SEQ ID NO: 302 or polypeptides that are at least 90% or 95% identical thereto.

**[000312]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 284; SEQ ID NO: 286; and SEQ ID NO: 288 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 281 or the variable heavy chain sequence of SEQ ID NO: 282 or sequences that are at least 90% or 95% identical thereto.

**[000313]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 304; SEQ ID NO: 306; and SEQ ID NO: 308 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 301 or the variable light chain sequence of SEQ ID NO: 302 or sequences that are at least 90% or 95% identical thereto.

**[000314]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 283; SEQ ID NO: 285; SEQ ID NO: 287; and SEQ ID NO: 289 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 281 or the variable heavy chain sequence of SEQ ID NO: 282 or sequences that are at least 90% or 95% identical thereto.

**[000315]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 303; SEQ ID NO: 305; SEQ ID NO: 307; and SEQ ID NO: 309 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 301 or the variable light chain sequence of SEQ ID NO: 302 or sequences that are at least 90% or 95% identical thereto.

**[000316]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 282; the variable light chain region of SEQ ID NO: 302; the complementarity-determining regions (SEQ ID NO: 284; SEQ ID NO: 286; and SEQ ID NO: 288) of the variable heavy chain region of SEQ ID NO: 282; and the complementarity-determining regions (SEQ ID NO: 304; SEQ ID NO: 306; and SEQ ID NO: 308) of the variable light chain region of SEQ ID NO: 302 or sequences that are at least 90% or 95% identical thereto.

**[000317]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 282; the variable light chain region of SEQ ID NO: 302; the framework regions (SEQ ID NO: 283; SEQ ID NO: 285; SEQ ID NO: 287; and SEQ ID NO: 289) of the variable heavy chain region of SEQ ID NO: 282; and the framework regions (SEQ ID NO: 303; SEQ ID NO: 305; SEQ ID NO: 307; and SEQ ID NO: 309) of the variable light chain region of SEQ ID NO: 302.

**[000318]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab8, comprising, or alternatively consisting of, SEQ ID NO: 281 and SEQ ID NO: 301, or an antibody or antibody fragment comprising the CDRs of Ab8 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab8 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab8 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab8.

**[000319]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab8, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 282 and the variable light chain sequence of SEQ ID NO: 302 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 282 and/or SEQ ID NO: 302 which retain the binding specificity for HGF.

**[000320]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab8. In another embodiment of the invention, anti-HGF antibodies such as Ab8 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000321]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab8 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab9

**[000322]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGIDLNSNGMSWVRQAPGEGLEWIGASSIDG
TTYYTNWAKGRFTISKTSSTTVDLKITSPTTEDTATYFCTRGEYAGVVGSNYFD
LWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 321).

**[000323]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGIDLNSNGMSWVRQAPGEGLEWIGASSIDG
TTYYTNWAKGRFTISKTSSTTVDLKITSPTTEDTATYFCTRGEYAGVVGSNYFD
LWGQGTLVTVSS (SEQ ID NO: 322).

**[000324]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab9 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 330).

**[000325]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: QVLTQTPPSVSAVVGGTVTINCQSSQRIYSNWLSWYQQKPGQTPKPLIYAASSL ASGVPSRFKGSGSGTQFTLTISDLECDDAASYYCAGYYSGHIYSFGGGTEVVVK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ ESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 341).

**[000326]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: QVLTQTPPSVSAVVGGTVTINCQSSQRIYSNWLSWYQQKPGQTPKPLIYAASSL ASGVPSRFKGSGSGTQFTLTISDLECDDAASYYCAGYYSGHIYSFGGGTEVVVK R (SEQ ID NO: 342).

**[000327]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab9 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 350).

**[000328]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 324; SEQ ID NO: 326; and SEQ ID NO: 328 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 321 or which contain the variable heavy chain sequence of SEQ ID NO: 322, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 344; SEQ ID NO: 346; and SEQ ID NO: 348 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 341 or which contain the variable light chain sequence of SEQ ID NO: 342, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000329]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 323; SEQ ID NO: 325; SEQ ID NO: 327; and SEQ ID NO: 329 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 321 or the variable heavy chain sequence of SEQ ID NO: 322, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 343; SEQ ID NO: 345; SEQ ID NO: 347; and SEQ ID NO: 349 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 341 or the variable light chain sequence of SEQ ID NO: 342, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000330]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000331]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 321 or SEQ ID NO: 322 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 341 or SEQ ID NO: 342 or polypeptides that are at least 90% or 95% identical thereto.

**[000332]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 324; SEQ ID NO: 326; and SEQ ID NO: 328 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 321 or the variable heavy chain sequence of SEQ ID NO: 322 or sequences that are at least 90% or 95% identical thereto.

**[000333]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 344; SEQ ID NO: 346; and SEQ ID NO: 348 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 341 or the variable light chain sequence of SEQ ID NO: 342 or sequences that are at least 90% or 95% identical thereto.

**[000334]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 323; SEQ ID NO: 325; SEQ ID NO: 327; and SEQ ID NO: 329 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 321 or the variable heavy chain sequence of SEQ ID NO: 322 or sequences that are at least 90% or 95% identical thereto.

**[000335]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 343; SEQ ID NO: 345; SEQ ID NO: 347; and SEQ ID NO: 349 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 341 or the variable light chain sequence of SEQ ID NO: 342 or sequences that are at least 90% or 95% identical thereto.

**[000336]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 322; the variable light chain region of SEQ ID NO: 342; the complementarity-determining regions (SEQ ID NO: 324; SEQ ID NO: 326; and SEQ ID NO: 328) of the variable heavy chain region of SEQ ID NO: 322; and the complementarity-determining regions (SEQ ID NO: 344; SEQ ID NO: 346; and SEQ ID NO: 348) of the variable light chain region of SEQ ID NO: 342 or sequences that are at least 90% or 95% identical thereto.

**[000337]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 322; the variable light chain region of SEQ ID NO: 342; the framework regions (SEQ ID NO: 323; SEQ ID NO: 325; SEQ ID NO: 327; and SEQ ID NO: 329) of the variable heavy chain region of SEQ ID NO: 322; and the framework regions (SEQ ID NO: 343; SEQ ID NO: 345; SEQ ID NO: 347; and SEQ ID NO: 349) of the variable light chain region of SEQ ID NO: 342.

**[000338]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab9, comprising, or alternatively consisting of, SEQ ID NO: 321 and SEQ ID NO: 341, or an antibody or antibody fragment comprising the CDRs of Ab9 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab9 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab9 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab9.

**[000339]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab9, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 322 and the variable light chain sequence of SEQ ID NO: 342 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 322 and/or SEQ ID NO: 342 which retain the binding specificity for HGF.

**[000340]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab9. In another embodiment of the invention, anti-HGF antibodies such as Ab9 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000341]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab9 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab10

**[000342]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNGMSWVRQAPGKGLEWVGASS
IDGTTYYTNSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGEYAGVVG
SNYFDLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN
TKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 361).

**[000343]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNGMSWVRQAPGKGLEWVGASS
IDGTTYYTNSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGEYAGVVG
SNYFDLWGQGTLVTVSS (SEQ ID NO: 362).

**[000344]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab10 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 370).

**[000345]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DIQMTQSPSSVSASVGDRVTITCQSSQRIYSNWLSWYQQKPGKAPKLLIYAASS LASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAGYYSGHIYSFGGGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ ESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 381).

**[000346]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DIQMTQSPSSVSASVGDRVTITCQSSQRIYSNWLSWYQQKPGKAPKLLIYAASS LASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAGYYSGHIYSFGGGTKVEIK R (SEQ ID NO: 382).

**[000347]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab10 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 390).

**[000348]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 364; SEQ ID NO: 366; and SEQ ID NO: 368 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 361 or which contain the variable heavy chain sequence of SEQ ID NO: 362, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 384; SEQ ID NO: 386; and SEQ ID NO: 388 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 381 or which contain the variable light chain sequence of SEQ ID NO: 382, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000349]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 363; SEQ ID NO: 365; SEQ ID NO: 367; and SEQ ID NO: 369 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 361 or the variable heavy chain sequence of SEQ ID NO: 362, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 383; SEQ ID NO: 385; SEQ ID NO: 387; and SEQ ID NO: 389 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 381 or the variable light chain sequence of SEQ ID NO: 382, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000350]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000351]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 361 or SEQ ID NO: 362 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 381 or SEQ ID NO: 382 or polypeptides that are at least 90% or 95% identical thereto.

**[000352]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 364; SEQ ID NO: 366; and SEQ ID NO: 368 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 361 or the variable heavy chain sequence of SEQ ID NO: 362 or sequences that are at least 90% or 95% identical thereto.

**[000353]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 384; SEQ ID NO: 386; and SEQ ID NO: 388 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 381 or the variable light chain sequence of SEQ ID NO: 382 or sequences that are at least 90% or 95% identical thereto.

**[000354]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 363; SEQ ID NO: 365; SEQ ID NO: 367; and SEQ ID NO: 369 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 361 or the variable heavy chain sequence of SEQ ID NO: 362 or sequences that are at least 90% or 95% identical thereto.

**[000355]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 383; SEQ ID NO: 385; SEQ ID NO: 387; and SEQ ID NO: 389 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 381 or the variable light chain sequence of SEQ ID NO: 382 or sequences that are at least 90% or 95% identical thereto.

**[000356]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 362; the variable light chain region of SEQ ID NO: 382; the complementarity-determining regions (SEQ ID NO: 364; SEQ ID NO: 366; and SEQ ID NO: 368) of the variable heavy chain region of SEQ ID NO: 362; and the complementarity-determining regions (SEQ ID NO: 384; SEQ ID NO: 386; and SEQ ID NO: 388) of the variable light chain region of SEQ ID NO: 382 or sequences that are at least 90% or 95% identical thereto.

**[000357]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 362; the variable light chain region of SEQ ID NO: 382; the framework regions (SEQ ID NO: 363; SEQ ID NO: 365; SEQ ID NO: 367; and SEQ ID NO: 369) of the variable heavy chain region of SEQ ID NO: 362; and the framework regions (SEQ ID NO: 383; SEQ ID NO: 385; SEQ ID NO: 387; and SEQ ID NO: 389) of the variable light chain region of SEQ ID NO: 382.

**[000358]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab10, comprising, or alternatively consisting of, SEQ ID NO: 361 and SEQ ID NO: 381, or an antibody or antibody fragment comprising the CDRs of Ab10 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab10 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab10 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab10.

**[000359]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab10, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 362 and the variable light chain sequence of SEQ ID NO: 382 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 362 and/or SEQ ID NO: 382 which retain the binding specificity for HGF.

**[000360]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab10. In another embodiment of the invention, anti-HGF antibodies such as Ab10 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000361]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab10 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab11

**[000362]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSMEESGGRLVTPGTPLTLTCTVSGFSLSDYALSWVRQAPGKGLEWIGMISSGD
NTYYASWAKGRFTISKASTTVDLKITSPTTEDTATYFCARDKDASSGGYLVLDL
LDVPDGMDLWGPGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
KPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV
TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQV
SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 401).

**[000363]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSMEESGGRLVTPGTPLTLTCTVSGFSLSDYALSWVRQAPGKGLEWIGMISSGD
NTYYASWAKGRFTISKASTTVDLKITSPTTEDTATYFCARDKDASSGGYLVLDL
LDVPDGMDLWGPGTLVTVSS (SEQ ID NO: 402).

**[000364]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab11 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 410).

**[000365]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AVLTQTPSPVSAAVGGTVTIKCQSSQSVYNNNLLSWYQQKPGQPPKLLIWGAS YLPSGVPDRFSGSGSGTQFTLTISGVQCDDAATYYCLGGYDGDADTYNTFGGG TEVVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL QSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC (SEQ ID NO: 421).

**[000366]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AVLTQTPSPVSAAVGGTVTIKCQSSQSVYNNNLLSWYQQKPGQPPKLLIWGAS YLPSGVPDRFSGSGSGTQFTLTISGVQCDDAATYYCLGGYDGDADTYNTFGGG TEVVVKR (SEQ ID NO: 422).

**[000367]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab11 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 430).

**[000368]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 404; SEQ ID NO: 406; and SEQ ID NO: 408 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 401 or which contain the variable heavy chain sequence of SEQ ID NO: 402, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 424; SEQ ID NO: 426; and SEQ ID NO: 428 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 421 or which contain the variable light chain sequence of SEQ ID NO: 422, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000369]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 403; SEQ ID NO: 405; SEQ ID NO: 407; and SEQ ID NO: 409 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 401 or the variable heavy chain sequence of SEQ ID NO: 402, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 423; SEQ ID NO: 425; SEQ ID NO: 427; and SEQ ID NO: 429 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 421 or the variable light chain sequence of SEQ ID NO: 422, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000370]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000371]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 401 or SEQ ID NO: 402 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 421 or SEQ ID NO: 422 or polypeptides that are at least 90% or 95% identical thereto.

**[000372]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 404; SEQ ID NO: 406; and SEQ ID NO: 408 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 401 or the variable heavy chain sequence of SEQ ID NO: 402 or sequences that are at least 90% or 95% identical thereto.

**[000373]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 424; SEQ ID NO: 426; and SEQ ID NO: 428 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 421 or the variable light chain sequence of SEQ ID NO: 422 or sequences that are at least 90% or 95% identical thereto.

**[000374]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 403; SEQ ID NO: 405; SEQ ID NO: 407; and SEQ ID NO: 409 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 401 or the variable heavy chain sequence of SEQ ID NO: 402 or sequences that are at least 90% or 95% identical thereto.

**[000375]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 423; SEQ ID NO: 425; SEQ ID NO: 427; and SEQ ID NO: 429 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 421 or the variable light chain sequence of SEQ ID NO: 422 or sequences that are at least 90% or 95% identical thereto.

**[000376]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 402; the variable light chain region of SEQ ID NO: 422; the complementarity-determining regions (SEQ ID NO: 404; SEQ ID NO: 406; and SEQ ID NO: 408) of the variable heavy chain region of SEQ ID NO: 402; and the complementarity-determining regions (SEQ ID NO: 424; SEQ ID NO: 426; and SEQ ID NO: 428) of the variable light chain region of SEQ ID NO: 422 or sequences that are at least 90% or 95% identical thereto.

**[000377]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 402; the variable light chain region of SEQ ID NO: 422; the framework regions (SEQ ID NO: 403; SEQ ID NO: 405; SEQ ID NO: 407; and SEQ ID NO: 409) of the variable heavy chain region of SEQ ID NO: 402; and the framework regions (SEQ ID NO: 423; SEQ ID NO: 425; SEQ ID NO: 427; and SEQ ID NO: 429) of the variable light chain region of SEQ ID NO: 422.

**[000378]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab11, comprising, or alternatively consisting of, SEQ ID NO: 401 and SEQ ID NO: 421, or an antibody or antibody fragment comprising the CDRs of Ab11 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab11 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab11 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab11.

**[000379]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab11, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 402 and the variable light chain sequence of SEQ ID NO: 422 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 402 and/or SEQ ID NO: 422 which retain the binding specificity for HGF.

**[000380]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab11. In another embodiment of the invention, anti-HGF antibodies such as Ab11 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000381]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab11 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

fragments: the variable heavy chain region of SEQ ID NO: 402; the variable light chain region of SEQ ID NO: 422; the framework regions (SEQ ID NO: 403; SEQ ID NO: 405; SEQ ID NO: 407; and SEQ ID NO: 409) of the variable heavy chain region of SEQ ID NO: 402; and the framework regions (SEQ ID NO: 423; SEQ ID NO: 425; SEQ ID NO: 427; and SEQ ID NO: 429) of the variable light chain region of SEQ ID NO: 422.

**[000378]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab11, comprising, or alternatively consisting of, SEQ ID NO: 401 and SEQ ID NO: 421, or an antibody or antibody fragment comprising the CDRs of Ab11 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab11 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab11 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab11.

**[000379]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab11, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 402 and the variable light chain sequence of SEQ ID NO: 422 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 402 and/or SEQ ID NO: 422 which retain the binding specificity for HGF.

**[000380]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab11. In another embodiment of the invention, anti-HGF antibodies such as Ab11 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000381]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab11 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab12

**[000382]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGGSLTLTCTVSGIDLSSNAISWVRQAPEKGLEWIAVIYVVG
ATDYASWAKGRFTISRTSTTVDLKMTSLTTEDTATYFCARVYDSGWNHFNLW
GPGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG
ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV
EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED
PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK (SEQ ID NO: 441).

**[000383]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGGSLTLTCTVSGIDLSSNAISWVRQAPEKGLEWIAVIYVVG
ATDYASWAKGRFTISRTSTTVDLKMTSLTTEDTATYFCARVYDSGWNHFNLW
GPGTLVTVSS (SEQ ID NO: 442).

**[000384]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab12 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 450).

**[000385]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQVSQSISSWLSWYQKKPGQRPKLLIYRAST LASGVSSRFKGSGSGTEFTLTISGVECADAATYYCQQAYSVSNVDNAFGGGTE VVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC (SEQ ID NO: 461).

**[000386]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQVSQSISSWLSWYQKKPGQRPKLLIYRAST LASGVSSRFKGSGSGTEFTLTISGVECADAATYYCQQAYSVSNVDNAFGGGTE VVVKR (SEQ ID NO: 462).

**[000387]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab12 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 470).

**[000388]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 444; SEQ ID NO: 446; and SEQ ID NO: 448 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 441 or which contain the variable heavy chain sequence of SEQ ID NO: 442, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 464; SEQ ID NO: 466; and SEQ ID NO: 468 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 461 or which contain the variable light chain sequence of SEQ ID NO: 462, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000389]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 443; SEQ ID NO: 445; SEQ ID NO: 447; and SEQ ID NO: 449 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 441 or the variable heavy chain sequence of SEQ ID NO: 442, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 463; SEQ ID NO: 465; SEQ ID NO: 467; and SEQ ID NO: 469 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 461 or the variable light chain sequence of SEQ ID NO: 462, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000390]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000391]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 441 or SEQ ID NO: 442 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 461 or SEQ ID NO: 462 or polypeptides that are at least 90% or 95% identical thereto.

**[000392]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 444; SEQ ID NO: 446; and SEQ ID NO: 448 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 441 or the variable heavy chain sequence of SEQ ID NO: 442 or sequences that are at least 90% or 95% identical thereto.

**[000393]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 464; SEQ ID NO: 466; and SEQ ID NO: 468 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 461 or the variable light chain sequence of SEQ ID NO: 462 or sequences that are at least 90% or 95% identical thereto.

**[000394]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 443; SEQ ID NO: 445; SEQ ID NO: 447; and SEQ ID NO: 449 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 441 or the variable heavy chain sequence of SEQ ID NO: 442 or sequences that are at least 90% or 95% identical thereto.

**[000395]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 463; SEQ ID NO: 465; SEQ ID NO: 467; and SEQ ID NO: 469 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 461 or the variable light chain sequence of SEQ ID NO: 462 or sequences that are at least 90% or 95% identical thereto.

**[000396]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 442; the variable light chain region of SEQ ID NO: 462; the complementarity-determining regions (SEQ ID NO: 444; SEQ ID NO: 446; and SEQ ID NO: 448) of the variable heavy chain region of SEQ ID NO: 442; and the complementarity-determining regions (SEQ ID NO: 464; SEQ ID NO: 466; and SEQ ID NO: 468) of the variable light chain region of SEQ ID NO: 462 or sequences that are at least 90% or 95% identical thereto.

**[000397]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 442; the variable light chain region of SEQ ID NO: 462; the framework regions (SEQ ID NO: 443; SEQ ID NO: 445; SEQ ID NO: 447; and SEQ ID NO: 449) of the variable heavy chain region of SEQ ID NO: 442; and the framework regions (SEQ ID NO: 463; SEQ ID NO: 465; SEQ ID NO: 467; and SEQ ID NO: 469) of the variable light chain region of SEQ ID NO: 462.

**[000398]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab12, comprising, or alternatively consisting of, SEQ ID NO: 441 and SEQ ID NO: 461, or an antibody or antibody fragment comprising the CDRs of Ab12 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab12 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab12 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab12.

**[000399]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab12, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 442 and the variable light chain sequence of SEQ ID NO: 462 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 442 and/or SEQ ID NO: 462 which retain the binding specificity for HGF.

**[000400]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab12. In another embodiment of the invention, anti-HGF antibodies such as Ab12 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000401]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab12 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab13

**[000402]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNAISWVRQAPGKGLEWVAVIYV
VGATDYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSGWNH
FNLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 481).

**[000403]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNAISWVRQAPGKGLEWVAVIYV
VGATDYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSGWNH
FNLWGQGTLVTVSS (SEQ ID NO: 482).

**[000404]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab13 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 490).

**[000405]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DYQMTQSPSTLSASVGDRVTITCQVSQSISSWLSWYQQKPGKAPKLLIYRASTL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVSNVDNAFGGGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C (SEQ ID NO: 501).

**[000406]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DYQMTQSPSTLSASVGDRVTITCQVSQSISSWLSWYQQKPGKAPKLLIYRASTL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVSNVDNAFGGGTKVE IKR (SEQ ID NO: 502).

**[000407]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab13 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 510).

**[000408]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 484; SEQ ID NO: 486; and SEQ ID NO: 488 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 481 or which contain the variable heavy chain sequence of SEQ ID NO: 482, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 504; SEQ ID NO: 506; and SEQ ID NO: 508 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 501 or which contain the variable light chain sequence of SEQ ID NO: 502, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000409]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 483; SEQ ID NO: 485; SEQ ID NO: 487; and SEQ ID NO: 489 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 481 or the variable heavy chain sequence of SEQ ID NO: 482, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 503; SEQ ID NO: 505; SEQ ID NO: 507; and SEQ ID NO: 509 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 501 or the variable light chain sequence of SEQ ID NO: 502, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000410]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000411]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 481 or SEQ ID NO: 482 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 501 or SEQ ID NO: 502 or polypeptides that are at least 90% or 95% identical thereto.

**[000412]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 484; SEQ ID NO: 486; and SEQ ID NO: 488 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 481 or the variable heavy chain sequence of SEQ ID NO: 482 or sequences that are at least 90% or 95% identical thereto.

**[000413]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 504; SEQ ID NO: 506; and SEQ ID NO: 508 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 501 or the variable light chain sequence of SEQ ID NO: 502 or sequences that are at least 90% or 95% identical thereto.

**[000414]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 483; SEQ ID NO: 485; SEQ ID NO: 487; and SEQ ID NO: 489 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 481 or the variable heavy chain sequence of SEQ ID NO: 482 or sequences that are at least 90% or 95% identical thereto.

**[000415]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 503; SEQ ID NO: 505; SEQ ID NO: 507; and SEQ ID NO: 509 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 501 or the variable light chain sequence of SEQ ID NO: 502 or sequences that are at least 90% or 95% identical thereto.

**[000416]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 482; the variable light chain region of SEQ ID NO: 502; the complementarity-determining regions (SEQ ID NO: 484; SEQ ID NO: 486; and SEQ ID NO: 488) of the variable heavy chain region of SEQ ID NO: 482; and the complementarity-determining regions (SEQ ID NO: 504; SEQ ID NO: 506; and SEQ ID NO: 508) of the variable light chain region of SEQ ID NO: 502 or sequences that are at least 90% or 95% identical thereto.

**[000417]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 482; the variable light chain region of SEQ ID NO: 502; the framework regions (SEQ ID NO: 483; SEQ ID NO: 485; SEQ ID NO: 487; and SEQ ID NO: 489) of the variable heavy chain region of SEQ ID NO: 482; and the framework regions (SEQ ID NO: 503; SEQ ID NO: 505; SEQ ID NO: 507; and SEQ ID NO: 509) of the variable light chain region of SEQ ID NO: 502.

**[000418]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab13, comprising, or alternatively consisting of, SEQ ID NO: 481 and SEQ ID NO: 501, or an antibody or antibody fragment comprising the CDRs of Ab13 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab13 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab13 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab13.

**[000419]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab13, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 482 and the variable light chain sequence of SEQ ID NO: 502 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 482 and/or SEQ ID NO: 502 which retain the binding specificity for HGF.

**[000420]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab13. In another embodiment of the invention, anti-HGF antibodies such as Ab13 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000421]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab13 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab14

**[000422]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below: QSVEESGGRLVTPGTPLTLTCTVSGFSLSNYAMTWVRQAPGKGLEWIGVISFGG NTYYANWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARWDAENNEILNLWG QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK (SEQ ID NO: 521).

**[000423]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below: QSVEESGGRLVTPGTPLTLTCTVSGFSLSNYAMTWVRQAPGKGLEWIGVISFGG NTYYANWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARWDAENNEILNLWG QGTLVTVSS (SEQ ID NO: 522).

**[000424]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab14 and which contain a constant heavy chain sequence comprising the sequence set forth below: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK (SEQ ID NO: 530).

**[000425]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESIESYLAWYQQKSGQPPKLLIYRASTL ASGVSSRFKGSGSGTQFTLTISGVECADAATYYCQQGDAWSNVDNVFGGGTE VVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC (SEQ ID NO: 541).

**[000426]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESIESYLAWYQQKSGQPPKLLIYRASTL ASGVSSRFKGSGSGTQFTLTISGVECADAATYYCQQGDAWSNVDNVFGGGTE VVVKR (SEQ ID NO: 542).

**[000427]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab14 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 550).

**[000428]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 524; SEQ ID NO: 526; and SEQ ID NO: 528 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 521 or which contain the variable heavy chain sequence of SEQ ID NO: 522, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 544; SEQ ID NO: 546; and SEQ ID NO: 548 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 541 or which contain the variable light chain sequence of SEQ ID NO: 542, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000429]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 523; SEQ ID NO: 525; SEQ ID NO: 527; and SEQ ID NO: 529 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 521 or the variable heavy chain sequence of SEQ ID NO: 522, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 543; SEQ ID NO: 545; SEQ ID NO: 547; and SEQ ID NO: 549 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 541 or the variable light chain sequence of SEQ ID NO: 542, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000430]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000431]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 521 or SEQ ID NO: 522 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 541 or SEQ ID NO: 542 or polypeptides that are at least 90% or 95% identical thereto.

**[000432]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 524; SEQ ID NO: 526; and SEQ ID NO: 528 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 521 or the variable heavy chain sequence of SEQ ID NO: 522 or sequences that are at least 90% or 95% identical thereto.

**[000433]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 544; SEQ ID NO: 546; and SEQ ID NO: 548 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 541 or the variable light chain sequence of SEQ ID NO: 542 or sequences that are at least 90% or 95% identical thereto.

**[000434]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 523; SEQ ID NO: 525; SEQ ID NO: 527; and SEQ ID NO: 529 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 521 or the variable heavy chain sequence of SEQ ID NO: 522 or sequences that are at least 90% or 95% identical thereto.

**[000435]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 543; SEQ ID NO: 545; SEQ ID NO: 547; and SEQ ID NO: 549 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 541 or the variable light chain sequence of SEQ ID NO: 542 or sequences that are at least 90% or 95% identical thereto.

**[000436]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 522; the variable light chain region of SEQ ID NO: 542; the complementarity-determining regions (SEQ ID NO: 524; SEQ ID NO: 526; and SEQ ID NO: 528) of the variable heavy chain region of SEQ ID NO: 522; and the complementarity-determining regions (SEQ ID NO: 544; SEQ ID NO: 546; and SEQ ID NO: 548) of the variable light chain region of SEQ ID NO: 542 or sequences that are at least 90% or 95% identical thereto.

**[000437]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 522; the variable light chain region of SEQ ID NO: 542; the framework regions (SEQ ID NO: 523; SEQ ID NO: 525; SEQ ID NO: 527; and SEQ ID NO: 529) of the variable heavy chain region of SEQ ID NO: 522; and the framework regions (SEQ ID NO: 543; SEQ ID NO: 545; SEQ ID NO: 547; and SEQ ID NO: 549) of the variable light chain region of SEQ ID NO: 542.

**[000438]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab14, comprising, or alternatively consisting of, SEQ ID NO: 521 and SEQ ID NO: 541, or an antibody or antibody fragment comprising the CDRs of Ab14 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab14 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab14 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab14.

**[000439]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab14, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 522 and the variable light chain sequence of SEQ ID NO: 542 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 522 and/or SEQ ID NO: 542 which retain the binding specificity for HGF.

**[000440]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab14. In another embodiment of the invention, anti-HGF antibodies such as Ab14 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000441]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab14 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab15

**[000442]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below: QSVEESGGRLVTPGTPLTLTCTVSGFSLSNYAMTWVRQAPGKGLEWIGVISFGG NTYYANWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARWDAENNEILNLWG PGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK (SEQ ID NO: 561).

**[000443]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below: QSVEESGGRLVTPGTPLTLTCTVSGFSLSNYAMTWVRQAPGKGLEWIGVISFGG NTYYANWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARWDAENNEILNLWG PGTLVTVSS (SEQ ID NO: 562).

**[000444]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab15 and which contain a constant heavy chain sequence comprising the sequence set forth below: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK (SEQ ID NO: 570).

**[000445]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESISSYLAWYQQKSGQPPKLLIYRASTL ASGVSSRFKGSGSGTQFTLTISGVECADAATYYCQQGDAWSNVDNVFGGGTE VVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC (SEQ ID NO: 581).

**[000446]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESISSYLAWYQQKSGQPPKLLIYRASTL ASGVSSRFKGSGSGTQFTLTISGVECADAATYYCQQGDAWSNVDNVFGGGTE VVVKR (SEQ ID NO: 582).

**[000447]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab15 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 590).

**[000448]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 564; SEQ ID NO: 566; and SEQ ID NO: 568 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 561 or which contain the variable heavy chain sequence of SEQ ID NO: 562, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 584; SEQ ID NO: 586; and SEQ ID NO: 588 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 581 or which contain the variable light chain sequence of SEQ ID NO: 582, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000449]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 563; SEQ ID NO: 565; SEQ ID NO: 567; and SEQ ID NO: 569 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 561 or the variable heavy chain sequence of SEQ ID NO: 562, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 583; SEQ ID NO: 585; SEQ ID NO: 587; and SEQ ID NO: 589 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 581 or the variable light chain sequence of SEQ ID NO: 582, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000450]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000451]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 561 or SEQ ID NO: 562 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 581 or SEQ ID NO: 582 or polypeptides that are at least 90% or 95% identical thereto.

**[000452]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 564; SEQ ID NO: 566; and SEQ ID NO: 568 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 561 or the variable heavy chain sequence of SEQ ID NO: 562 or sequences that are at least 90% or 95% identical thereto.

**[000453]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 584; SEQ ID NO: 586; and SEQ ID NO: 588 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 581 or the variable light chain sequence of SEQ ID NO: 582 or sequences that are at least 90% or 95% identical thereto.

**[000454]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 563; SEQ ID NO: 565; SEQ ID NO: 567; and SEQ ID NO: 569 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 561 or the variable heavy chain sequence of SEQ ID NO: 562 or sequences that are at least 90% or 95% identical thereto.

**[000455]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 583; SEQ ID NO: 585; SEQ ID NO: 587; and SEQ ID NO: 589 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 581 or the variable light chain sequence of SEQ ID NO: 582 or sequences that are at least 90% or 95% identical thereto.

**[000456]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 562; the variable light chain region of SEQ ID NO: 582; the complementarity-determining regions (SEQ ID NO: 564; SEQ ID NO: 566; and SEQ ID NO: 568) of the variable heavy chain region of SEQ ID NO: 562; and the complementarity-determining regions (SEQ ID NO: 584; SEQ ID NO: 586; and SEQ ID NO: 588) of the variable light chain region of SEQ ID NO: 582 or sequences that are at least 90% or 95% identical thereto.

**[000457]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 562; the variable light chain region of SEQ ID NO: 582; the framework regions (SEQ ID NO: 563; SEQ ID NO: 565; SEQ ID NO: 567; and SEQ ID NO: 569) of the variable heavy chain region of SEQ ID NO: 562; and the framework regions (SEQ ID NO: 583; SEQ ID NO: 585; SEQ ID NO: 587; and SEQ ID NO: 589) of the variable light chain region of SEQ ID NO: 582.

**[000458]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab15, comprising, or alternatively consisting of, SEQ ID NO: 561 and SEQ ID NO: 581, or an antibody or antibody fragment comprising the CDRs of Ab15 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab15 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab15 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab15.

**[000459]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab15, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 562 and the variable light chain sequence of SEQ ID NO: 582 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 562 and/or SEQ ID NO: 582 which retain the binding specificity for HGF.

**[000460]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab15. In another embodiment of the invention, anti-HGF antibodies such as Ab15 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000461]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab15 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab16

**[000462]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGIDLSNYAMGWVRQAPGKGLEYIGMIGVN
GRAWYATWAKGRFTISKTSPTVDLKITSPTTEDTATYFCARLIDERSTYSYVFD
LWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 601).

**[000463]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGIDLSNYAMGWVRQAPGKGLEYIGMIGVN
GRAWYATWAKGRFTISKTSPTVDLKITSPTTEDTATYFCARLIDERSTYSYVFD
LWGQGTLVTVSS (SEQ ID NO: 602).

**[000464]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab16 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 610).

**[000465]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: QVLTQTPSPVSAAVGGTVTINCQGSQSLYNNNAFSWYQQKPGQPPKLLIYDAS TLASGVPSRFKGSGSGTQFTLTISGVQCADAATYYCQGEFSCGDVDCIAFGGGT EVVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSF NRGEC (SEQ ID NO: 621).

**[000466]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: QVLTQTPSPVSAAVGGTVTINCQGSQSLYNNNAFSWYQQKPGQPPKLLIYDAS TLASGVPSRFKGSGSGTQFTLTISGVQCADAATYYCQGEFSCGDVDCIAFGGGT EVVVKR (SEQ ID NO: 622).

**[000467]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab16 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 630).

**[000468]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 604; SEQ ID NO: 606; and SEQ ID NO: 608 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 601 or which contain the variable heavy chain sequence of SEQ ID NO: 602, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 624; SEQ ID NO: 626; and SEQ ID NO: 628 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 621 or which contain the variable light chain sequence of SEQ ID NO: 622, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000469]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 603; SEQ ID NO: 605; SEQ ID NO: 607; and SEQ ID NO: 609 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 601 or the variable heavy chain sequence of SEQ ID NO: 602, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 623; SEQ ID NO: 625; SEQ ID NO: 627; and SEQ ID NO: 629 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 621 or the variable light chain sequence of SEQ ID NO: 622, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000470]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000471]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 601 or SEQ ID NO: 602 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 621 or SEQ ID NO: 622 or polypeptides that are at least 90% or 95% identical thereto.

**[000472]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 604; SEQ ID NO: 606; and SEQ ID NO: 608 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 601 or the variable heavy chain sequence of SEQ ID NO: 602 or sequences that are at least 90% or 95% identical thereto.

**[000473]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 624; SEQ ID NO: 626; and SEQ ID NO: 628 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 621 or the variable light chain sequence of SEQ ID NO: 622 or sequences that are at least 90% or 95% identical thereto.

**[000474]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 603; SEQ ID NO: 605; SEQ ID NO: 607; and SEQ ID NO: 609 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 601 or the variable heavy chain sequence of SEQ ID NO: 602 or sequences that are at least 90% or 95% identical thereto.

**[000475]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 623; SEQ ID NO: 625; SEQ ID NO: 627; and SEQ ID NO: 629 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 621 or the variable light chain sequence of SEQ ID NO: 622 or sequences that are at least 90% or 95% identical thereto.

**[000476]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 602; the variable light chain region of SEQ ID NO: 622; the complementarity-determining regions (SEQ ID NO: 604; SEQ ID NO: 606; and SEQ ID NO: 608) of the variable heavy chain region of SEQ ID NO: 602; and the complementarity-determining regions (SEQ ID NO: 624; SEQ ID NO: 626; and SEQ ID NO: 628) of the variable light chain region of SEQ ID NO: 622 or sequences that are at least 90% or 95% identical thereto.

**[000477]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 602; the variable light chain region of SEQ ID NO: 622; the framework regions (SEQ ID NO: 603; SEQ ID NO: 605; SEQ ID NO: 607; and SEQ ID NO: 609) of the variable heavy chain region of SEQ ID NO: 602; and the framework regions (SEQ ID NO: 623; SEQ ID NO: 625; SEQ ID NO: 627; and SEQ ID NO: 629) of the variable light chain region of SEQ ID NO: 622.

**[000478]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab16, comprising, or alternatively consisting of, SEQ ID NO: 601 and SEQ ID NO: 621, or an antibody or antibody fragment comprising the CDRs of Ab16 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab16 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab16 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab16.

**[000479]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab16, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 602 and the variable light chain sequence of SEQ ID NO: 622 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 602 and/or SEQ ID NO: 622 which retain the binding specificity for HGF.

**[000480]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab16. In another embodiment of the invention, anti-HGF antibodies such as Ab16 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000481]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab16 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab17

**[000482]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below: QSVEESGGRLVPPGTPLTLTCTVSGIDLSSYAMGWVRQAPGKGLEYIGMIDVSG STYYADWAKGRLTISKTPTTVDLEITSPTTEDTATYFCARLIDERSTYSYAFDLW GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKC KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM HEALHNHYTQKSLSLSPGK (SEQ ID NO: 641).

**[000483]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below: QSVEESGGRLVPPGTPLTLTCTVSGIDLSSYAMGWVRQAPGKGLEYIGMIDVSG STYYADWAKGRLTISKTPTTVDLEITSPTTEDTATYFCARLIDERSTYSYAFDLW GQGTLVTVSS (SEQ ID NO: 642).

**[000484]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab17 and which contain a constant heavy chain sequence comprising the sequence set forth below: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK (SEQ ID NO: 650).

**[000485]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: QVLTQTPSPVSAAVGGTVTINCQASQSFYNNGAFSWYQQKPGQPPKLLIYDAS TLASGVPSRFKGSGSGTQFTLTISGVQCGDAATYYCQGEFSCGSADCVAFGGG TEVVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL QSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC (SEQ ID NO: 661).

**[000486]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: QVLTQTPSPVSAAVGGTVTINCQASQSFYNNGAFSWYQQKPGQPPKLLIYDAS TLASGVPSRFKGSGSGTQFTLTISGVQCGDAATYYCQGEFSCGSADCVAFGGG TEVVVKR (SEQ ID NO: 662).

**[000487]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab17 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 670).

**[000488]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 644; SEQ ID NO: 646; and SEQ ID NO: 648 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 641 or which contain the variable heavy chain sequence of SEQ ID NO: 642, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 664; SEQ ID NO: 666; and SEQ ID NO: 668 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 661 or which contain the variable light chain sequence of SEQ ID NO: 662, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000489]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 643; SEQ ID NO: 645; SEQ ID NO: 647; and SEQ ID NO: 649 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 641 or the variable heavy chain sequence of SEQ ID NO: 642, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 663; SEQ ID NO: 665; SEQ ID NO: 667; and SEQ ID NO: 669 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 661 or the variable light chain sequence of SEQ ID NO: 662, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000490]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000491]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 641 or SEQ ID NO: 642 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 661 or SEQ ID NO: 662 or polypeptides that are at least 90% or 95% identical thereto.

**[000492]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 644; SEQ ID NO: 646; and SEQ ID NO: 648 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 641 or the variable heavy chain sequence of SEQ ID NO: 642 or sequences that are at least 90% or 95% identical thereto.

**[000493]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 664; SEQ ID NO: 666; and SEQ ID NO: 668 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 661 or the variable light chain sequence of SEQ ID NO: 662 or sequences that are at least 90% or 95% identical thereto.

**[000494]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 643; SEQ ID NO: 645; SEQ ID NO: 647; and SEQ ID NO: 649 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 641 or the variable heavy chain sequence of SEQ ID NO: 642 or sequences that are at least 90% or 95% identical thereto.

**[000495]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 663; SEQ ID NO: 665; SEQ ID NO: 667; and SEQ ID NO: 669 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 661 or the variable light chain sequence of SEQ ID NO: 662 or sequences that are at least 90% or 95% identical thereto.

**[000496]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 642; the variable light chain region of SEQ ID NO: 662; the complementarity-determining regions (SEQ ID NO: 644; SEQ ID NO: 646; and SEQ ID NO: 648) of the variable heavy chain region of SEQ ID NO: 642; and the complementarity-determining regions (SEQ ID NO: 664; SEQ ID NO: 666; and SEQ ID NO: 668) of the variable light chain region of SEQ ID NO: 662 or sequences that are at least 90% or 95% identical thereto.

**[000497]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 642; the variable light chain region of SEQ ID NO: 662; the framework regions (SEQ ID NO: 643; SEQ ID NO: 645; SEQ ID NO: 647; and SEQ ID NO: 649) of the variable heavy chain region of SEQ ID NO: 642; and the framework regions (SEQ ID NO: 663; SEQ ID NO: 665; SEQ ID NO: 667; and SEQ ID NO: 669) of the variable light chain region of SEQ ID NO: 662.

**[000498]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab17, comprising, or alternatively consisting of, SEQ ID NO: 641 and SEQ ID NO: 661, or an antibody or antibody fragment comprising the CDRs of Ab17 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab17 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab17 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab17.

**[000499]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab17, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 642 and the variable light chain sequence of SEQ ID NO: 662 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 642 and/or SEQ ID NO: 662 which retain the binding specificity for HGF.

**[000500]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab17. In another embodiment of the invention, anti-HGF antibodies such as Ab17 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000501]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab17 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab18

**[000502]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGTPLTLTCTASGFSLSSYDMSWVRQAPGKGLEWIGIIYAGS
ASTWFASWVKGRFTISKTSTTVDLKMTSLTTEDTATYFCARVGYSGYGYDDNL
DMWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 681).

**[000503]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGTPLTLTCTASGFSLSSYDMSWVRQAPGKGLEWIGIIYAGS
ASTWFASWVKGRFTISKTSTTVDLKMTSLTTEDTATYFCARVGYSGYGYDDNL
DMWGQGTLVTVSS (SEQ ID NO: 682).

**[000504]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab18 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 690).

**[000505]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASQSISTALAWYQQKPGQRPKLLIYDASK LASGVSSRFKGSGSGAQFTLTISGVECADAATYYCHQGYSSSNVDNTFGGGTE VVVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC (SEQ ID NO: 701).

**[000506]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASQSISTALAWYQQKPGQRPKLLIYDASK LASGVSSRFKGSGSGAQFTLTISGVECADAATYYCHQGYSSSNVDNTFGGGTE VVVKR (SEQ ID NO: 702).

**[000507]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab18 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 710).

**[000508]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 684; SEQ ID NO: 686; and SEQ ID NO: 688 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 681 or which contain the variable heavy chain sequence of SEQ ID NO: 682, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 704; SEQ ID NO: 706; and SEQ ID NO: 708 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 701 or which contain the variable light chain sequence of SEQ ID NO: 702, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000509]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 683; SEQ ID NO: 685; SEQ ID NO: 687; and SEQ ID NO: 689 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 681 or the variable heavy chain sequence of SEQ ID NO: 682, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 703; SEQ ID NO: 705; SEQ ID NO: 707; and SEQ ID NO: 709 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 701 or the variable light chain sequence of SEQ ID NO: 702, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000510]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000511]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 681 or SEQ ID NO: 682 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 701 or SEQ ID NO: 702 or polypeptides that are at least 90% or 95% identical thereto.

**[000512]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 684; SEQ ID NO: 686; and SEQ ID NO: 688 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 681 or the variable heavy chain sequence of SEQ ID NO: 682 or sequences that are at least 90% or 95% identical thereto.

**[000513]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 704; SEQ ID NO: 706; and SEQ ID NO: 708 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 701 or the variable light chain sequence of SEQ ID NO: 702 or sequences that are at least 90% or 95% identical thereto.

**[000514]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 683; SEQ ID NO: 685; SEQ ID NO: 687; and SEQ ID NO: 689 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 681 or the variable heavy chain sequence of SEQ ID NO: 682 or sequences that are at least 90% or 95% identical thereto.

**[000515]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 703; SEQ ID NO: 705; SEQ ID NO: 707; and SEQ ID NO: 709 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 701 or the variable light chain sequence of SEQ ID NO: 702 or sequences that are at least 90% or 95% identical thereto.

**[000516]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 682; the variable light chain region of SEQ ID NO: 702; the complementarity-determining regions (SEQ ID NO: 684; SEQ ID NO: 686; and SEQ ID NO: 688) of the variable heavy chain region of SEQ ID NO: 682; and the complementarity-determining regions (SEQ ID NO: 704; SEQ ID NO: 706; and SEQ ID NO: 708) of the variable light chain region of SEQ ID NO: 702 or sequences that are at least 90% or 95% identical thereto.

**[000517]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 682; the variable light chain region of SEQ ID NO: 702; the framework regions (SEQ ID NO: 683; SEQ ID NO: 685; SEQ ID NO: 687; and SEQ ID NO: 689) of the variable heavy chain region of SEQ ID NO: 682; and the framework regions (SEQ ID NO: 703; SEQ ID NO: 705; SEQ ID NO: 707; and SEQ ID NO: 709) of the variable light chain region of SEQ ID NO: 702.

**[000518]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab18, comprising, or alternatively consisting of, SEQ ID NO: 681 and SEQ ID NO: 701, or an antibody or antibody fragment comprising the CDRs of Ab18 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab18 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab18 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab18.

**[000519]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab18, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 682 and the variable light chain sequence of SEQ ID NO: 702 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 682 and/or SEQ ID NO: 702 which retain the binding specificity for HGF.

**[000520]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab18. In another embodiment of the invention, anti-HGF antibodies such as Ab18 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000521]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab18 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab19

**[000522]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTASGFSLSNYWMGWVRQAPGEGLEWIGTISYD
GNTYYASWAKGRFTISRTSTTVDLKMTSLTTEDTAIYFCATVNYPDYSTGAFNI
WGPGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS
GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE
DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO: 721).

**[000523]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTASGFSLSNYWMGWVRQAPGEGLEWIGTISYD
GNTYYASWAKGRFTISRTSTTVDLKMTSLTTEDTAIYFCATVNYPDYSTGAFNI
WGPGTLVTVSS (SEQ ID NO: 722).

**[000524]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab19 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 730).

**[000525]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DVVMTQTPASVSEPVGGTVTIKCQASQSIDNYLAWYQQKPGQRPRLLIYYTST LASGVPSRFKGSGSGTEYTLTISDLECADAATYYCQFTAYYSTYIGAFGGGTEV VVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC (SEQ ID NO: 741).

**[000526]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DVVMTQTPASVSEPVGGTVTIKCQASQSIDNYLAWYQQKPGQRPRLLIYYTST LASGVPSRFKGSGSGTEYTLTISDLECADAATYYCQFTAYYSTYIGAFGGGTEV VVKR (SEQ ID NO: 742).

**[000527]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab19 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 750).

**[000528]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 724; SEQ ID NO: 726; and SEQ ID NO: 728 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 721 or which contain the variable heavy chain sequence of SEQ ID NO: 722, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 744; SEQ ID NO: 746; and SEQ ID NO: 748 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 741 or which contain the variable light chain sequence of SEQ ID NO: 742, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000529]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 723; SEQ ID NO: 725; SEQ ID NO: 727; and SEQ ID NO: 729 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 721 or the variable heavy chain sequence of SEQ ID NO: 722, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 743; SEQ ID NO: 745; SEQ ID NO: 747; and SEQ ID NO: 749 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 741 or the variable light chain sequence of SEQ ID NO: 742, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000530]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000531]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 721 or SEQ ID NO: 722 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 741 or SEQ ID NO: 742 or polypeptides that are at least 90% or 95% identical thereto.

**[000532]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 724; SEQ ID NO: 726; and SEQ ID NO: 728 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 721 or the variable heavy chain sequence of SEQ ID NO: 722 or sequences that are at least 90% or 95% identical thereto.

**[000533]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 744; SEQ ID NO: 746; and SEQ ID NO: 748 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 741 or the variable light chain sequence of SEQ ID NO: 742 or sequences that are at least 90% or 95% identical thereto.

**[000534]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 723; SEQ ID NO: 725; SEQ ID NO: 727; and SEQ ID NO: 729 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 721 or the variable heavy chain sequence of SEQ ID NO: 722 or sequences that are at least 90% or 95% identical thereto.

**[000535]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 743; SEQ ID NO: 745; SEQ ID NO: 747; and SEQ ID NO: 749 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 741 or the variable light chain sequence of SEQ ID NO: 742 or sequences that are at least 90% or 95% identical thereto.

**[000536]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 722; the variable light chain region of SEQ ID NO: 742; the complementarity-determining regions (SEQ ID NO: 724; SEQ ID NO: 726; and SEQ ID NO: 728) of the variable heavy chain region of SEQ ID NO: 722; and the complementarity-determining regions (SEQ ID NO: 744; SEQ ID NO: 746; and SEQ ID NO: 748) of the variable light chain region of SEQ ID NO: 742 or sequences that are at least 90% or 95% identical thereto.

**[000537]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 722; the variable light chain region of SEQ ID NO: 742; the framework regions (SEQ ID NO: 723; SEQ ID NO: 725; SEQ ID NO: 727; and SEQ ID NO: 729) of the variable heavy chain region of SEQ ID NO: 722; and the framework regions (SEQ ID NO: 743; SEQ ID NO: 745; SEQ ID NO: 747; and SEQ ID NO: 749) of the variable light chain region of SEQ ID NO: 742.

**[000538]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab19, comprising, or alternatively consisting of, SEQ ID NO: 721 and SEQ ID NO: 741, or an antibody or antibody fragment comprising the CDRs of Ab19 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab19 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab19 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab19.

**[000539]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab19, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 722 and the variable light chain sequence of SEQ ID NO: 742 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 722 and/or SEQ ID NO: 742 which retain the binding specificity for HGF.

**[000540]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab19. In another embodiment of the invention, anti-HGF antibodies such as Ab19 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000541]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab19 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab20

**[000542]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSNYWMGWVRQAPGKGLEWIGTIS
YDGNTYYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCATVNYPDYS
TGAFNIWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN
TKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 761).

**[000543]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSNYWMGWVRQAPGKGLEWIGTIS
YDGNTYYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCATVNYPDYS
TGAFNIWGQGTLVTVSS (SEQ ID NO: 762).

**[000544]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab20 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 770).

**[000545]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DIQMTQSPSSLSASVGDRVTITCQASQSIDNYLAWYQQKPGKVPKLLIYYTSTL ASGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQFTAYYSTYIGAFGGGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C (SEQ ID NO: 781).

**[000546]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DIQMTQSPSSLSASVGDRVTITCQASQSIDNYLAWYQQKPGKVPKLLIYYTSTL ASGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQFTAYYSTYIGAFGGGTKVEI KR (SEQ ID NO: 782).

**[000547]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab20 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 790).

**[000548]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 764; SEQ ID NO: 766; and SEQ ID NO: 768 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 761 or which contain the variable heavy chain sequence of SEQ ID NO: 762, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 784; SEQ ID NO: 786; and SEQ ID NO: 788 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 781 or which contain the variable light chain sequence of SEQ ID NO: 782, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000549]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 763; SEQ ID NO: 765; SEQ ID NO: 767; and SEQ ID NO: 769 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 761 or the variable heavy chain sequence of SEQ ID NO: 762, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 783; SEQ ID NO: 785; SEQ ID NO: 787; and SEQ ID NO: 789 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 781 or the variable light chain sequence of SEQ ID NO: 782, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000550]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000551]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 761 or SEQ ID NO: 762 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 781 or SEQ ID NO: 782 or polypeptides that are at least 90% or 95% identical thereto.

**[000552]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 764; SEQ ID NO: 766; and SEQ ID NO: 768 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 761 or the variable heavy chain sequence of SEQ ID NO: 762 or sequences that are at least 90% or 95% identical thereto.

**[000553]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 784; SEQ ID NO: 786; and SEQ ID NO: 788 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 781 or the variable light chain sequence of SEQ ID NO: 782 or sequences that are at least 90% or 95% identical thereto.

**[000554]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 763; SEQ ID NO: 765; SEQ ID NO: 767; and SEQ ID NO: 769 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 761 or the variable heavy chain sequence of SEQ ID NO: 762 or sequences that are at least 90% or 95% identical thereto.

**[000555]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 783; SEQ ID NO: 785; SEQ ID NO: 787; and SEQ ID NO: 789 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 781 or the variable light chain sequence of SEQ ID NO: 782 or sequences that are at least 90% or 95% identical thereto.

**[000556]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 762; the variable light chain region of SEQ ID NO: 782; the complementarity-determining regions (SEQ ID NO: 764; SEQ ID NO: 766; and SEQ ID NO: 768) of the variable heavy chain region of SEQ ID NO: 762; and the complementarity-determining regions (SEQ ID NO: 784; SEQ ID NO: 786; and SEQ ID NO: 788) of the variable light chain region of SEQ ID NO: 782 or sequences that are at least 90% or 95% identical thereto.

**[000557]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 762; the variable light chain region of SEQ ID NO: 782; the framework regions (SEQ ID NO: 763; SEQ ID NO: 765; SEQ ID NO: 767; and SEQ ID NO: 769) of the variable heavy chain region of SEQ ID NO: 762; and the framework regions (SEQ ID NO: 783; SEQ ID NO: 785; SEQ ID NO: 787; and SEQ ID NO: 789) of the variable light chain region of SEQ ID NO: 782.

**[000558]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab20, comprising, or alternatively consisting of, SEQ ID NO: 761 and SEQ ID NO: 781, or an antibody or antibody fragment comprising the CDRs of Ab20 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab20 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab20 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab20.

**[000559]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab20, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 762 and the variable light chain sequence of SEQ ID NO: 782 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 762 and/or SEQ ID NO: 782 which retain the binding specificity for HGF.

**[000560]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab20. In another embodiment of the invention, anti-HGF antibodies such as Ab20 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000561]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab20 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab21

**[000562]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGFSLSTYYMSWVRQAPGKGLEWIGIIYVSGI
TDYARWAKGRFTISKTSTTVDLKMTSLTTEDTATYFCARHIDSSGWDGLGIWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK (SEQ ID NO: 801).

**[000563]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGFSLSTYYMSWVRQAPGKGLEWIGIIYVSGI
TDYARWAKGRFTISKTSTTVDLKMTSLTTEDTATYFCARHIDSSGWDGLGIWG
QGTLVTVSS (SEQ ID NO: 802).

**[000564]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab21 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 810).

**[000565]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESISSYLNWYQQKLGQPPKLLIYRASTL TSGVSSRFKGSGSGTEYTLTISDLECADAATYYCQQTYGYSDTDNSFGGGTEV VVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC (SEQ ID NO: 821).

**[000566]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESISSYLNWYQQKLGQPPKLLIYRASTL TSGVSSRFKGSGSGTEYTLTISDLECADAATYYCQQTYGYSDTDNSFGGGTEV VVKR (SEQ ID NO: 822).

**[000567]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab21 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 830).

**[000568]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 804; SEQ ID NO: 806; and SEQ ID NO: 808 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 801 or which contain the variable heavy chain sequence of SEQ ID NO: 802, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 824; SEQ ID NO: 826; and SEQ ID NO: 828 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 821 or which contain the variable light chain sequence of SEQ ID NO: 822, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000569]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 803; SEQ ID NO: 805; SEQ ID NO: 807; and SEQ ID NO: 809 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 801 or the variable heavy chain sequence of SEQ ID NO: 802, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 823; SEQ ID NO: 825; SEQ ID NO: 827; and SEQ ID NO: 829 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 821 or the variable light chain sequence of SEQ ID NO: 822, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000570]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000571]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 801 or SEQ ID NO: 802 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 821 or SEQ ID NO: 822 or polypeptides that are at least 90% or 95% identical thereto.

**[000572]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 804; SEQ ID NO: 806; and SEQ ID NO: 808 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 801 or the variable heavy chain sequence of SEQ ID NO: 802 or sequences that are at least 90% or 95% identical thereto.

**[000573]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 824; SEQ ID NO: 826; and SEQ ID NO: 828 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 821 or the variable light chain sequence of SEQ ID NO: 822 or sequences that are at least 90% or 95% identical thereto.

**[000574]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 803; SEQ ID NO: 805; SEQ ID NO: 807; and SEQ ID NO: 809 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 801 or the variable heavy chain sequence of SEQ ID NO: 802 or sequences that are at least 90% or 95% identical thereto.

**[000575]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 823; SEQ ID NO: 825; SEQ ID NO: 827; and SEQ ID NO: 829 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 821 or the variable light chain sequence of SEQ ID NO: 822 or sequences that are at least 90% or 95% identical thereto.

**[000576]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 802; the variable light chain region of SEQ ID NO: 822; the complementarity-determining regions (SEQ ID NO: 804; SEQ ID NO: 806; and SEQ ID NO: 808) of the variable heavy chain region of SEQ ID NO: 802; and the complementarity-determining regions (SEQ ID NO: 824; SEQ ID NO: 826; and SEQ ID NO: 828) of the variable light chain region of SEQ ID NO: 822 or sequences that are at least 90% or 95% identical thereto.

**[000577]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 802; the variable light chain region of SEQ ID NO: 822; the framework regions (SEQ ID NO: 803; SEQ ID NO: 805; SEQ ID NO: 807; and SEQ ID NO: 809) of the variable heavy chain region of SEQ ID NO: 802; and the framework regions (SEQ ID NO: 823; SEQ ID NO: 825; SEQ ID NO: 827; and SEQ ID NO: 829) of the variable light chain region of SEQ ID NO: 822.

**[000578]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab21, comprising, or alternatively consisting of, SEQ ID NO: 801 and SEQ ID NO: 821, or an antibody or antibody fragment comprising the CDRs of Ab21 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab21 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab21 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab21.

**[000579]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab21, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 802 and the variable light chain sequence of SEQ ID NO: 822 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 802 and/or SEQ ID NO: 822 which retain the binding specificity for HGF.

**[000580]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab21. In another embodiment of the invention, anti-HGF antibodies such as Ab21 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000581]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab21 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab23

**[000582]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below: QSLEESGGRLVTPGTPLTLTCTASGFTIGRYYMSWVRQAPGKGLEWIGIIYTHG VNPDYASWAKGRFTISRPSTTVDLKITSPTTEDTATYFCARVGGFNDYSDIWGP GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK (SEQ ID NO: 841).

**[000583]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below: QSLEESGGRLVTPGTPLTLTCTASGFTIGRYYMSWVRQAPGKGLEWIGIIYTHG VNPDYASWAKGRFTISRPSTTVDLKITSPTTEDTATYFCARVGGFNDYSDIWGP GTLVTVSS (SEQ ID NO: 842).

**[000584]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab23 and which contain a constant heavy chain sequence comprising the sequence set forth below: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK (SEQ ID NO: 850).

**[000585]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESISTYLAWYQQKPGQPPKLLIYRASTL ASGVSSRFKGSGSGTQFTLTISGVECADAATYYCQQGYSYSNVDNAFGGGTEV VVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC (SEQ ID NO: 861).

**[000586]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: AYDMTQTPASVEVAVGGTVTIKCQASESISTYLAWYQQKPGQPPKLLIYRASTL ASGVSSRFKGSGSGTQFTLTISGVECADAATYYCQQGYSYSNVDNAFGGGTEV VVKR (SEQ ID NO: 862).

**[000587]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab23 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 870).

**[000588]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 844; SEQ ID NO: 846; and SEQ ID NO: 848 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 841 or which contain the variable heavy chain sequence of SEQ ID NO: 842, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 864; SEQ ID NO: 866; and SEQ ID NO: 868 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 861 or which contain the variable light chain sequence of SEQ ID NO: 862, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000589]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 843; SEQ ID NO: 845; SEQ ID NO: 847; and SEQ ID NO: 849 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 841 or the variable heavy chain sequence of SEQ ID NO: 842, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 863; SEQ ID NO: 865; SEQ ID NO: 867; and SEQ ID NO: 869 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 861 or the variable light chain sequence of SEQ ID NO: 862, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000590]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000591]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 841 or SEQ ID NO: 842 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 861 or SEQ ID NO: 862 or polypeptides that are at least 90% or 95% identical thereto.

**[000592]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 844; SEQ ID NO: 846; and SEQ ID NO: 848 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 841 or the variable heavy chain sequence of SEQ ID NO: 842 or sequences that are at least 90% or 95% identical thereto.

**[000593]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 864; SEQ ID NO: 866; and SEQ ID NO: 868 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 861 or the variable light chain sequence of SEQ ID NO: 862 or sequences that are at least 90% or 95% identical thereto.

**[000594]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 843; SEQ ID NO: 845; SEQ ID NO: 847; and SEQ ID NO: 849 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 841 or the variable heavy chain sequence of SEQ ID NO: 842 or sequences that are at least 90% or 95% identical thereto.

**[000595]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 863; SEQ ID NO: 865; SEQ ID NO: 867; and SEQ ID NO: 869 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 861 or the variable light chain sequence of SEQ ID NO: 862 or sequences that are at least 90% or 95% identical thereto.

**[000596]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 842; the variable light chain region of SEQ ID NO: 862; the complementarity-determining regions (SEQ ID NO: 844; SEQ ID NO: 846; and SEQ ID NO: 848) of the variable heavy chain region of SEQ ID NO: 842; and the complementarity-determining regions (SEQ ID NO: 864; SEQ ID NO: 866; and SEQ ID NO: 868) of the variable light chain region of SEQ ID NO: 862 or sequences that are at least 90% or 95% identical thereto.

**[000597]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 842; the variable light chain region of SEQ ID NO: 862; the framework regions (SEQ ID NO: 843; SEQ ID NO: 845; SEQ ID NO: 847; and SEQ ID NO: 849) of the variable heavy chain region of SEQ ID NO: 842; and the framework regions (SEQ ID NO: 863; SEQ ID NO: 865; SEQ ID NO: 867; and SEQ ID NO: 869) of the variable light chain region of SEQ ID NO: 862.

**[000598]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab23, comprising, or alternatively consisting of, SEQ ID NO: 841 and SEQ ID NO: 861, or an antibody or antibody fragment comprising the CDRs of Ab23 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab23 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab23 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab23.

**[000599]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab23, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 842 and the variable light chain sequence of SEQ ID NO: 862 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 842 and/or SEQ ID NO: 862 which retain the binding specificity for HGF.

**[000600]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab23. In another embodiment of the invention, anti-HGF antibodies such as Ab23 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000601]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab23 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab24

**[000602]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVGRYYMSWVRQAPGKGLEWIGIIYT
HGVNPDYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVGGFNDY
SDIWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 881).

**[000603]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVGRYYMSWVRQAPGKGLEWIGIIYT
HGVNPDYASSAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVGGFNDY
SDIWGQGTLVTVSS (SEQ ID NO: 882).

**[000604]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab24 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 890).

**[000605]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DIQMTQSPSSLSASVGDRVTITCQASESISTYLAWYQQKPGKVPKLLIYRASTLA SGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQQGYSYSNVDNAFGGGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C (SEQ ID NO: 901).

**[000606]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DIQMTQSPSSLSASVGDRVTITCQASESISTYLAWYQQKPGKVPKLLIYRASTLA SGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQQGYSYSNVDNAFGGGTKVEI KR (SEQ ID NO: 902).

**[000607]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab24 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 910).

**[000608]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 884; SEQ ID NO: 886; and SEQ ID NO: 888 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 881 or which contain the variable heavy chain sequence of SEQ ID NO: 882, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 904; SEQ ID NO: 906; and SEQ ID NO: 908 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 901 or which contain the variable light chain sequence of SEQ ID NO: 902, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000609]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 883; SEQ ID NO: 885; SEQ ID NO: 887; and SEQ ID NO: 889 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 881 or the variable heavy chain sequence of SEQ ID NO: 882, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 903; SEQ ID NO: 905; SEQ ID NO: 907; and SEQ ID NO: 909 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 901 or the variable light chain sequence of SEQ ID NO: 902, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000610]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000611]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 881 or SEQ ID NO: 882 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 901 or SEQ ID NO: 902 or polypeptides that are at least 90% or 95% identical thereto.

**[000612]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 884; SEQ ID NO: 886; and SEQ ID NO: 888 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 881 or the variable heavy chain sequence of SEQ ID NO: 882 or sequences that are at least 90% or 95% identical thereto.

**[000613]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 904; SEQ ID NO: 906; and SEQ ID NO: 908 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 901 or the variable light chain sequence of SEQ ID NO: 902 or sequences that are at least 90% or 95% identical thereto.

**[000614]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 883; SEQ ID NO: 885; SEQ ID NO: 887; and SEQ ID NO: 889 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 881 or the variable heavy chain sequence of SEQ ID NO: 882 or sequences that are at least 90% or 95% identical thereto.

**[000615]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 903; SEQ ID NO: 905; SEQ ID NO: 907; and SEQ ID NO: 909 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 901 or the variable light chain sequence of SEQ ID NO: 902 or sequences that are at least 90% or 95% identical thereto.

**[000616]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 882; the variable light chain region of SEQ ID NO: 902; the complementarity-determining regions (SEQ ID NO: 884; SEQ ID NO: 886; and SEQ ID NO: 888) of the variable heavy chain region of SEQ ID NO: 882; and the complementarity-determining regions (SEQ ID NO: 904; SEQ ID NO: 906; and SEQ ID NO: 908) of the variable light chain region of SEQ ID NO: 902 or sequences that are at least 90% or 95% identical thereto.

**[000617]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 882; the variable light chain region of SEQ ID NO: 902; the framework regions (SEQ ID NO: 883; SEQ ID NO: 885; SEQ ID NO: 887; and SEQ ID NO: 889) of the variable heavy chain region of SEQ ID NO: 882; and the framework regions (SEQ ID NO: 903; SEQ ID NO: 905; SEQ ID NO: 907; and SEQ ID NO: 909) of the variable light chain region of SEQ ID NO: 902.

**[000618]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab24, comprising, or alternatively consisting of, SEQ ID NO: 881 and SEQ ID NO: 901, or an antibody or antibody fragment comprising the CDRs of Ab24 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab24 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab24 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab24.

**[000619]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab24, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 882 and the variable light chain sequence of SEQ ID NO: 902 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 882 and/or SEQ ID NO: 902 which retain the binding specificity for HGF.

**[000620]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab24. In another embodiment of the invention, anti-HGF antibodies such as Ab24 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000621]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab24 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab25

**[000622]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGTPLTLTCTASGFSLSSYAMGWFRQAPGKGLEWIAYIFASG
STYYASWAKGRFTISKTSTTVELKITSLTTEDTATYFCARGSGARFFPNYFAIWG
PGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK (SEQ ID NO: 921).

**[000623]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSLEESGGRLVTPGTPLTLTCTASGFSLSSYAMGWFRQAPGKGLEWIAYIFASG
STYYASWAKGRFTISKTSTTVELKITSLTTEDTATYFCARGSGARFFPNYFAIWG
PGTLVTVSS (SEQ ID NO: 922).

**[000624]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab25 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 930).

**[000625]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: QVLTQTASSVSAAVGGTVTISCQSSQSVTNNNDLAWYQQKPGQPPKLLIYQAS KLASGVPSRFKGSGSGTQFTLTISDLECDDAATYYCQGSYSGGICAFGGGTEVV VKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC (SEQ ID NO: 941).

**[000626]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: QVLTQTASSVSAAVGGTVTISCQSSQSVTNNNDLAWYQQKPGQPPKLLIYQAS KLASGVPSRFKGSGSGTQFTLTISDLECDDAATYYCQGSYSGGICAFGGGTEVV VKR (SEQ ID NO: 942).

**[000627]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab25 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 950).

**[000628]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 924; SEQ ID NO: 926; and SEQ ID NO: 928 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 921 or which contain the variable heavy chain sequence of SEQ ID NO: 922, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 944; SEQ ID NO: 946; and SEQ ID NO: 948 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 941 or which contain the variable light chain sequence of SEQ ID NO: 942, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000629]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 923; SEQ ID NO: 925; SEQ ID NO: 927; and SEQ ID NO: 929 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 921 or the variable heavy chain sequence of SEQ ID NO: 922, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 943; SEQ ID NO: 945; SEQ ID NO: 947; and SEQ ID NO: 949 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 941 or the variable light chain sequence of SEQ ID NO: 942, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000630]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000631]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 921 or SEQ ID NO: 922 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 941 or SEQ ID NO: 942 or polypeptides that are at least 90% or 95% identical thereto.

**[000632]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 924; SEQ ID NO: 926; and SEQ ID NO: 928 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 921 or the variable heavy chain sequence of SEQ ID NO: 922 or sequences that are at least 90% or 95% identical thereto.

**[000633]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 944; SEQ ID NO: 946; and SEQ ID NO: 948 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 941 or the variable light chain sequence of SEQ ID NO: 942 or sequences that are at least 90% or 95% identical thereto.

**[000634]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 923; SEQ ID NO: 925; SEQ ID NO: 927; and SEQ ID NO: 929 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 921 or the variable heavy chain sequence of SEQ ID NO: 922 or sequences that are at least 90% or 95% identical thereto.

**[000635]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 943; SEQ ID NO: 945; SEQ ID NO: 947; and SEQ ID NO: 949 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 941 or the variable light chain sequence of SEQ ID NO: 942 or sequences that are at least 90% or 95% identical thereto.

**[000636]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 922; the variable light chain region of SEQ ID NO: 942; the complementarity-determining regions (SEQ ID NO: 924; SEQ ID NO: 926; and SEQ ID NO: 928) of the variable heavy chain region of SEQ ID NO: 922; and the complementarity-determining regions (SEQ ID NO: 944; SEQ ID NO: 946; and SEQ ID NO: 948) of the variable light chain region of SEQ ID NO: 942 or sequences that are at least 90% or 95% identical thereto.

**[000637]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 922; the variable light chain region of SEQ ID NO: 942; the framework regions (SEQ ID NO: 923; SEQ ID NO: 925; SEQ ID NO: 927; and SEQ ID NO: 929) of the variable heavy chain region of SEQ ID NO: 922; and the framework regions (SEQ ID NO: 943; SEQ ID NO: 945; SEQ ID NO: 947; and SEQ ID NO: 949) of the variable light chain region of SEQ ID NO: 942.

**[000638]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab25, comprising, or alternatively consisting of, SEQ ID NO: 921 and SEQ ID NO: 941, or an antibody or antibody fragment comprising the CDRs of Ab25 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab25 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab25 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab25.

**[000639]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab25, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 922 and the variable light chain sequence of SEQ ID NO: 942 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 922 and/or SEQ ID NO: 942 which retain the binding specificity for HGF.

**[000640]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab25. In another embodiment of the invention, anti-HGF antibodies such as Ab25 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000641]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab25 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab26

**[000642]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGFSLSTYTMNWVRQAPGKGLEYIGFISSSSS
IDYVSWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARDFYADYIGGGYPYIWG
PGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK (SEQ ID NO: 961).

**[000643]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSVEESGGRLVTPGTPLTLTCTVSGFSLSTYTMNWVRQAPGKGLEYIGFISSSSS
IDYVSWAKGRFTISKTSTTVDLKITSPTTEDTATYFCARDFYADYIGGGYPYIWG
PGTLVTVSS (SEQ ID NO: 962).

**[000644]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab26 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 970).

**[000645]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: ADVVMTQTPASVSEPVGGTVTIKCQASQSISSYLSWYQQKPGQPPKLLIYGASK LTSGVPSRFKGSGSGTEYTLTISDLECADAATYYCQSNYDIYSYAFGGGTEVVV KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C (SEQ ID NO: 981).

**[000646]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: ADVVMTQTPASVSEPVGGTVTIKCQASQSISSYLSWYQQKPGQPPKLLIYGASK LTSGVPSRFKGSGSGTEYTLTISDLECADAATYYCQSNYDIYSYAFGGGTEVVV KR (SEQ ID NO: 982).

**[000647]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab26 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 990).

**[000648]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 964; SEQ ID NO: 966; and SEQ ID NO: 968 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 961 or which contain the variable heavy chain sequence of SEQ ID NO: 962, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 984; SEQ ID NO: 986; and SEQ ID NO: 988 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 981 or which contain the variable light chain sequence of SEQ ID NO: 982, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof comprise, or alternatively consist of,

combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000649]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 963; SEQ ID NO: 965; SEQ ID NO: 967; and SEQ ID NO: 969 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 961 or the variable heavy chain sequence of SEQ ID NO: 962, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 983; SEQ ID NO: 985; SEQ ID NO: 987; and SEQ ID NO: 989 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 981 or the variable light chain sequence of SEQ ID NO: 982, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000650]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000651]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 961 or SEQ ID NO: 962 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 981 or SEQ ID NO: 982 or polypeptides that are at least 90% or 95% identical thereto.

**[000652]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 964; SEQ ID NO: 966; and SEQ ID NO: 968 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 961 or the variable heavy chain sequence of SEQ ID NO: 962 or sequences that are at least 90% or 95% identical thereto.

**[000653]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or

three of the polypeptide sequences of SEQ ID NO: 984; SEQ ID NO: 986; and SEQ ID NO: 988 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 981 or the variable light chain sequence of SEQ ID NO: 982 or sequences that are at least 90% or 95% identical thereto.

**[000654]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 963; SEQ ID NO: 965; SEQ ID NO: 967; and SEQ ID NO: 969 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 961 or the variable heavy chain sequence of SEQ ID NO: 962 or sequences that are at least 90% or 95% identical thereto.

**[000655]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 983; SEQ ID NO: 985; SEQ ID NO: 987; and SEQ ID NO: 989 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 981 or the variable light chain sequence of SEQ ID NO: 982 or sequences that are at least 90% or 95% identical thereto.

**[000656]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 962; the variable light chain region of SEQ ID NO: 982; the complementarity-determining regions (SEQ ID NO: 964; SEQ ID NO: 966; and SEQ ID NO: 968) of the variable heavy chain region of SEQ ID NO: 962; and the complementarity-determining regions (SEQ ID NO: 984; SEQ ID NO: 986; and SEQ ID NO: 988) of the variable light chain region of SEQ ID NO: 982 or sequences that are at least 90% or 95% identical thereto.

**[000657]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody

fragments: the variable heavy chain region of SEQ ID NO: 962; the variable light chain region of SEQ ID NO: 982; the framework regions (SEQ ID NO: 963; SEQ ID NO: 965; SEQ ID NO: 967; and SEQ ID NO: 969) of the variable heavy chain region of SEQ ID NO: 962; and the framework regions (SEQ ID NO: 983; SEQ ID NO: 985; SEQ ID NO: 987; and SEQ ID NO: 989) of the variable light chain region of SEQ ID NO: 982.

**[000658]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab26, comprising, or alternatively consisting of, SEQ ID NO: 961 and SEQ ID NO: 981, or an antibody or antibody fragment comprising the CDRs of Ab26 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab26 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab26 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab26.

**[000659]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab26, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 962 and the variable light chain sequence of SEQ ID NO: 982 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 962 and/or SEQ ID NO: 982 which retain the binding specificity for HGF.

**[000660]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab26. In another embodiment of the invention, anti-HGF antibodies such as Ab26 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000661]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab26 as well as fragments, variants, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable

light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab27

**[000662]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
QSLEESGGDLVKPGGTLTLTCTASGFSFSDDHYMCWVRQAPGKGLQWIACMY
VGSSGATYYASWAKGRFTISKTSSTTVTLQMTSLTAADTATYFCARDDWTSYY
AWGYWALWGPGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE
PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKP
SNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC
VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 1001).

**[000663]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
QSLEESGGDLVKPGGTLTLTCTASGFSFSDDHYMCWVRQAPGKGLQWIACMY
VGSSGATYYASWAKGRFTISKTSSTTVTLQMTSLTAADTATYFCARDDWTSYY
AWGYWALWGPGTLVTVSS (SEQ ID NO: 1002).

**[000664]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab27 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 1010).

**[000665]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: ADIVMTQNPASVSEPVGGTVTIKCQASQSVNSWLSWYQQKPGQPPKFLIYKAS TLASGVSSRFKGSGIGTEFTLTISDLECADAATYYCQFSNSGTIYGSGFGGGTEV VVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC (SEQ ID NO: 1021).

**[000666]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: ADIVMTQNPASVSEPVGGTVTIKCQASQSVNSWLSWYQQKPGQPPKFLIYKAS TLASGVSSRFKGSGIGTEFTLTISDLECADAATYYCQFSNSGTIYGSGFGGGTEV VVKR (SEQ ID NO: 1022).

**[000667]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab27 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 1030).

**[000668]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 1004; SEQ ID NO: 1006; and SEQ ID NO: 1008 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1001 or which contain the variable heavy chain sequence of SEQ ID NO: 1002, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 1024; SEQ ID NO: 1026; and SEQ ID NO: 1028 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 1021 or which contain the variable light chain sequence of SEQ ID NO: 1022, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof

comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000669]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1003; SEQ ID NO: 1005; SEQ ID NO: 1007; and SEQ ID NO: 1009 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 1001 or the variable heavy chain sequence of SEQ ID NO: 1002, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1023; SEQ ID NO: 1025; SEQ ID NO: 1027; and SEQ ID NO: 1029 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 1021 or the variable light chain sequence of SEQ ID NO: 1022, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000670]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000671]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 1001 or SEQ ID NO: 1002 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 1021 or SEQ ID NO: 1022 or polypeptides that are at least 90% or 95% identical thereto.

**[000672]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 1004; SEQ ID NO: 1006; and SEQ ID NO: 1008 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1001 or the variable heavy chain sequence of SEQ ID NO: 1002 or sequences that are at least 90% or 95% identical thereto.

**[000673]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 1024; SEQ ID NO: 1026; and SEQ ID NO: 1028 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 1021 or the variable light chain sequence of SEQ ID NO: 1022 or sequences that are at least 90% or 95% identical thereto.

**[000674]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1003; SEQ ID NO: 1005; SEQ ID NO: 1007; and SEQ ID NO: 1009 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 1001 or the variable heavy chain sequence of SEQ ID NO: 1002 or sequences that are at least 90% or 95% identical thereto.

**[000675]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1023; SEQ ID NO: 1025; SEQ ID NO: 1027; and SEQ ID NO: 1029 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 1021 or the variable light chain sequence of SEQ ID NO: 1022 or sequences that are at least 90% or 95% identical thereto.

**[000676]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 1002; the variable light chain region of SEQ ID NO: 1022; the complementarity-determining regions (SEQ ID NO: 1004; SEQ ID NO: 1006; and SEQ ID NO: 1008) of the variable heavy chain region of SEQ ID NO: 1002; and the complementarity-determining regions (SEQ ID NO: 1024; SEQ ID NO: 1026; and SEQ ID NO: 1028) of the variable light chain region of SEQ ID NO: 1022 or sequences that are at least 90% or 95% identical thereto.

**[000677]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention,

fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 1002; the variable light chain region of SEQ ID NO: 1022; the framework regions (SEQ ID NO: 1003; SEQ ID NO: 1005; SEQ ID NO: 1007; and SEQ ID NO: 1009) of the variable heavy chain region of SEQ ID NO: 1002; and the framework regions (SEQ ID NO: 1023; SEQ ID NO: 1025; SEQ ID NO: 1027; and SEQ ID NO: 1029) of the variable light chain region of SEQ ID NO: 1022.

**[000678]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab27, comprising, or alternatively consisting of, SEQ ID NO: 1001 and SEQ ID NO: 1021, or an antibody or antibody fragment comprising the CDRs of Ab27 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab27 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab27 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab27.

**[000679]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab27, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 1002 and the variable light chain sequence of SEQ ID NO: 1022 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 1002 and/or SEQ ID NO: 1022 which retain the binding specificity for HGF.

**[000680]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab27. In another embodiment of the invention, anti-HGF antibodies such as Ab27 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000681]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab27 as well as fragments, variants,

combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

Antibody Ab28

**[000682]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess a heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNAISWVRQAPGKGLEWVGVIYV
IGVTDYASSAQGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSGWNH
FNLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DARVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 1041).

**[000683]** In one embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable heavy chain sequence comprising the sequence set forth below:
EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNAISWVRQAPGKGLEWVGVIYV
IGVTDYASSAQGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVYDSGWNH
FNLWGQGTLVTVSS (SEQ ID NO: 1042).

**[000684]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that possess the same epitopic specificity as Ab28 and which contain a constant heavy chain sequence comprising the sequence set forth below:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK (SEQ ID NO: 1050).

**[000685]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a light chain sequence comprising the sequence set forth below: DIQMTQSPSTLSASVGDRVTITCQASQSISSWLAWYQQKPGKAPKLLIYEASKL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVANVDNAFGGGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C (SEQ ID NO: 1061).

**[000686]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain a variable light chain sequence comprising the sequence set forth below: DIQMTQSPSTLSASVGDRVTITCQASQSISSWLAWYQQKPGKAPKLLIYEASKL ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQAYSVANVDNAFGGGTKVE IKR (SEQ ID NO: 1062).

**[000687]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that bind the same epitope as Ab28 which contain a constant light chain sequence comprising the sequence set forth below: TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 1070).

**[000688]** In another embodiment, the invention includes antibodies and antibody fragments having binding specificity to HGF that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 1044; SEQ ID NO: 1046; and SEQ ID NO: 1048 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1041 or which contain the variable heavy chain sequence of SEQ ID NO: 1042, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 1064; SEQ ID NO: 1066; and SEQ ID NO: 1068 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 1061 or which contain the variable light chain sequence of SEQ ID NO: 1062, or antibodies or fragments containing combinations of sequences which are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention or fragments thereof

comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

**[000689]** The invention further contemplates anti-HGF antibodies and antibody fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1043; SEQ ID NO: 1045; SEQ ID NO: 1047; and SEQ ID NO: 1049 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 1041 or the variable heavy chain sequence of SEQ ID NO: 1042, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1063; SEQ ID NO: 1065; SEQ ID NO: 1067; and SEQ ID NO: 1069 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 1061 or the variable light chain sequence of SEQ ID NO: 1062, or combinations of these polypeptide sequences or sequences which are at least 80%, 90% or 95% identical therewith.

**[000690]** In another embodiment of the invention, the antibodies and antibody fragments of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000691]** In another embodiment of the invention, the anti-HGF antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 1041 or SEQ ID NO: 1042 or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, antibody fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 1061 or SEQ ID NO: 1062 or polypeptides that are at least 90% or 95% identical thereto.

**[000692]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 1044; SEQ ID NO: 1046; and SEQ ID NO: 1048 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1041 or the variable heavy chain sequence of SEQ ID NO: 1042 or sequences that are at least 90% or 95% identical thereto.

**[000693]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, or three of the polypeptide sequences of SEQ ID NO: 1064; SEQ ID NO: 1066; and SEQ ID NO: 1068 which correspond to the complementarity-determining regions (CDRs, or hypervariable regions) of the light chain sequence of SEQ ID NO: 1061 or the variable light chain sequence of SEQ ID NO: 1062 or sequences that are at least 90% or 95% identical thereto.

**[000694]** In a further embodiment of the invention, the antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1043; SEQ ID NO: 1045; SEQ ID NO: 1047; and SEQ ID NO: 1049 which correspond to the framework regions (FRs or constant regions) of the heavy chain sequence of SEQ ID NO: 1041 or the variable heavy chain sequence of SEQ ID NO: 1042 or sequences that are at least 90% or 95% identical thereto.

**[000695]** In a further embodiment of the invention, the subject antibody or antibody fragment having binding specificity to HGF comprises, or alternatively consists of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 1063; SEQ ID NO: 1065; SEQ ID NO: 1067; and SEQ ID NO: 1069 which correspond to the framework regions (FRs or constant regions) of the light chain sequence of SEQ ID NO: 1061 or the variable light chain sequence of SEQ ID NO: 1062 or sequences that are at least 90% or 95% identical thereto.

**[000696]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 1042; the variable light chain region of SEQ ID NO: 1062; the complementarity-determining regions (SEQ ID NO: 1044; SEQ ID NO: 1046; and SEQ ID NO: 1048) of the variable heavy chain region of SEQ ID NO: 1042; and the complementarity-determining regions (SEQ ID NO: 1064; SEQ ID NO: 1066; and SEQ ID NO: 1068) of the variable light chain region of SEQ ID NO: 1062 or sequences that are at least 90% or 95% identical thereto.

**[000697]** The invention also contemplates antibody fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention,

fragments of the antibodies having binding specificity to HGF comprise, or alternatively consist of, one, two, three or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 1042; the variable light chain region of SEQ ID NO: 1062; the framework regions (SEQ ID NO: 1043; SEQ ID NO: 1045; SEQ ID NO: 1047; and SEQ ID NO: 1049) of the variable heavy chain region of SEQ ID NO: 1042; and the framework regions (SEQ ID NO: 1063; SEQ ID NO: 1065; SEQ ID NO: 1067; and SEQ ID NO: 1069) of the variable light chain region of SEQ ID NO: 1062.

**[000698]** In a particularly preferred embodiment of the invention, the anti-HGF antibody is Ab28, comprising, or alternatively consisting of, SEQ ID NO: 1041 and SEQ ID NO: 1061, or an antibody or antibody fragment comprising the CDRs of Ab28 and having at least one of the biological activities set forth herein or is an anti-HGF antibody that competes with Ab28 in binding HGF, preferably one containing sequences that are at least 90% or 95% identical to that of Ab28 or an antibody that binds to the same or overlapping epitope(s) on HGF as Ab28.

**[000699]** In a further particularly preferred embodiment of the invention, antibody fragments comprise, or alternatively consist of, Fab (fragment antigen binding) fragments having binding specificity for HGF. With respect to antibody Ab28, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 1042 and the variable light chain sequence of SEQ ID NO: 1062 or sequences that are at least 90% or 95% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 1042 and/or SEQ ID NO: 1062 which retain the binding specificity for HGF.

**[000700]** In one embodiment of the invention described herein (infra), Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab28. In another embodiment of the invention, anti-HGF antibodies such as Ab28 or Fab fragments thereof may be produced via expression in mammalian cells such as CHO, NSO or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example haploid or diploid yeast such as haploid or diploid Pichia) and other yeast strains. Suitable Pichia species include, but are not limited to, Pichia pastoris.

**[000701]** In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to HGF, including the heavy and/or light chains of Ab28 as well as fragments, variants,

combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them or sequences which are at least 90% or 95% identical thereto.

**[000702]**

**[000703]** In another embodiment, the invention contemplates an isolated anti-HGF antibody comprising any of the afore-identified $V_H$ polypeptide sequences; and further comprising any of the afore-identified $V_L$ polypeptide sequence, wherein one or more of the framework residues (FR residues) in said $V_H$ or $V_L$ polypeptide has been substituted with another amino acid residue resulting in an anti-HGF antibody that specifically binds HGF. The invention contemplates humanized and chimeric forms of these antibodies. The chimeric antibodies may include an Fc derived from IgG1, IgG2, IgG3, IgG4, IgG5, IgG6, IgG7, IgG8, IgG9, IgG10, IgG11, IgG12, IgG13, IgG14, IgG15, IgG16, IgG17, IgG18 or IgG19, IgG20, IgG21 and other antibody constant regions, which optionally may be mutagenized or fragmented.

**[000704]** In one embodiment of the invention, the antibodies or $V_H$ or $V_L$ polypeptides originate or are selected from one or more rabbit B cell populations prior to initiation of the humanization process referenced herein.

**[000705]** In another embodiment of the invention, the anti-HGF antibodies and fragments thereof which have binding specificity for human HGF and allelic variants of human HGF may also bind to non-human HGF polypeptides including primate homologs of human HGF such as HGF expressed in chimpanzee, monkey, ape, gibbon, gorilla, lemur and other primates, and potentially to non-primate HGF polypeptides such as rabbit, canine, rodent, feline, and other HGF species homologs.

**[000706]** In another embodiment of the invention, the anti-HGF antibodies and fragments thereof do not have binding specificity for HGFR (c-met). In a further embodiment of the invention, the anti-HGF antibodies and fragments thereof inhibit the association of HGF with HGFR. In another embodiment of the invention, the anti-HGF antibodies and fragments thereof inhibit the association of HGF with HGFR and/or multimers thereof and/or antagonizes the biological effects thereof.

**[000707]** In adition, the subject anti-HGF antibodies and fragments thereof may be modified post-translationally to add effector moieties such as chemical linkers, detectable moieties such as for example fluorescent dyes, enzymes, substrates, bioluminescent materials, radioactive materials, and chemiluminescent moieties, or

functional moieties such as for example streptavidin, avidin, biotin, a cytotoxin, a cytotoxic agent, and radioactive materials.

**[000708]** Regarding detectable moieties, further exemplary enzymes include, but are not limited to, horseradish peroxidase, acetylcholinesterase, alkaline phosphatase, beta-galactosidase and luciferase. Further exemplary fluorescent materials include, but are not limited to, rhodamine, fluorescein, fluorescein isothiocyanate, umbelliferone, dichlorotriazinylamine, phycoerythrin and dansyl chloride. Further exemplary chemiluminescent moieties include, but are not limited to, luminol. Further exemplary bioluminescent materials include, but are not limited to, luciferin and aequorin. Further exemplary radioactive materials include, but are not limited to, Iodine 125 ($^{125}I$), Carbon 14 ($^{14}C$), Sulfur 35 ($^{35}S$), Tritium ($^{3}H$) and Phosphorus 32 ($^{32}P$).

**[000709]** In another embodiment the subject anti-HGF antibodies and fragments may be attached or administered in combination therapies with one or more other functional moieties, exemplary cytotoxic agents include, but are not limited to, methotrexate, aminopterin, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine; alkylating agents such as mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU), mitomycin C, lomustine (CCNU), 1-methylnitrosourea, cyclothosphamide, mechlorethamine, busulfan, dibromomannitol, streptozotocin, mitomycin C, cis-dichlorodiamine platinum (II) (DDP) cisplatin and carboplatin (paraplatin); anthracyclines include daunorubicin (formerly daunomycin), doxorubicin (adriamycin), detorubicin, carminomycin, idarubicin, epirubicin, mitoxantrone and bisantrene; antibiotics include dactinomycin (actinomycin D), bleomycin, calicheamicin, mithramycin, and anthramycin (AMC); and antimytotic agents such as the vinca alkaloids, vincristine and vinblastine. Other cytotoxic agents include paclitaxel (taxol), ricin, pseudomonas exotoxin, gemcitabine, cytochalasin B, gramicidin D, ethidium bromide, emetine, etoposide, tenoposide, colchicin, dihydroxy anthracin dione, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, puromycin, procarbazine, hydroxyurea, asparaginase, corticosteroids, mytotane (O,P'-(DDD)), interferons, and mixtures of these cytotoxic agents.

**[000710]** Further cytotoxic agents include, but are not limited to, chemotherapeutic agents such as carboplatin, cisplatin, paclitaxel, gemcitabine, calicheamicin, doxorubicin, 5-fluorouracil, mitomycin C, actinomycin D, cyclophosphamide, vincristine and bleomycin. Toxic proteins from plants and bacteria such as ricin,

diphtheria toxin and Pseudomonas toxin may be conjugated to the humanized or chimeric antibodies, or binding fragments thereof, to generate cell-type-specific-killing reagents (Youle, et al., Proc. Nat'l Acad. Sci. USA 77:5483 (1980); Gilliland, et al., Proc. Nat'l Acad. Sci. USA 77:4539 (1980); Krolick, et al., Proc. Nat'l Acad. Sci. USA 77:5419 (1980)).

**[000711]** Other cytotoxic agents which may be used in combination with the subject anti-HGF antibodies and fragments include cytotoxic ribonucleases as described by Goldenberg in U.S. Pat. No. 6,653,104. Embodiments of the invention also relate to radioimmunoconjugates where a radionuclide that emits alpha or beta particles is stably coupled to the antibody, or binding fragments thereof, with or without the use of a complex-forming agent. Such radionuclides include beta-emitters such as Phosphorus-32 ($^{32}$P), Scandium-47 ($^{47}$Sc), Copper-67 ($^{67}$Cu), Gallium-67 ($^{67}$Ga), Yttrium-88 ($^{88}$Y), Yttrium-90 ($^{90}$Y), Iodine-125 ($^{125}$I), Iodine-131 ($^{131}$I), Samarium-153 ($^{153}$Sm), Lutetium-177 ($^{177}$Lu), Rhenium-186 ($^{186}$Re) or Rhenium-188 ($^{188}$Re), and alpha-emitters such as Astatine-211 ($^{211}$At), Lead-212 ($^{212}$Pb), Bismuth-212 ($^{212}$Bi) or Bismuth-213 ($^{21}$3Bi) or Actinium-225 ($^{225}$Ac). The term "cytotoxic agent" as used herein broadly includes any substance that inhibits or prevents the function of cells and/or causes destruction of cells and "chemotherapeutic agent" useful in the treatment of cancer The term is intended to include radioactive isotopes, chemotherapeutic agents e.g. methotrexate, adriamicin, vinca alkaloids (vincristine, vinblastine, etoposide), doxorubicin, melphalan, mitomycin C, chlorambucil, daunorubicin or other intercalating agents, enzymes and fragments thereof such as nucleolytic enzymes, antibiotics, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, including fragments and/or variants thereof, and the various antitumor or anticancer agents disclosed below. Other cytotoxic agents are described below. A tumoricidal agent causes destruction of tumor cells.

**[000712]** A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of chemotherapeutic agents include alkylating agents such as thiotepa and CYTOXAN ®. cyclosphosphamide; alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, trietylenephosphoramide, triethiylenethiophosphoramide and trimethylolomelamine; acetogenins (especially bullatacin and bullatacinone); a

camptothecin (including the synthetic analogue topotecan); bryostatin; callystatin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogues); cryptophycins (particularly cryptophycin 1 and cryptophycin 8); dolastatin; duocarmycin (including the synthetic analogues, KW-2189 and CB1-TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimustine; antibiotics such as the enediyne antibiotics (e.g., calicheamicin, especially calicheamicin gamma1I and calicheamicin omegaI1 (see, e.g., Agnew, Chem Intl. Ed. Engl., 33: 183-186 (1994)); dynemicin, including dynemicin A; bisphosphonates, such as clodronate; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromophores), aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, ADRIAMYCIN® doxorubicin (including morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidanmol; nitraerine; pentostatin; phenamet; pirarubicin;

losoxantrone; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK® polysaccharide complex (JHS Natural Products, Eugene, Oreg.); razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2"-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g., TAXOL® paclitaxel (Bristol-Myers Squibb Oncology, Princeton, N.J.), ABRAXANE.TM. Cremophor-free, albumin-engineered nanoparticle formulation of paclitaxel (American Pharmaceutical Partners, Schaumberg, Ill.), and TAXOTERE® doxetaxel (Rhone-Poulenc Rorer, Antony, France); chloranbucil; GEMZAR® gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitoxantrone; vincristine; NAVELBINE® vinorelbine; novantrone; teniposide; edatrexate; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoids such as retinoic acid; capecitabine; and pharmaceutically acceptable salts, acids or derivatives of any of the above. Also included in the definition of "chemotherapeutic agent" above are anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens and selective estrogen receptor modulators (SERMs), including, for example, tamoxifen (including NOLVADEX® tamoxifen), raloxifene, droloxifene, 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and FARESTON. toremifene; aromatase inhibitors that inhibit the enzyme aromatase, which regulates estrogen production in the adrenal glands, such as, for example, 4(5)-imidazoles, aminoglutethimide, MEGASE® megestrol acetate, AROMASIN® exemestane, formestanie, fadrozole, RIVISOR® vorozole, FEMARA® letrozole, and ARIMIDEX® anastrozole; and anti-androgens such as flutamide, nilutamide, bicalutamide, leuprolide, and goserelin; as well as troxacitabine (a 1,3-dioxolane nucleoside cytosine analog); antisense oligonucleotides, particularly those which inhibit expression of genes in signaling pathways implicated in abherant cell proliferation, such as, for example, PKC-alpha, Ralf and H-Ras; ribozymes such as a VEGF expression inhibitor (e.g., ANGIOZYME® ribozyme) and a HER2 expression inhibitor; vaccines such as gene therapy vaccines, for example, ALLOVECTIN® vaccine, LEUVECTIN® vaccine, and VAXID® vaccine; PROLEUKIN® rIL-2; LURTOTECAN® topoisomerase 1 inhibitor;

ABARELIX® rmRH; and pharmaceutically acceptable salts, acids or derivatives of any of the above. Preferred examples of cytotoxic agents used in association with the subject anti- HGF antibodies and fragments are Erlotinib, Gemcitabine, Premetrexed, Docetaxel, Folfox Chemotherapy Regime Combinations, Paclitaxel and Bevacizumab.

**[000713]** Other cytotoxic agents include cytotoxic ribonucleases as described by Goldenberg in U.S. Pat. No. 6,653,104. Embodiments of the invention also relate to radioimmunoconjugates where a radionuclide that emits alpha or beta particles is stably coupled to the antibody, or binding fragments thereof, with or without the use of a complex-forming agent. Such radionuclides include beta-emitters such as Phosphorus-32 ($^{32}$P), Scandium-47 ($^{47S}$c), Copper-67 ($^{67}$Cu), Gallium-67 ($^{67}$Ga), Yttrium-88 ($^{88}$Y), Yttrium-90 ($^{90}$Y), Iodine-125 ($^{125}$I), Iodine-131 ($^{131}$I), Samarium-153 ($^{153}$Sm), Lutetium-177 ($^{177}$Lu), Rhenium-186 ($^{186}$Re) or Rhenium-188 ($^{188}$Re), and alpha-emitters such as Astatine-211 ($^{211}$At), Lead-212 ($^{212}$Pb), Bismuth-212 ($^{212}$Bi) or -213 ($^{213}$Bi) or Actinium-225 ($^{225}$Ac).

**[000714]** Methods are known in the art for conjugating an antibody or binding fragment thereof to a detectable moiety and the like, such as for example those methods described by Hunter et al, Nature 144:945 (1962); David et al, Biochemistry 13:1014 (1974); Pain et al, J. Immunol. Meth. 40:219 (1981); and Nygren, J., Histochem. and Cytochem. 30:407 (1982).

**[000715]** Embodiments described herein further include variants and equivalents that are substantially homologous to the antibodies, antibody fragments, diabodies, SMIPs, camelbodies, nanobodies, IgNAR, polypeptides, variable regions and CDRs set forth herein. These may contain, e.g., conservative substitution mutations, (i.e., the substitution of one or more amino acids by similar amino acids). For example, conservative substitution refers to the substitution of an amino acid with another within the same general class, e.g., one acidic amino acid with another acidic amino acid, one basic amino acid with another basic amino acid, or one neutral amino acid by another neutral amino acid. What is intended by a conservative amino acid substitution is well known in the art.

**[000716]** In another embodiment, the invention contemplates polypeptide sequences having at least 90% or greater sequence homology to any one or more of the polypeptide sequences of antibody fragments, variable regions and CDRs set forth herein. More preferably, the invention contemplates polypeptide sequences having at

least 95% or greater sequence homology, even more preferably at least 98% or greater sequence homology, and still more preferably at least 99% or greater sequence homology to any one or more of the polypeptide sequences of antibody fragments, variable regions and CDRs set forth herein. Methods for determining homology between nucleic acid and amino acid sequences are well known to those of ordinary skill in the art.

**[000717]** In another embodiment, the invention further contemplates the above-recited polypeptide homologs of the antibody fragments, variable regions and CDRs set forth herein further having anti-HGF activity. Non-limiting examples of anti-HGF activity are set forth herein.

**[000718]** In another embodiment, the invention further contemplates the generation and use of anti-idiotypic antibodies that bind any of the foregoing sequences. In an exemplary embodiment, such an anti-idiotypic antibody could be administered to a subject who has received an anti-HGF antibody to modulate, reduce, or neutralize, the effect of the anti-HGF antibody. Such anti-idiotypic antibodies could also be useful for treatment of an autoimmune disease characterized by the presence of anti-HGF antibodies. A further exemplary use of such anti-idiotypic antibodies is for detection of the anti-HGF antibodies of the present invention, for example to monitor the levels of the anti-HGF antibodies present in a subject's blood or other bodily fluids.

**[000719]** The present invention also contemplates anti-HGF antibodies comprising any of the polypeptide or polynucleotide sequences described herein substituted for any of the other polynucleotide sequences described herein. For example, without limitation thereto, the present invention contemplates antibodies comprising the combination of any of the variable light chain and variable heavy chain sequences described herein, and further contemplates antibodies resulting from substitution of any of the CDR sequences described herein for any of the other CDR sequences described herein.

***Additional Exemplary Embodiments of the Invention***

**[000720]** In another embodiment, the invention contemplates one or more anti-human HGF antibodies or antibody fragments which specifically bind to the same linear or conformational epitope(s) and/or competes for binding to the same linear or conformational epitope(s) on an intact human HGF polypeptide or fragment thereof as an anti-human HGF antibody selected from the group consisting of Ab1, Ab2, Ab3,

Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13 Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28. In a preferred embodiment, the anti-human HGF antibody or fragment specifically binds to the same linear or conformational epitope(s) and/or competes for binding to the same linear or conformational epitope(s) on an intact human HGF polypeptide or a fragment thereof as Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, and Ab28.

**[000721]** In another embodiment of the invention, the anti-human HGF antibody which specifically binds to the same linear or conformational epitopes on an intact HGF polypeptide or fragment thereof that is (are) specifically bound by one of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13 Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28 binds to HGF epitope(s) ascertained by epitopic mapping using overlapping linear peptide fragments which span the full length of the native human HGF polypeptide.

**[000722]** The invention is also directed to an anti-HGF antibody that binds with the same HGF epitope and/or competes with an anti-HGF antibody for binding to HGF as an antibody or antibody fragment disclosed herein, including but not limited to an anti-HGF antibody selected from of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13 Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28 or preferably one of Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, or Ab28. In another embodiment, the invention is also directed to an isolated anti-HGF antibody or antibody fragment comprising one or more of the CDRs contained in the VH polypeptide of an anti-HGF antibody selected from of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13 Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28 or preferably one of as Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, and Ab28.

**[000723]** In one embodiment of the invention, the anti-human HGF antibody comprises at least 2 complementarity determining regions (CDRs) in each the variable light and the variable heavy regions which are identical to those contained in an anti-human HGF antibody selected from the group consisting of an anti-HGF antibody selected from of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13 Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26,

Ab27 and Ab28 or preferably one of Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, and Ab28.

**[000724]** In a preferred embodiment, the anti-human HGF antibody discussed above comprises at least 2 complementarity determining regions (CDRs) in each the variable light and the variable heavy regions which are identical to those contained in an anti-HGF antibody selected from of Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, and Ab28. In another embodiment, all of the CDRs of the anti-human HGF antibody discussed above are identical to the CDRs contained in an anti-human HGF antibody selected from the group consisting of an anti-HGF antibody selected from of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13 Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28 or preferably one of as Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, and Ab28. In a preferred embodiment of the invention, all of the CDRs of the anti-human HGF antibody discussed above are identical to the CDRs contained in of Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, or Ab28 or preferably one of Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25, and Ab28.

**[000725]** The invention further contemplates that the one or more anti-human HGF antibodies discussed above are aglycosylated; that contain an Fc region that has been modified to alter effector function, half-life, proteolysis, and/or glycosylation; are human, humanized, single chain or chimeric; and are a humanized antibody derived from a rabbit (parent) anti-human HGF antibody.

**[000726]** The invention further contemplates one or more anti-human HGF antibodies wherein the framework regions (FRs) in the variable light region and the variable heavy regions of said antibody respectively are human FRs which are unmodified or which have been modified by the substitution of at most 2 or 3 human FR residues in the variable light or heavy chain region with the corresponding FR residues of the parent rabbit antibody, and wherein said human FRs have been derived from human variable heavy and light chain antibody sequences which have been selected from a library of human germline antibody sequences based on their high level of homology to the corresponding rabbit variable heavy or light chain regions relative to other human germline antibody sequences contained in the library.

**[000727]** In one embodiment of the invention, the anti-human HGF antibody or fragment specifically binds to HGF expressing human cells and/or to circulating soluble HGF molecules in vivo, including HGF expressed on or by human cells in a patient with a disease associated with cells that express HGF.

**[000728]** In another embodiment, the disease is selected from cancers, including ovarian cancer, breast cancer, lung cancer (small cell or non-small cell), colon cancer, prostate cancer, pancreatic cancer, renal cancer, gastric cancer, liver cancer, head-and-neck tumors, melanoma, sarcomas, and brain tumors (e.g., glioblastomas), of children or adults; leukemias; lymphomas; macular degeneration; Alzheimer's disease; and malarial infection. In a preferred embodiment, the disease is selected from a cancer or macular degeneration. In a particularly preferred embodiment, the disease is a cancer such as ovarian cancer, breast cancer, lung cancer (small cell or non-small cell), colon cancer, prostate cancer, pancreatic cancer, renal cancer, gastric cancer, liver cancer, head-and-neck tumors, melanoma, sarcomas, and brain tumors (e.g., glioblastomas), of children or adults; leukemias; lymphomas or another cancer.

**[000729]** The invention further contemplates anti-human HGF antibodies or fragments directly or indirectly attached to a detectable label or therapeutic agent.

**[000730]** The invention also contemplates one or more nucleic acid sequences which result in the expression of an anti-human HGF antibody or antibody fragment as set forth above, including those comprising, or alternatively consisting of, yeast or human preferred codons. The invention also contemplates vectors (including plasmids or recombinant viral vectors) comprising said nucleic acid sequence(s). The invention also contemplates host cells or recombinant host cells expressing at least one of the antibodies set forth above, including a mammalian, yeast, bacterial, and insect cells. In a preferred embodiment, the host cell is a yeast cell. In a further preferred embodiment, the yeast cell is a diploidal yeast cell. In a more preferred embodiment, the yeast cell is a Pichia yeast.

**[000731]** The invention also contemplates a method of treatment comprising administering to a patient with a disease or condition associated with HGF expressing cells a therapeutically effective amount of at least one anti-human HGF antibody or fragment described herein. The invention also contemplates that the treatment method may involve the administration of two or more anti-HGF antibodies or fragments thereof and disclosed herein. If more than one antibody is administered to the patient,

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# JUMBO APPLICATIONS/PATENTS

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# CLAIMS

*What is claimed is*:

**1**. An anti-human hepatocyte growth factor (HGF) antibody or antibody fragment which:

(1) specifically binds to the same or overlapping epitope(s) and/or competes for binding to the same or overlapping epitope(s) on an intact human HGF polypeptide or fragment thereof as an anti-human HGF antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(2) specifically binds to the same linear or conformational epitope(s) and/or competes for binding to the same or overlapping epitope(s) on an intact human HGF polypeptide or a fragment thereof as an anti-human HGF antibody selected from Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab13 Ab14, Ab19, Ab21, Ab23, Ab24, Ab25 and Ab28;

(3) specifically binds to the same epitope(s) on an intact human HGF polypeptide or fragment thereof as an anti-human HGF antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28; and/or

(4) specifically binds to the same epitope(s) on an intact human HGF polypeptide or a fragment thereof as an anti-human HGF antibody selected from Ab1, Ab2, Ab7, Ab8, Ab9, Ab10, Ab12, Ab13, Ab14, Ab19, Ab21, Ab23, Ab24, Ab25 and Ab28, wherein said epitope(s) are optionally identified using a binding assay that detects the binding of said anti-human HGF antibody to one or more peptides in a library of 10-15-mer peptides which are overlapping peptide fragments of human HGF that correspond to all or substantially all of the length of the human HGF polypeptide, wherein binding assay further

optionally is a Western immunoblot assay which detects specific binding of the antibody or antibody fragment to one or more of said 10-15 mer peptides in said library by the use of a chemiluminescent label which emits a detectable chemiluminescent signal when specific binding of said antibody or antibody fragment to a peptide in said library occurs.

**2.** An anti-human HGF antibody or antibody fragment according to Claim 1, wherein:

(1) said anti-human HGF antibody or antibody fragment contains at least 2 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(2) said anti-human HGF antibody or antibody fragment contains at least 3 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(3) said anti-human HGF antibody or antibody fragment contains at least 4 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(4) said anti-human HGF antibody or antibody fragment contains at least 5 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28; or

(5) said anti-human HGF antibody or antibody fragment contains all 6 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11,

Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

3. An anti-human HGF antibody or antibody fragment according to Claim 1 or 2, wherein:

(1) said anti-human HGF antibody contains at least one residue other than a CDR residue which has been modified, which modification does not affect HGF binding;

(2) said anti-human HGF antibody is chimeric and contains human constant domains;

(3) said anti-HGF antibody is a human or humanized antibody or fragment thereof;

(4) said anti-human HGF antibody or antibody fragment contains:

(a) a variable heavy chain comprising a CDR1 sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 44, SEQ ID NO: 84, SEQ ID NO: 124, SEQ ID NO: 164, SEQ ID NO: 204, SEQ ID NO: 244, SEQ ID NO: 284, SEQ ID NO: 324, SEQ ID NO: 364, SEQ ID NO: 404, SEQ ID NO: 444, SEQ ID NO: 484, SEQ ID NO: 524, SEQ ID NO: 564, SEQ ID NO: 604, SEQ ID NO: 644, SEQ ID NO: 684, SEQ ID NO: 724, SEQ ID NO: 764, SEQ ID NO: 804, SEQ ID NO: 844, SEQ ID NO: 884, SEQ ID NO: 924, SEQ ID NO: 964, SEQ ID NO:1004, and SEQ ID NO:1044; a CDR2 sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 46, SEQ ID NO: 86, SEQ ID NO: 126, SEQ ID NO: 166, SEQ ID NO: 206, SEQ ID NO: 246, SEQ ID NO: 286, SEQ ID NO: 326, SEQ ID NO: 366, SEQ ID NO: 406, SEQ ID NO: 446, SEQ ID NO: 486, SEQ ID NO: 526, SEQ ID NO: 566, SEQ ID NO: 606, SEQ ID NO: 646, SEQ ID NO: 686, SEQ ID NO: 726, SEQ ID NO: 766, SEQ ID NO: 806, SEQ ID NO: 846, SEQ ID NO: 886, SEQ ID NO: 926, SEQ ID NO:966, SEQ ID NO:1006, and SEQ ID NO:1046; and a CDR3 sequence selected from the group consisting of SEQ ID NO: 8, SEQ ID NO: 48, SEQ ID NO: 88, SEQ ID NO: 128, SEQ ID NO: 168, SEQ ID NO: 208, SEQ ID NO:

248, SEQ ID NO: 288, SEQ ID NO: 328, SEQ ID NO: 368, SEQ ID NO: 408, SEQ ID NO: 448, SEQ ID NO: 488, SEQ ID NO: 528, SEQ ID NO: 568, SEQ ID NO: 608, SEQ ID NO: 648, SEQ ID NO: 688, SEQ ID NO: 728, SEQ ID NO: 768, SEQ ID NO: 808, SEQ ID NO: 848, SEQ ID NO: 888, and SEQ ID NO: 928, SEQ ID NO:968, SEQ ID NO:1008, and SEQ ID NO:1048; and/or

(b) a variable light chain comprising a CDR1 sequence selected from the group consisting of SEQ ID NO: 24, SEQ ID NO: 64, SEQ ID NO: 104, SEQ ID NO: 144, SEQ ID NO: 184, SEQ ID NO: 224, SEQ ID NO: 264, SEQ ID NO: 304, SEQ ID NO: 344, SEQ ID NO: 384, SEQ ID NO: 424, SEQ ID NO: 464, SEQ ID NO: 504, SEQ ID NO: 544, SEQ ID NO: 584, SEQ ID NO: 624, SEQ ID NO: 664, SEQ ID NO: 704, SEQ ID NO: 744, SEQ ID NO: 784, SEQ ID NO: 824, SEQ ID NO: 864, SEQ ID NO: 904, SEQ ID NO: 944, SEQ ID NO:984, SEQ ID NO:1024, and SEQ ID NO:1064; a CDR2 sequence selected from the group consisting of SEQ ID NO: 26, SEQ ID NO: 66, SEQ ID NO: 106, SEQ ID NO: 146, SEQ ID NO: 186, SEQ ID NO: 226, SEQ ID NO: 266, SEQ ID NO: 306, SEQ ID NO: 346, SEQ ID NO: 386, SEQ ID NO: 426, SEQ ID NO: 466, SEQ ID NO: 506, SEQ ID NO: 546, SEQ ID NO: 586, SEQ ID NO: 626, SEQ ID NO: 666, SEQ ID NO: 706, SEQ ID NO: 746, SEQ ID NO: 786, SEQ ID NO: 826, SEQ ID NO: 866, SEQ ID NO: 906, SEQ ID NO: 946, SEQ ID NO:986, SEQ ID NO:1026, and SEQ ID NO:1066 ; and a CDR3 sequence selected from the group consisting of SEQ ID NO: 28, SEQ ID NO: 68, SEQ ID NO: 108, SEQ ID NO: 148, SEQ ID NO: 188, SEQ ID NO: 228, SEQ ID NO: 268, SEQ ID NO: 308, SEQ ID NO: 348, SEQ ID NO: 388, SEQ ID NO: 428, SEQ ID NO: 468, SEQ ID NO: 508, SEQ ID NO: 548, SEQ ID NO: 588, SEQ ID NO: 628, SEQ ID NO: 668, SEQ ID NO: 708, SEQ ID NO: 748, SEQ ID NO: 788, SEQ ID NO: 828, SEQ ID NO: 868, SEQ ID NO: 908, SEQ ID NO: 948, SEQ ID NO:988, SEQ ID NO:1028, and SEQ ID NO:1068; with the further proviso that one or two residues of any of the afore-identified CDR polypeptides may be substituted with another amino acid, preferably a conservative amino acid substitution;

(5) the variable heavy chain of said antibody or antibody fragment comprises the CDR1 sequence of SEQ ID NO: 4, the CDR2 sequence of SEQ ID NO: 6, and the

CDR3 sequence of SEQ ID NO: 8; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 24, the CDR2 sequence of SEQ ID NO: 26, and the CDR3 sequence of SEQ ID NO: 28;

(6) said anti-human HGF antibody or antibody fragment contains a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 44, the CDR2 sequence of SEQ ID NO: 46, and the CDR3 sequence of SEQ ID NO: 48; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 64, the CDR2 sequence of SEQ ID NO: 66, and the CDR3 sequence of SEQ ID NO: 68;

(7) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 84, the CDR2 sequence of SEQ ID NO: 86, and the CDR3 sequence of SEQ ID NO: 88; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 104, the CDR2 sequence of SEQ ID NO: 106, and the CDR3 sequence of SEQ ID NO: 108;

(8) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 124, the CDR2 sequence of SEQ ID NO: 126, and the CDR3 sequence of SEQ ID NO: 128; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 144, the CDR2 sequence of SEQ ID NO: 146, and the CDR3 sequence of SEQ ID NO: 148;

(9) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 164, the CDR2 sequence of SEQ ID NO: 166, and the CDR3 sequence of SEQ ID NO: 168; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 184, the CDR2 sequence of SEQ ID NO: 186, and the CDR3 sequence of SEQ ID NO: 188;

(10) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 204, the CDR2 sequence of SEQ ID NO: 206, and the CDR3 sequence of SEQ ID NO: 208; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 224, the CDR2 sequence of SEQ ID NO: 226, and the CDR3 sequence of SEQ ID NO: 228;

(11) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 244, the CDR2 sequence of SEQ ID NO: 246, and the CDR3 sequence of SEQ ID NO: 248; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 264, the CDR2 sequence of SEQ ID NO: 266, and the CDR3 sequence of SEQ ID NO: 268;

(12) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 284, the CDR2 sequence of SEQ ID NO: 286, and the CDR3 sequence of SEQ ID NO: 288; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 304, the CDR2 sequence of SEQ ID NO: 306, and the CDR3 sequence of SEQ ID NO: 308;

(13) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 324, the CDR2 sequence of SEQ ID NO: 326, and the CDR3 sequence of SEQ ID NO: 328; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 344, the CDR2 sequence of SEQ ID NO: 346, and the CDR3 sequence of SEQ ID NO: 348;

(14) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 364, the CDR2 sequence of SEQ ID NO: 366, and the CDR3 sequence of SEQ ID NO: 368; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 384, the CDR2 sequence of SEQ ID NO: 386, and the CDR3 sequence of SEQ ID NO: 388;

(15) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 404, the CDR2 sequence of SEQ ID NO: 406, and the CDR3 sequence of SEQ ID NO: 408; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 424, the CDR2 sequence of SEQ ID NO: 426, and the CDR3 sequence of SEQ ID NO: 428;

(16) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 444, the CDR2 sequence of SEQ ID NO: 446, and the CDR3 sequence of SEQ ID NO: 448; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 464, the CDR2 sequence of SEQ ID NO: 466, and the CDR3 sequence of SEQ ID NO: 468;

(17) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 484, the CDR2 sequence of SEQ ID NO: 486, and the CDR3 sequence of SEQ ID NO: 488; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 504, the CDR2 sequence of SEQ ID NO: 506, and the CDR3 sequence of SEQ ID NO: 508;

(18) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 524, the CDR2 sequence of SEQ ID NO: 526, and the CDR3 sequence of SEQ ID NO: 528; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 544, the CDR2 sequence of SEQ ID NO: 546, and the CDR3 sequence of SEQ ID NO: 548;

(19) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 564, the CDR2 sequence of SEQ ID NO: 566, and the CDR3 sequence of SEQ ID NO: 568; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 584, the CDR2 sequence of SEQ ID NO: 586, and the CDR3 sequence of SEQ ID NO: 588;

(20) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 604, the CDR2 sequence of SEQ ID NO: 606, and the CDR3 sequence of SEQ ID NO: 608; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 624, the CDR2 sequence of SEQ ID NO: 626, and the CDR3 sequence of SEQ ID NO: 628;

(21) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 644, the CDR2 sequence of SEQ ID NO: 646, and the CDR3 sequence of SEQ ID NO: 648; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 664, the CDR2 sequence of SEQ ID NO: 666, and the CDR3 sequence of SEQ ID NO: 668;

(22) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 684, the CDR2 sequence of SEQ ID NO: 686, and the CDR3 sequence of SEQ ID NO: 688; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 704, the CDR2 sequence of SEQ ID NO: 706, and the CDR3 sequence of SEQ ID NO: 708;

(23) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 724, the CDR2 sequence of SEQ ID NO: 726, and the CDR3 sequence of SEQ ID NO: 728; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 744, the CDR2 sequence of SEQ ID NO: 746, and the CDR3 sequence of SEQ ID NO: 748;

(24) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the anti-human HGF antibody or antibody fragment of any one of Claims 1-10, wherein the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 764, the CDR2 sequence of SEQ ID NO: 766, and the CDR3 sequence of SEQ ID NO: 768; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 784, the CDR2 sequence of SEQ ID NO: 786, and the CDR3 sequence of SEQ ID NO: 788;

(25) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 804, the CDR2 sequence of SEQ ID NO: 806, and the CDR3 sequence of SEQ ID NO: 808; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 824, the CDR2 sequence of SEQ ID NO: 826, and the CDR3 sequence of SEQ ID NO: 828;

(26) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the variable heavy chain comprises the CDR1 sequence of SEQ ID NO: 844, the CDR2 sequence of SEQ ID NO: 846, and the CDR3 sequence of SEQ ID NO: 848; and/or the variable light chain comprises the CDR1 sequence of SEQ ID

NO: 864, the CDR2 sequence of SEQ ID NO: 866, and the CDR3 sequence of SEQ ID NO: 868;

(27) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 884, the CDR2 sequence of SEQ ID NO: 886, and the CDR3 sequence of SEQ ID NO: 888; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 904, the CDR2 sequence of SEQ ID NO: 906, and the CDR3 sequence of SEQ ID NO: 908;

(28) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 924, the CDR2 sequence of SEQ ID NO: 926, and the CDR3 sequence of SEQ ID NO: 928; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 944, the CDR2 sequence of SEQ ID NO: 946, and the CDR3 sequence of SEQ ID NO: 948;

(29) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 964, the CDR2 sequence of SEQ ID NO: 966, and the CDR3 sequence of SEQ ID NO: 968; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 984, the CDR2 sequence of SEQ ID NO: 986, and the CDR3 sequence of SEQ ID NO: 988;

(30) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 1004, the CDR2 sequence of SEQ ID NO: 1006, and the CDR3 sequence of SEQ ID NO: 1008; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 1024, the CDR2 sequence of SEQ ID NO: 1026, and the CDR3 sequence of SEQ ID NO: 1028;

(31) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprising the CDR1 sequence of SEQ ID NO: 1044, the CDR2 sequence of SEQ ID NO: 1046, and the CDR3 sequence of SEQ ID NO: 1048; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 1064, the CDR2 sequence of SEQ ID NO: 1066, and the CDR3 sequence of SEQ ID NO: 1068;

(32) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain that comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 2 and/or the variable light chain comprises SEQ ID NO: 22;

(33) said anti-human HGF antibody or antibody fragment comprises a variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 2 and SEQ ID NO: 22, respectively;

(34) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 42 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 62;

(35) said anti-human HGF antibody or antibody fragment comprises a variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 42 and SEQ ID NO: 62, respectively;

(36) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprises a sequence which is at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 82 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 102;

(37) said anti-human HGF antibody or antibody fragment comprises a variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 82 and SEQ ID NO: 102, respectively;

(38) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain that comprises a sequence which is at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 122 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 142;

(39) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 122 and SEQ ID NO: 142, respectively;

(40) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence that is at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 162 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 182;

(41) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 162 and SEQ ID NO: 182, respectively;

(42) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 202 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 222;

(43) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 202 and SEQ ID NO: 222, respectively;

(44) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain that comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 242 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 262;

(45) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 242 and SEQ ID NO: 262, respectively;

(46) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 282 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 302;

(47) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 282 and SEQ ID NO: 302, respectively;

(48) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 322 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 342;

(49) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 322 and SEQ ID NO: 342, respectively;

(50) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 362 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 382;

(51) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 362 and SEQ ID NO: 382, respectively;

(52) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 402 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 422;

(53) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 402 and SEQ ID NO: 422, respectively;

(54) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 442 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 462;

(55) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 442 and SEQ ID NO: 462, respectively;

(56) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 482 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 502;

(57) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 482 and SEQ ID NO: 502, respectively;

(58) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 522 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 542;

(59) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 522 and SEQ ID NO: 542, respectively;

(60) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 562 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 582;

(61) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 562 and SEQ ID NO: 582, respectively;

(62) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 602 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 622;

(63) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 602 and SEQ ID NO: 622, respectively;

(64) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 642 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 662;

(65) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 642 and SEQ ID NO: 662, respectively;

(66) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 682 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 702;

(67) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 682 and SEQ ID NO: 702, respectively;

(68) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 722 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 742;

(69) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 722 and SEQ ID NO: 742, respectively;

(70) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 762 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 782;

(71) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 762 and SEQ ID NO: 782, respectively;

(72) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 802 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 822;

(73) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 802 and SEQ ID NO: 822, respectively;

(74) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 842 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 862;

(75) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 842 and SEQ ID NO: 862, respectively;

(76) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 882 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 902;

(77) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 882 and SEQ ID NO: 902, respectively;

(78) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 922 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 942;

(79) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains which re each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 922 and SEQ ID NO: 942, respectively;

(80) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 962 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 982;

(81) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 962 and SEQ ID NO: 982, respectively;

(82) said anti-human HGF antibody or antibody fragment a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1002 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1022;

(83) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 1002 and SEQ ID NO: 1022, respectively;

(84) said anti-human HGF antibody or antibody fragment comprises a variable heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1042 and the variable light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1062;

(85) said anti-human HGF antibody or antibody fragment comprises variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 1042 and SEQ ID NO: 1062, respectively;

(86) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 21;

(87) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 41 and a light chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 61;

(88) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 81 and a light chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 101;

(89) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 121 and a light chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 141;

(90) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 161 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 181;

(91) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 201 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 221;

(92) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 241 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 261;

(93) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 281 and the light chain comprises SEQ ID NO: 301;

(94) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises SEQ ID NO: 321 and a light chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 341;

(95) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 361 and the light chain comprises SEQ ID NO: 381;

(96) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises SEQ ID NO: 401 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 421;

(97) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 441 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 461;

(98) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 481 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 501;

(99) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 521 and the light chain comprises SEQ ID NO: 541;

(100) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises SEQ ID NO: 561 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 581;

(101) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 601 and the light chain comprises SEQ ID NO: 621;

(102) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises SEQ ID NO: 641 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 661;

(103) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 681 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 701;

(104) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 721 and the light chain comprises SEQ ID NO: 741;

(105) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises SEQ ID NO: 761 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 781;

(106) said anti-human HGF antibody or antibody fragment comprises a heavy chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 801 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 821;

(107) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 841 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 861;

(108) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 881 and the light chain comprises SEQ ID NO: 901;

(109) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises SEQ ID NO: 921 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 941;

(110) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises SEQ ID NO: 961 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 981;

(111) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises SEQ ID NO: 1001 and the light chain comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1021; and

(112) said anti-human HGF antibody or antibody fragment comprises a heavy chain which comprises SEQ ID NO: 1041 and the light chain comprises a sequence at

least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1061; or any combination of the foregoing.

**4.** The anti-human HGF antibody or antibody fragment of claims 1, 2 or 3, wherein the antibody or antibody fragment comprises:

(1) a chimeric, humanized, and human antibody or antibody fragment;

(2) an scFv, camelbody, nanobody, IgNAR, Fab fragment, Fab' fragment, MetMab like antibody, monovalent antibody fragment, and /or an F(ab')2 fragment;

(3) an antibody or antibody fragment that substantially or entirely lacks N-glycosylation and/or O-glycosylation;

(4) an antibody or antibody fragment which comprises a human constant domain;

(5) a human which contains human IgG1, IgG2, IgG3, or IgG4 antibody constant regions;

(6) an antibody or antibody fragment which comprises an Fc region that has been modified to alter at least one of effector function, half-life, proteolysis, or glycosylation;

(7) an antibody which contains an Fc region which contains one or more mutations that alters or eliminates N- and/or O-glycosylation;

(8) a humanized antibody or antibody fragment;

(9) an antibody or antibody fragment which binds to HGF with a dissociation constant ($K_D$) of less than or equal to $10^{-2}$ M, $5x10^{-3}$ M, $10^{-3}$ M, $5x10^{-4}$ M, $10^{-4}$ M, $5x10^{-5}$ M, $10^{-5}$ M, $5x10^{-6}$ M, $10^{-6}$ M, $5x10^{-7}$ M, $10^{-7}$ M, $5x10^{-8}$ M, $10^{-8}$ M, $5x10^{-9}$ M, $10^{-9}$ M, $5x10^{-10}$ M, $10^{-10}$ M, $5x10^{-11}$ M, $10^{-11}$ M, $5x10^{-12}$ M, $10^{-12}$ M, $5x10^{-13}$ M, or $10^{-13}$ M;

(10) an antibody or antibody fragment binds to HGF with a dissociation constant ($K_D$) of less than or equal to $10^{-11}$ M, $5x10^{-12}$ M, or $10^{-12}$ M;

(11) an antibody or antibody fragment that binds to HGF with an off-rate ($K_{off}$) of less than or equal to $10^{-4}$ $S^{-1}$, $5x10^{-5}$ $S^{-1}$, 10-5 $S^{-1}$, $5x10^{-6}$ $S^{-1}$, $10^{-6}$ S-1, $5x10^{-7}$ $S^{-1}$, or 10-7 $S^{-1}$;

(12) an antibody or antibody fragment which directly or indirectly attached to a detectable label or therapeutic agent;

(13) an antibody or antibody fragment which when administered to a human subject inhibits or neutralizes at least one biological effect elicited by HGF;

(14) an antibody or antibody fragment which binds to HGF with a $K_D$ that is less than about 100 nM;

(15) an antibody or antibody fragment which binds to HGF with a $K_D$ that is less than about 10 nM;

(16) an antibody or antibody fragment which binds to HGF with a $K_D$ that is less than about 1 nM;

(17) an antibody or antibody fragment which binds to HGF with a $K_D$ that is between about 1 and about 10 nM;

(18) the antibody or antibody fragment binds to HGF with a $K_D$ that is between about 0.1 and about 1 nM;

(19) an antibody or antibody fragment which is attached to at least one effector moiety, optionally comprising a chemical linker;

(20) an antibody or antibody fragment which is attached to one or more detectable moieties;

(21) an antibody or antibody fragment which is attached to a detectable moiety that comprises a fluorescent dye, enzyme, substrate, bioluminescent material, radioactive material, chemiluminescent moiety, or mixtures thereof;

(22) an antibody or antibody fragment which is attached to one or more functional moieties; and/or

(23) an anti-idiotypic antibody produced against an anti-human HGF antibody or antibody fragment according to any one of the foregoing.

**5**. A composition suitable for therapeutic, prophylaxis, or a diagnostic use comprising a therapeutically, prophylactically or diagnostically effective amount of at least one antibody or antibody fragment according to any one of claims 1-4.

**6**. A composition according to claim 5, wherein:

(1) it is suitable for administration by a means selected from buccal, epicutaneous, epidural, inhalation, intraarterial, intracardial, intracerebroventricular, intradermal, intramuscular, intranasal, intraocular, intraperitoneal, intraspinal, intrathecal, intravenous, oral, parenteral, topical, rectally via an enema or suppository, subcutaneous, subdermal, sublingual, transdermal, and transmucosal;

(2) it comprises a powder, liquid, gel, drop, liposomal, or other dosage form;

(3) it is lyophilized;

(4) it comprises a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, preservative, or mixture thereof;

(5) it comprises another active agent;

(6) it comprises another active agent comprising a drug useful for treating a condition selected from cancer, macular degeneration, Alzheimer's disease, and malarial infection;

(7) it comprises another active agent for treating a cancer is selected from cancer ovarian cancer, breast cancer, lung cancer (small cell or non-small cell), colon and colorectal cancer, prostate cancer, pancreatic cancer, renal cancer, gastric cancer, liver cancer, bladder cancer, thyroid cancer, endometrial cancer, head-and-neck tumors, melanoma, sarcomas, leukemias, lymphomas, and brain tumors (e.g., glioblastomas), of children or adults;

(8) it comprises another active agent selected from chemotherapy agents, statins, cytokines, immunosuppressive agents, gene therapy agents, anti-coagulants,

anti-cachexia agents, anti-weakness agent, anti-fatigue agent, anti-fever agent, anti-nausea agents, antiemetic agents, IL-6 antagonists, cytotoxic agents, analgesics, antipyretics, anti-inflammatory agents, antibiotics, antiviral agents, anti-cytokine agents, anti-angiogenesis agents, or any combination thereof;

(9) it comprises another active agent which is a chemotherapy agent selected from: VEGF antagonists, EGFR antagonists, platins, taxols, irinotecan, 5-fluorouracil, gemcitabine, leucovorin, steroids, cyclophosphamide, melphalan, vinca alkaloids, vinblastine, vincristine, vindesine, vinorelbine, mustines, tyrosine kinase inhibitors, radiotherapy, sex hormone antagonists, selective androgen receptor modulators, selective estrogen receptor modulators, PDGF antagonists, TNF antagonists, IL-I antagonists, interleukins, IL-12, IL-2, IL-12R antagonists, Toxin conjugated monoclonal antibodies, tumor antigen specific monoclonal antibodies, Erbitux™, Avastin™, Pertuzumab, anti-CD20 antibodies, Rituxan®, ocrelizumab, ofatumumab, DXL625, Herceptin®, or any combination thereof;

(10) it comprises another active agent which is an anti-coagulant selected from: abciximab (ReoPro™), acenocoumarol, antithrombin IE, argatroban, aspirin, bivalirudin (Angiomax™), clopidogrel, dabigatran, dabigatran etexilate (Pradaxa™/Pradax™), desirudin (Revasc™/Iprivask™), dipyridamole, eptifibatide (Integrilin™), fondaparinux, heparin, hirudin, idraparinux, lepirudin (Refludan™), low molecular weight heparin, Melagatran, phenindione, phenprocoumon, ticlopidine, tirofiban (Aggrastat™), warfarin, ximelagatran, ximelagatran (Exanta™/ Exarta™), or any combination thereof;

(11) it comprises another active agent which is a statin selected from: atorvastatin, cerivastatin, fluvastatin, lovastatin, mevastatin, pravastatin, pravastatin, rosuvastatin, simvastatin, or any combination thereof;

(12) it comprises another active agent which is an antagonist of a factor selected from tumor necrosis factor-alpha, Interferon gamma, Interleukin 1 alpha, Interleukin 1 beta, Interleukin 6, proteolysis inducing factor, leukemia-inhibitory factor, or any combination thereof;

(13) it comprises another active agent which is an anti-angiogenesis factor selected from soluble VEGFR-1, NRP-1, Angiopoietin 2, TSP-1 and TSP-2, angiostatin and related molecules, endostatin, vasostatin, calreticulin, platelet factor-4, TIMP, CDAI, Meth-1, Meth-2, IFN-α, -β and -γ, CXCL10, IL-4, IL-12, IL-18, prothrombin (kringle domain-2), antithrombin III fragment, prolactin, VEGI, SPARC, osteopontin, maspin, and canstatin;

(14) it comprises another active agent which is an anti-cachexia agent comprising: cannabis, dronabinol (Marinol™), nabilone (Cesamet), cannabidiol, cannabichromene, tetrahydrocannabinol, Sativex, megestrol acetate, or any combination thereof;

(15) it comprises another active agent which is an anti-nausea agent or antiemetic agent is comprising: 5-HT3 receptor antagonists, ajwain, alizapride, anticholinergics, antihistamines, aprepitant, benzodiazepines, cannabichromene, cannabidiol, cannabinoids, cannabis, casopitant, chlorpromazine, cyclizine, dexamethasone, dexamethasone, dimenhydrinate (Gravol™), diphenhydramine, dolasetron, domperidone, dopamine antagonists, doxylamine, dronabinol (Marinol™), droperidol, emetrol, ginger, granisetron, haloperidol, hydroxyzine, hyoscine, lorazepam, meclizine, metoclopramide, midazolam, muscimol, nabilone (Cesamet), nk1 receptor antagonists, ondansetron, palonosetron, peppermint, Phenergan, prochlorperazine, Promacot, promethazine, Pentazine, propofol, sativex, tetrahydrocannabinol, trimethobenzamide, tropisetron, nandrolone, stilbestrol, thalidomide, lenalidomide, ghrelin agonists, myostatin antagonists, anti-myostatin antibodies, selective androgen receptor modulators, selective estrogen receptor modulators, angiotensin All antagonists, beta two adenergic receptor agonists, beta three adenergic receptor agonists, or any combination thereof;

(16) it comprises another active agent which is selected from tamoxifen, BCL-2 antagonists, estrogen, bisphosphonates, teriparatide, strontium ranelate, sodium alendronate (Fosamax), risedronate (Actonel), raloxifene, ibandronate (Boniva), Obatoclax, ABT-263, gossypol, gefitinib, epidermal growth factor receptor tyrosine kinase inhibitors, erlotinib, epidermal growth factor receptor inhibitors, psoralens, trioxysalen, methoxsalen, bergapten, retinoids, etretinate, acitretin, infliximab

(Remicade®), adalimumab, infliximab, etanercept, Zenapax™, Cyclosporine, Methotrexate, granulocyte-colony stimulating factor, filgrastim, lenograstim, Neupogen, Neulasta, 2-Arylpropionic acids, Aceclofenac, Acemetacin, Acetylsalicylic acid (Aspirin), Alclofenac, Alminoprofen, Amoxiprin, Ampyrone, Arylalkanoic acids, Azapropazone, Benorylate/Benorilate, Benoxaprofen, Bromfenac, Carprofen, Celecoxib, Choline magnesium salicylate, Clofezone, COX-2 inhibitors, Dexibuprofen, Dexketoprofen, Diclofenac, Diflunisal, Droxicam, Ethenzamide, Etodolac, Etoricoxib, Faislamine, fenamic acids, Fenbufen, Fenoprofen, Flufenamic acid, Flunoxaprofen, Flurbiprofen, Ibuprofen, Ibuproxam, Indometacin, Indoprofen, Kebuzone, Ketoprofen, Ketorolac, Lornoxicam, Loxoprofen, Lumiracoxib, Magnesium salicylate, Meclofenamic acid, Mefenamic acid, Meloxicam, Metamizole, Methyl salicylate, Mofebutazone, Nabumetone, Naproxen, N-Arylanthranilic acids, Oxametacin, Oxaprozin, Oxicams, Oxyphenbutazone, Parecoxib, Phenazone, Phenylbutazone, Phenylbutazone, Piroxicam, Pirprofen, profens, Proglumetacin, Pyrazolidine derivatives, Rofecoxib, Salicyl salicylate, Salicylamide, Salicylates, Sulfinpyrazone, Sulindac, Suprofen, Tenoxicam, Tiaprofenic acid, Tolfenamic acid, Tolmetin, and Valdecoxib; Antibiotics; Amikacin, Aminoglycosides, Amoxicillin, Ampicillin, Ansamycins, Arsphenamine, Azithromycin, Azlocillin, Aztreonam, Bacitracin, Carbacephem, Carbapenems, Carbenicillin, Cefaclor, Cefadroxil, Cefalexin, Cefalothin, Cefalotin, Cefamandole, Cefazolin, Cefdinir, Cefditoren, Cefepime, Cefixime, Cefoperazone, Cefotaxime, Cefoxitin, Cefpodoxime, Cefprozil, Ceftazidime, Ceftibuten, Ceftizoxime, Ceftobiprole, Ceftriaxone, Cefuroxime, Cephalosporins, Chloramphenicol, Cilastatin, Ciprofloxacin, Clarithromycin, Clindamycin, Cloxacillin, Colistin, Co-trimoxazole, Dalfopristin, Demeclocycline, Dicloxacillin, Dirithromycin, Doripenem, Doxycycline, Enoxacin, Ertapenem, Erythromycin, Ethambutol, Flucloxacillin, Fosfomycin, Furazolidone, Fusidic acid, Gatifloxacin, Geldanamycin, Gentamicin, Glycopeptides, Herbimycin, Imipenem, Isoniazid, Kanamycin, Levofloxacin, Lincomycin, Linezolid, Lomefloxacin, Loracarbef, Macrolides, Mafenide, Meropenem, Meticillin, Metronidazole, Mezlocillin, Minocycline, Monobactams, Moxifloxacin, Mupirocin, Nafcillin, Neomycin, Netilmicin, Nitrofurantoin, Norfloxacin, Ofloxacin, Oxacillin, Oxytetracycline, Paromomycin, Penicillin, Penicillins, Piperacillin, Platensimycin, Polymyxin B, Polypeptides, Prontosil, Pyrazinamide, Quinolones, Quinupristin, Rifampicin, Rifampin,

Roxithromycin, Spectinomycin, Streptomycin, Sulfacetamide, Sulfamethizole, Sulfanamide, Sulfasalazine, Sulfisoxazole, Sulfonamides, Teicoplanin, Telithromycin, Tetracycline, Tetracyclines, Ticarcillin, Tinidazole, Tobramycin, Trimethoprim, Trimethoprim-Sulfamethoxazole, Troleandomycin, Trovafloxacin, Vancomycin; Aldosterone, Beclometasone, Betamethasone, Corticosteroids, Cortisol, Cortisone acetate, Deoxycorticosterone acetate, Dexamethasone, Fludrocortisone acetate, Glucocorticoids, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone, Steroids, and Triamcinolone; Antiviral agents including by way of example abacavir, aciclovir, acyclovir, adefovir, amantadine, amprenavir, an antiretroviral fixed dose combination, an antiretroviral synergistic enhancer, arbidol, atazanavir, atripla, brivudine, cidofovir, combivir, darunavir, delavirdine, didanosine, docosanol, edoxudine, efavirenz, emtricitabine, enfuvirtide, entecavir, entry inhibitors, famciclovir, fomivirsen, fosamprenavir, foscarnet, fosfonet, fusion inhibitor, ganciclovir, gardasil, ibacitabine, idoxuridine, imiquimod, imunovir, indinavir, inosine, integrase inhibitor, interferon, interferon type I, interferon type II, interferon type III, lamivudine, lopinavir, loviride, maraviroc, MK-0518, moroxydine, nelfinavir, nevirapine, nexavir, nucleoside analogues, oseltamivir, penciclovir, peramivir, pleconaril, podophyllotoxin, protease inhibitor, reverse transcriptase inhibitor, ribavirin, rimantadine, ritonavir, saquinavir, stavudine, tenofovir, tenofovir disoproxil, tipranavir, trifluridine, trizivir, tromantadine, truvada, valaciclovir, valganciclovir, vicriviroc, vidarabine, viramidine, zalcitabine, zanamivir, zidovudine, or any combination thereof;

(17) it comprises another active agent which is a cytotoxic agent, chemotherapeutic agent, or immunosuppressive agent is comprising: 1-dehydrotestosterone, 1-methylnitrosourea, 5-fluorouracil, 6-mercaptopurine, 6-mercaptopurine, 6-thioguanine, Abatacept, abraxane, acitretin, aclarubicin, Actinium-225 ($^{225}$Ac), actinomycin, Adalimumab, adenosine deaminase inhibitors, Afelimomab, Aflibercept, Afutuzumab, Alefacept, alitretinoin, alkyl sulfonates, alkylating agents, altretamine, alvocidib, aminolevulinic acid/methyl aminolevulinate, aminopterin, aminopterin, amrubicin, amsacrine, amsacrine, anagrelide, Anakinra, anthracenediones, anthracyclines, anthracyclines, anthracyclines, anthramycin (AMC); antimytotic agents, antibiotics, anti-CD20 antibodies, antifolates, Anti-lymphocyte globulin, Antimetabolites, Anti-thymocyte globulin, arsenic trioxide, Aselizumab, asparaginase,

asparagine depleters, Astatine-211 ($^{211}$At), Atlizumab, Atorolimumab, atrasentan, Avastin™, azacitidine, Azathioprine, azelastine, aziridines, Basiliximab, BAYX antibodies, Belatacept, Belimumab, belotecan, bendamustine, Bertilimumab, bexarotene, bisantrene, Bismuth -213 ($^{213}$Bi), Bismuth-212 ($^{212}$Bi), bleomycin, bleomycin, bleomycin, BLyS antibodies, bortezomib, busulfan, busulfan, Calcineurin inhibitors, calicheamicin, camptothecin, camptothecins, capecitabine, carboplatin (paraplatin), carboquone, carminomycin, carmofur, carmustine, carmustine (BSNU), CAT antibodies, CDl1a antibodies, CD147/Basigin antibodies, CD154 antibodies, CD18 antibodies, CD20 antibodies, CD23 antibodies, CD3 antibodies, CD4 antibodies, CD40 antibodies, CD62L/L-selectin antibodies, CD80 antibodies, CDK inhibitors, Cedelizumab, celecoxib, Certolizumab pegol, chlorambucil, chlorambucils, Cyclosporin, cis-dichlorodiamine platinum (II) (DDP) cisplatin, cladribine, Clenoliximab, clofarabine, colchicin, Complement component 5 antibodies, Copper-67 (67Cu), corticosteroids, CTLA-4 antibodies, CTLA-4 fusion proteins, Cyclophilin inhibitors, cyclophosphamides, cyclothosphamide, cytarabine, cytarabine, cytochalasin B, cytotoxic ribonucleases, dacarbazine, Daclizumab, dactinomycin, dactinomycin (actinomycin D), daunorubicin, daunorubicin, daunorubicin (formerly daunomycin), decitabine, Deforolimus, demecolcine, detorubicin, dibromomannitol, diethylcarbamazine, dihydrofolate reductase inhibitors, dihydroxy anthracin dione, diphtheria toxin, DNA polymerase inhibitors, docetaxel, Dorlimomab aritox, Dorlixizumab, doxorubicin (adriamycin), DXL625, Eculizumab, Efalizumab, efaproxiral, EGFR antagonists, elesclomol, elsamitrucin, Elsilimomab, emetine, endothelin receptor antagonists, epipodophyllotoxins, epirubicin, epothilones, Erbitux™, Erlizumab, estramustine, Etanercept, ethidium bromide, etoglucid, etoposide, etoposide phosphate, Everolimus, Faralimomab, farnesyltransferase inhibitors, FKBP inhibitors, floxuridine, fludarabine, fluorouracil, Fontolizumab, fotemustine, Galiximab, Gallium-67 (67Ga), Gantenerumab, Gavilimomab, gemcitabine, glucocorticoids, Golimumab, Gomiliximab, gramicidin D, Gusperimus, Herceptin®, hydrazines, hydroxyurea, hypomethylating agents, idarubicin, Idarubicine, ifosfamide, IL-1 antagonists, IL-1 receptor antagonists, IL-12, IL-12 antibodies, IL-12R antagonists, IL-13 antibodies, IL-2, IL-2 inhibitors, IL-2 receptor/CD25 antibodies, IL-6 antibodies, imatinib mesylate, Immunoglobulin E antibodies, IMP dehydrogenase inhibitors, Infliximab, Inolimomab, Integrin antibodies, Interferon antibodies,

interferons, Interleukin 5 antibodies, Interleukin-6 receptor antibodies, interleukins, Iodine-125 ($^{125}$I), Iodine-131 ($^{131}$I), Ipilimumab, irinotecan, ixabepilone, Keliximab, larotaxel, Lead-212 ($^{212}$Pb), Lebrilizumab, Leflunomide, Lenalidomide, Lerdelimumab, leucovorine, LFA-I antibodies, lidocaine, lipoxygenase inhibitors, lomustine (CCNU), lonidamine, lucanthone, Lumiliximab, Lutetium-177 ($^{177}$Lu), Macrolides, mannosulfan, Maslimomab, masoprocol, mechlorethamine, melphalan, Mepolizumab, mercaptopurine, Metelimumab, Methotrexate, microtubule assembly inhibitors, microtubule stability enhancers, mithramycin, mitobronitol, mitoguazone, mitomycin, mitomycin C, mitotane, mitoxantrone, Morolimumab, mTOR inhibitors, Muromonab-CD3, mustines, Mycophenolic acid, mytotane (O,P'-(DDD)), Natalizumab, nedaplatin, Nerelimomab, nimustine, nitrogen mustards, nitrosoureas, nordihydroguaiaretic acid, oblimersen, ocrelizumab, Ocrelizumab, Odulimomab, ofatumumab, olaparib, Omalizumab, ortataxel, Otelixizumab, oxaliplatin, oxaliplatin, paclitaxel (taxol), Pascolizumab, PDGF antagonists, pegaspargase, pemetrexed, Pentostatin, Pertuzumab, Pexelizumab, phosphodiesterase inhibitors, Phosphorus-32 ($^{32}$P), Pimecrolimus Abetimus, pirarubicin, pixantrone, platins, plicamycin, poly ADP ribose polymerase inhibitors, porfimer sodium, porphyrin derivatives, prednimustine, procaine, procarbazine, procarbazine, propranolol, proteasome inhibitors, pseudomonas exotoxin, Pseudomonas toxin, purine synthesis inhibitors, puromycin, pyrimidine synthesis inhibitors, radionuclides, radiotherapy, raltitrexed, ranimustine, Reslizumab, retinoid X receptor agonists, retinoids, Rhenium- 186 ($^{186}$Re), Rhenium- 188 ($^{188}$Re), ribonucleotide reductase inhibitors, ricin, Rilonacept, Rituxan®, Rovelizumab, rubitecan, Ruplizumab, Samarium-153 ($^{153}$Sm), satraplatin, Scandium-47 ($^{47}$Sc), selective androgen receptor modulators, selective estrogen receptor modulators, seliciclib, semustine, sex hormone antagonists, Siplizumab, Sirolimus, steroid aromatase inhibitors, steroids, streptozocin, streptozotocin, Tacrolimus, talaporfin, Talizumab, taxanes, taxols, tegafur, Telimomab aritox, temoporfin, temozolomide, temsirolimus, Temsirolimus, Teneliximab, teniposide, Teplizumab, Teriflunomide, tesetaxel, testolactone, tetracaine, Thalidomide, thioepa chlorambucil, thiopurines thioguanine, ThioTEPA, thymidylate synthase inhibitors, tiazofurin, tipifarnib, T-lymphocyte antibodies, TNF antagonists, TNF antibodies, TNF fusion proteins, TNF receptor fusion proteins, TNF-alpha inhibitors, Tocilizumab, topoisomerase inhibitors, topotecan, Toralizumab, trabectedin, Tremelimumab, treosulfan, tretinoin, triazenes,

triaziquone, triethylenemelamine, triplatin tetranitrate, trofosfamide, tumor antigen specific monoclonal antibodies, tyrosine kinase inhibitors, uramustine, Ustekinumab, valrubicin, Valrubicine, Vapaliximab, VEGF antagonists, Vepalimomab, verteporfin, vinblastine, vinca alkaloids, vincristine, vindesine, vinflunine, vinorelbine, Visilizumab, vorinostat, Yttrium-88 ($^{88}Y$), Yttrium-90 ($^{90}Y$), Zanolimumab, zileuton, Ziralimumab, Zolimomab aritox, zorubicin, Zotarolimus, or any combination thereof; and/or

(18) it comprises another active agent which is an agonist, antagonist, or modulator of a factor comprising: TNF-alpha, IL-2, IL-4, IL-6, IL-10, IL-12, IL-13, IL-18, ÏFN-alpha, IFN-gamma, BAFF, CXCL13, IP-10, VEGF, EPO, EGF, HRG, Hepatocyte Growth Factor (HGF), Hepcidin, or any combination thereof.

**7**. An anti-human HGF antibody or fragment or composition according to of any one of claims 1-6, which antibody or fragment:

(1) specifically binds to HGF expressing human cells and/or to circulating soluble HGF molecules in vivo;

(2) specifically binds to HGF expressed on or by human cells in a patient with a disease associated with cells that express HGF such as cancer, including ovarian cancer, breast cancer, lung cancer (small cell or non-small cell), colon and colorectal cancer, prostate cancer, pancreatic cancer, renal cancer, gastric cancer, liver cancer, bladder cancer, thyroid cancer, endometrial cancer, head-and-neck tumors, melanoma, sarcomas, leukemias; lymphomas; and brain tumors (e.g., glioblastomas), of children or adults; macular degeneration; Alzheimer's disease; and malarial infection;

(3) the $V_H$ or $V_L$ polypeptides contained in said antibody originated from one or more rabbit B cell populations;

(4) the antibody or fragment does not have binding specificity for HGFR; and/or

(5) the antibody or fragment inhibits the production of HGF/HGFR complexes and/or the production of HGF/HGFR multimers.

**8.** An isolated nucleic acid or nucleic acids which encode for and which when expressed in a suitable host cell result in the expression of an anti-human HGF

antibody or antibody fragment or the variable heavy or light chain thereof, which antibody or antibody fragment is (are) selected from:

(1) said antibody or antibody fragment encoded by said nucleic acid or nucleic acids competes with and/or specifically binds to the same or overlapping epitope(s) on human HGF as an anti-human HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(2) said expressed antibody or antibody fragment encoded by said nucleic acid or nucleic acids specifically binds to the same or overlapping epitope(s) on human HGF as an anti-human HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28, wherein said epitope(s) optionally can be identified is a binding assay that detects the binding of an anti-human HGF antibody to one or more peptides in a library of 10-15-mer peptides which are overlapping fragments that correspond to all or substantially all of the length of the human HGF polypeptide, wherein further optionally said binding assay is a Western immunoblot assay which detects specific binding of the antibody or antibody fragment to one or more of said 10-15 mer peptides in said library by the use of a chemiluminescent label which emits a detectable chemiluminescent signal when specific binding of said antibody or antibody fragment to a peptide in said library occurs;

(3) said expressed antibody or antibody fragment encoded by said nucleic acid or nucleic acids contains at least 2 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(4) said expressed anti-human anti- HGF antibody or antibody fragment encoded by said nucleic acid or nucleic acids contains at least 3 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group

consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(5) said expressed anti-human HGF antibody or antibody fragment encoded by said nucleic acid or nucleic acids contains at least 4 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23 Ab24, Ab25, Ab26, Ab27 and Ab28;

(6) said expressed anti-human HGF antibody or antibody fragment encoded by said nucleic acid or nucleic acids contains at least 5 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(7) said expressed antibody or antibody fragment encoded by said nucleic acid or nucleic acids contains all 6 complementarity determining regions (CDRs) of an anti-HGF antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab23, Ab24, Ab25, Ab26, Ab27 and Ab28;

(8) said expressed anti-human HGF antibody or antibody fragment encoded by said nucleic acid or nucleic acids contains (a) a variable heavy chain comprising a CDR1 sequence selected from the group consisting of:

(a) SEQ ID NO: 4, SEQ ID NO: 44, SEQ ID NO: 84, SEQ ID NO: 124, SEQ ID NO: 164, SEQ ID NO: 204, SEQ ID NO: 244, SEQ ID NO: 284, SEQ ID NO: 324, SEQ ID NO: 364, SEQ ID NO: 404, SEQ ID NO: 444, SEQ ID NO: 484, SEQ ID NO: 524, SEQ ID NO: 564, SEQ ID NO: 604, SEQ ID NO: 644, SEQ ID NO: 684, SEQ ID NO: 724, SEQ ID NO: 764, SEQ ID NO: 804, SEQ ID NO: 844, SEQ ID NO: 884, and SEQ ID NO: 924, SEQ ID NO:964, SEQ ID NO:1004, and SEQ ID NO:1044; a CDR2 sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 46, SEQ ID NO: 86, SEQ ID NO: 126, SEQ ID NO: 166, SEQ ID NO: 206, SEQ ID NO: 246, SEQ ID NO: 286,

SEQ ID NO: 326, SEQ ID NO: 366, SEQ ID NO: 406, SEQ ID NO: 446, SEQ ID NO: 486, SEQ ID NO: 526, SEQ ID NO: 566, SEQ ID NO: 606, SEQ ID NO: 646, SEQ ID NO: 686, SEQ ID NO: 726, SEQ ID NO: 766, SEQ ID NO: 806, SEQ ID NO: 846, SEQ ID NO: 886, and SEQ ID NO: 926, SEQ ID NO:966, SEQ ID NO:1006, and SEQ ID NO:1046; and a CDR3 sequence selected from the group consisting of SEQ ID NO: 8, SEQ ID NO: 48, SEQ ID NO: 88, SEQ ID NO: 128, SEQ ID NO: 168, SEQ ID NO: 208, SEQ ID NO: 248, SEQ ID NO: 288, SEQ ID NO: 328, SEQ ID NO: 368, SEQ ID NO: 408, SEQ ID NO: 448, SEQ ID NO: 488, SEQ ID NO: 528, SEQ ID NO: 568, SEQ ID NO: 608, SEQ ID NO: 648, SEQ ID NO: 688, SEQ ID NO: 728, SEQ ID NO: 768, SEQ ID NO: 808, SEQ ID NO: 848, SEQ ID NO: 888, and SEQ ID NO: 928, SEQ ID NO:968, SEQ ID NO:1008, and SEQ ID NO:1048; and/or

(b) a variable light chain comprising a CDR1 sequence selected from the group consisting of SEQ ID NO: 24, SEQ ID NO: 64, SEQ ID NO: 104, SEQ ID NO: 144, SEQ ID NO: 184, SEQ ID NO: 224, SEQ ID NO: 264, SEQ ID NO: 304, SEQ ID NO: 344, SEQ ID NO: 384, SEQ ID NO: 424, SEQ ID NO: 464, SEQ ID NO: 504, SEQ ID NO: 544, SEQ ID NO: 584, SEQ ID NO: 624, SEQ ID NO: 664, SEQ ID NO: 704, SEQ ID NO: 744, SEQ ID NO: 784, SEQ ID NO: 824, SEQ ID NO: 864, SEQ ID NO: 904, and SEQ ID NO: 944, SEQ ID NO:984, SEQ ID NO:1024, and SEQ ID NO:1064; a CDR2 sequence selected from the group consisting of SEQ ID NO: 26, SEQ ID NO: 66, SEQ ID NO: 106, SEQ ID NO: 146, SEQ ID NO: 186, SEQ ID NO: 226, SEQ ID NO: 266, SEQ ID NO: 306, SEQ ID NO: 346, SEQ ID NO: 386, SEQ ID NO: 426, SEQ ID NO: 466, SEQ ID NO: 506, SEQ ID NO: 546, SEQ ID NO: 586, SEQ ID NO: 626, SEQ ID NO: 666, SEQ ID NO: 706, SEQ ID NO: 746, SEQ ID NO: 786, SEQ ID NO: 826, SEQ ID NO: 866, SEQ ID NO: 906, and SEQ ID NO: 946, SEQ ID NO:986, SEQ ID NO:1026, and SEQ ID NO:1066; and a CDR3 sequence selected from the group consisting of SEQ ID NO: 28, SEQ ID NO: 68, SEQ ID NO: 108, SEQ ID NO: 148, SEQ ID NO: 188, SEQ ID NO: 228, SEQ ID NO: 268, SEQ ID NO: 308, SEQ ID NO: 348, SEQ ID NO: 388, SEQ ID NO: 428, SEQ ID NO: 468, SEQ ID NO: 508, SEQ ID NO: 548, SEQ ID NO: 588, SEQ ID NO: 628, SEQ ID NO: 668, SEQ ID NO: 708,

SEQ ID NO: 748, SEQ ID NO: 788, SEQ ID NO: 828, SEQ ID NO: 868, SEQ ID NO: 908, SEQ ID NO: 948, SEQ ID NO:988, SEQ ID NO:1028, and SEQ ID NO:1068 with the further proviso that one or two residues of any of the afore-identified CDR polypeptides may be substituted with another amino acid;

(9) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 4, the CDR2 sequence of SEQ ID NO: 6, and the CDR3 sequence of SEQ ID NO: 8; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 24, the CDR2 sequence of SEQ ID NO: 26, and the CDR3 sequence of SEQ ID NO: 28;

(10) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 44, the CDR2 sequence of SEQ ID NO: 46, and the CDR3 sequence of SEQ ID NO: 48; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 64, the CDR2 sequence of SEQ ID NO: 66, and the CDR3 sequence of SEQ ID NO: 68;

(11) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 84, the CDR2 sequence of SEQ ID NO: 86, and the CDR3 sequence of SEQ ID NO: 88; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 104, the CDR2 sequence of SEQ ID NO: 106, and the CDR3 sequence of SEQ ID NO: 108;

(12) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 124, the CDR2 sequence of SEQ ID NO: 126, and the CDR3 sequence of SEQ ID NO: 128; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 144, the CDR2 sequence of SEQ ID NO: 146, and the CDR3 sequence of SEQ ID NO: 148;

(13) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 164, the CDR2 sequence of SEQ ID NO: 166, and the CDR3 sequence of SEQ ID NO: 168; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 184, the CDR2 sequence of SEQ ID NO: 186, and the CDR3 sequence of SEQ ID NO: 188;

(14) said expressed anti-human HGF antibody or antibody fragment contains a variable heavy chain that comprises the CDR1 sequence of SEQ ID NO: 204, the CDR2 sequence of SEQ ID NO: 206, and the CDR3 sequence of SEQ ID NO: 208; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 224, the CDR2 sequence of SEQ ID NO: 226, and the CDR3 sequence of SEQ ID NO: 228;

(15) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 244, the CDR2 sequence of SEQ ID NO: 246, and the CDR3 sequence of SEQ ID NO: 248; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 264, the CDR2 sequence of SEQ ID NO: 266, and the CDR3 sequence of SEQ ID NO: 268;

(16) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 284, the CDR2 sequence of SEQ ID NO: 286, and the CDR3 sequence of SEQ ID NO: 288; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 304, the CDR2 sequence of SEQ ID NO: 306, and the CDR3 sequence of SEQ ID NO: 308;

(17) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 324, the CDR2 sequence of SEQ ID NO: 326, and the CDR3 sequence of SEQ ID NO: 328; and/or the variable light chain

comprises the CDR1 sequence of SEQ ID NO: 344, the CDR2 sequence of SEQ ID NO: 346, and the CDR3 sequence of SEQ ID NO: 348;

(18) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 364, the CDR2 sequence of SEQ ID NO: 366, and the CDR3 sequence of SEQ ID NO: 368; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 384, the CDR2 sequence of SEQ ID NO: 386, and the CDR3 sequence of SEQ ID NO: 388;

(19) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 404, the CDR2 sequence of SEQ ID NO: 406, and the CDR3 sequence of SEQ ID NO: 408; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 424, the CDR2 sequence of SEQ ID NO: 426, and the CDR3 sequence of SEQ ID NO: 428;

(20) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 444, the CDR2 sequence of SEQ ID NO: 446, and the CDR3 sequence of SEQ ID NO: 448; and the variable light chain comprises the CDR1 sequence of SEQ ID NO: 464, the CDR2 sequence of SEQ ID NO: 466, and the CDR3 sequence of SEQ ID NO: 468;

(21) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 484, the CDR2 sequence of SEQ ID NO: 486, and the CDR3 sequence of SEQ ID NO: 488; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 504, the CDR2 sequence of SEQ ID NO: 506, and the CDR3 sequence of SEQ ID NO: 508;

(22) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 524, the CDR2 sequence of SEQ ID NO: 526, and the CDR3 sequence of SEQ ID NO: 528; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 544, the CDR2 sequence of SEQ ID NO: 546, and the CDR3 sequence of SEQ ID NO: 548;

(23) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 564, the CDR2 sequence of SEQ ID NO: 566, and the CDR3 sequence of SEQ ID NO: 568; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 584, the CDR2 sequence of SEQ ID NO: 586, and the CDR3 sequence of SEQ ID NO: 588;

(24) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 604, the CDR2 sequence of SEQ ID NO: 606, and the CDR3 sequence of SEQ ID NO: 608; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 624, the CDR2 sequence of SEQ ID NO: 626, and the CDR3 sequence of SEQ ID NO: 628;

(25) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 644, the CDR2 sequence of SEQ ID NO: 646, and the CDR3 sequence of SEQ ID NO: 648; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 664, the CDR2 sequence of SEQ ID NO: 666, and the CDR3 sequence of SEQ ID NO: 668;

(26) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 684, the CDR2 sequence of SEQ ID NO: 686, and the CDR3 sequence of SEQ ID NO: 688; and/or the variable light chain

comprises the CDR1 sequence of SEQ ID NO: 704, the CDR2 sequence of SEQ ID NO: 706, and the CDR3 sequence of SEQ ID NO: 708;

(27) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 724, the CDR2 sequence of SEQ ID NO: 726, and the CDR3 sequence of SEQ ID NO: 728; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 744, the CDR2 sequence of SEQ ID NO: 746, and the CDR3 sequence of SEQ ID NO: 748;

(28) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 764, the CDR2 sequence of SEQ ID NO: 766, and the CDR3 sequence of SEQ ID NO: 768; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 784, the CDR2 sequence of SEQ ID NO: 786, and the CDR3 sequence of SEQ ID NO: 788;

(29) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 804, the CDR2 sequence of SEQ ID NO: 806, and the CDR3 sequence of SEQ ID NO: 808; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 824, the CDR2 sequence of SEQ ID NO: 826, and the CDR3 sequence of SEQ ID NO: 828;

(30) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 844, the CDR2 sequence of SEQ ID NO: 846, and the CDR3 sequence of SEQ ID NO: 848; and/or the variable light chain comprises the CDR1 sequence of SEQ ID NO: 864, the CDR2 sequence of SEQ ID NO: 866, and the CDR3 sequence of SEQ ID NO: 868;

(31) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 884, the CDR2 sequence of SEQ ID NO: 886, and the CDR3 sequence of SEQ ID NO: 888; and/or the variable light chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 904, the CDR2 sequence of SEQ ID NO: 906, and the CDR3 sequence of SEQ ID NO: 908;

(32) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 924, the CDR2 sequence of SEQ ID NO: 926, and the CDR3 sequence of SEQ ID NO: 928; and/or the variable light chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 944, the CDR2 sequence of SEQ ID NO: 946, and the CDR3 sequence of SEQ ID NO: 948;

(33) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 964, the CDR2 sequence of SEQ ID NO: 966, and the CDR3 sequence of SEQ ID NO: 968; and/or the variable light chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 984, the CDR2 sequence of SEQ ID NO: 986, and the CDR3 sequence of SEQ ID NO: 988;

(34) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 1004, the CDR2 sequence of SEQ ID NO: 1006, and the CDR3 sequence of SEQ ID NO: 1008; and/or the variable light chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 1024, the CDR2 sequence of SEQ ID NO: 1026, and the CDR3 sequence of SEQ ID NO: 1028;

(35) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 1044, the CDR2 sequence of SEQ ID NO: 1046, and the CDR3 sequence of SEQ ID NO: 1048; and/or the variable light chain encoded by said nucleic acid or nucleic acids comprises the CDR1 sequence of SEQ ID NO: 1064, the CDR2 sequence of SEQ ID NO: 1066, and the CDR3 sequence of SEQ ID NO: 1068;

(36) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 2 and/or the variable light chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 22;

(37) the variable heavy and light chains encoded by said nucleic acid are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 2 and SEQ ID NO: 22, respectively;

(38) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 42 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 62;

(39) the variable heavy and light chains encoded by said nucleic acid are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 42 and SEQ ID NO: 62, respectively;

(40) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 82 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 102;

(41) the variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 82 and SEQ ID NO: 102, respectively;

(42) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 122 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 142;

(43) the variable heavy and light chains encoded by said nucleic acid or acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 122 and SEQ ID NO: 142, respectively;

(44) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 162 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 182;

(45) the variable heavy and light chains encoded by said nucleic acid or acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 162 and SEQ ID NO: 182, respectively;

(46) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 202 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 222;

(47) the variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 202 and SEQ ID NO: 222, respectively;

(48) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 242 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 262;

(49) the variable heavy and light chains encoded by said nucleic acid(s) are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 242 and SEQ ID NO: 262, respectively;

(50) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 282 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 302;

(51) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 282 and SEQ ID NO: 302, respectively;

(52) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 322 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 342;

(53) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 322 and SEQ ID NO: 342, respectively;

(54) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 362 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 382;

(55) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 362 and SEQ ID NO: 382, respectively;

(56) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 402 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 422;

(57) the variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 402 and SEQ ID NO: 422, respectively;

(58) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 442 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 462;

(59) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 442 and SEQ ID NO: 462, respectively;

(60) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 482 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 502;

(61) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 482 and SEQ ID NO: 502, respectively;

(62) the variable heavy chain encoded by said nucleic acid or nucleic acids comprise a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 522 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 542;

(63) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 522 and SEQ ID NO: 542, respectively;

(64) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 562 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 582;

(65) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 562 and SEQ ID NO: 582, respectively;

(66) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID

NO: 602 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 622;

(67) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 602 and SEQ ID NO: 622, respectively;

(68) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 642 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 662;

(69) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 642 and SEQ ID NO: 662, respectively;

(70) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 682 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 702;

(71) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 682 and SEQ ID NO: 702, respectively;

(72) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 722 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 742;

(73) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 722 and SEQ ID NO: 742, respectively;

(74) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 762 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 782;

(75) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 762 and SEQ ID NO: 782, respectively;

(76) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 802 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 822;

(77) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 802 and SEQ ID NO: 822, respectively;

(78) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 842 and the variable light chain encoded by said nucleic acid or nucleic acids comprises s a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 862;

(79) the variable heavy and light chains are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 842 and SEQ ID NO: 862, respectively;

(80) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 882 and the variable light chain encoded by said nucleic acid or nucleic acids

comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 902;

(81) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 882 and SEQ ID NO: 902, respectively;

(82) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 922 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 942;

(83) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 922 and SEQ ID NO: 942, respectively;

(84) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 962 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 982;

(85) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 962 and SEQ ID NO: 982, respectively;

(86) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1002 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1022;

(87) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 1002 and SEQ ID NO: 1022, respectively;

(88) the variable heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1042 and the variable light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1062;

(89) the variable heavy and light chains encoded by said nucleic acid or nucleic acids are each at least 90% identical to the variable heavy and light chains in SEQ ID NO: 1042 and SEQ ID NO: 1062, respectively;

(90) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 21;

(91) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 41 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 61;

(92) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence is at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 81 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 101;

(93) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 121 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 141;

(94) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 161 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 181;

(95) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 201 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 221;

(96) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 241 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 261;

(97) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 281 and the light chain encoded by said nucleic acid or nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 301;

(98) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 321 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 341;

(99) heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 361 and the light chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 381;

(100) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 401 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 421;

(101) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 441 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 461;

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(102) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 481 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 501;

(103) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 521 and the light chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 541;

(104) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 561 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 581;

(105) the heavy chain encoded by said nucleic acid or nucleic acids a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 601 and the light chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 621;

(106) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 641 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 661;

(107) the heavy chain encoded by said nucleic acid or nucleic acids comprises s a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 681 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 701;

(108) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 721 and the light chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 741;

(109) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 761 and the light chain encoded by said nucleic acid or nucleic acids

comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 781;

(110) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence that is at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 801 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 821;

(111) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence that is at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 841 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 861;

(112) the heavy chain encoded by said nucleic acid or nucleic acids comprises a sequence that is at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 881 and the light chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 901;

(113) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 921 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 941;

(114) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 961 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 981;

(115) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 1001 and the light chain encoded by said nucleic acid or nucleic acids comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1021; and/or

(116) the heavy chain encoded by said nucleic acid or nucleic acids comprises SEQ ID NO: 1041 and the light chain encoded by said nucleic acid or nucleic acids

comprises a sequence at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 1061, or any combination of the foregoing.

**9.** The nucleic acid or nucleic acids of Claim 8 wherein the antibody or antibody fragment encoded by said nucleic acid or nucleic acids is selected from:

(1) chimeric, humanized, and human antibodies or antibody fragments;

(2) scFvs, camelbodies, nanobodies, IgNAR, Fab fragments, Fab' fragments, MetMabs, monovalent antibody fragments, and F(ab')2 fragments;

(3) the expressed antibody or antibody fragment encoded by said nucleic acid or nucleic acids substantially or entirely lacks N-glycosylation and/or O-glycosylation;

(4) the expressed antibody or antibody fragment encoded by said nucleic acid or nucleic acids comprises a human constant domain;

(5) the expressed antibody encoded by said nucleic acid or nucleic acids is an IgG1, IgG2, IgG3, or IgG4 antibody;

(6) said nucleic acid or nucleic acids comprise a sequence encoding a VH and a VL region at least 80, 90, 95, 96, 97, 98, 99 or 100% identical to SEQ ID NO: 12, SEQ ID NO: 32; SEQ ID NO: 52, SEQ ID NO: 72; SEQ ID NO: 92, SEQ ID NO: 112; SEQ ID NO: 132, SEQ ID NO: 152; SEQ ID NO: 172, SEQ ID NO: 192; SEQ ID NO: 212, SEQ ID NO: 232, SEQ ID NO: 252, SEQ ID NO: 272; SEQ ID NO: 292, SEQ ID NO: 312; SEQ ID NO: 332, SEQ ID NO: 352; SEQ ID NO: 372, SEQ ID NO: 392; SEQ ID NO: 412, SEQ ID NO: 432; SEQ ID NO: 452, SEQ ID NO: 472; SEQ ID NO: 492, SEQ ID NO: 512, SEQ ID NO: 532, SEQ ID NO: 552, SEQ ID NO: 572, SEQ ID NO: 592, SEQ ID NO: 612, SEQ ID NO: 632, SEQ ID NO: 652, SEQ ID NO: 672; SEQ ID NO: 692; SEQ ID NO: 712; SEQ ID NO: 732; SEQ ID NO: 752; SEQ ID NO: 772; SEQ ID NO: 792; SEQ ID NO: 812; SEQ ID NO: 832; SEQ ID NO: 852; SEQ ID NO: 872; SEQ ID NO: 892; SEQ ID NO: 912; SEQ ID NO: 932; SEQ ID NO: 952; SEQ ID NO:972, SEQ ID NO:992; SEQ ID NO:1012, SEQ ID NO:1032; SEQ ID NO:1052, and SEQ ID NO:1072; or a codon degenerate of any of the foregoing; and/or

(7) the nucleic acid sequence or sequences comprise Pichia or human preferred codons.

**10.** A vector or vectors comprising the nucleic acid sequence or sequences of any of Claims 8 or 9.

**11.** A host cell comprising nucleic acid sequence or sequences of any of Claims 8 or 9, or a vector or vectors according to Claim 10.

**12.** The host cell of claim 11, wherein said host cell is a mammalian, bacterial, fungal, yeast, avian or insect cell.

**13.** The host cell of Claim 12, which comprises:

(1) a filamentous fungi or a yeast;

(2) a filamentous fungi or yeast selected from Pichia pastoris, Pichia finlandica, Pichia trehalophila, Pichia koclamae, Pichia membranaefaciens, Pichia minuta (Ogataea minuta, Pichia lindneri), Pichia opuntiae, Pichia thermotolerans, Pichia salictaria, Pichia guercuum, Pichia pijperi, Pichia stiptis, Pichia methanolica, Pichia sp., Saccharomyces cerevisiae, Saccharomyces sp., Hansenula polymorpha, Kluyveromyces sp., Kluyveromyces lactis, Candida albicans, Aspergillus nidulans, Aspergillus niger, Aspergillus oryzae, Trichoderma reesei, Chrysosporium lucknowense, Fusarium sp., Fusarium gramineum, Fusarium venenatum, Physcomitrella patens Neurospora crassa, Pichia sp., any Saccharomyces sp., Hansenula polymorpha, any Kluyveromyces sp., Candida albicans, any Aspergillus sp., Trichoderma reesei, Chrysosporium lucknowense, any Fusarium sp. and Neurospora crassa;

(3) a mammalian cell; and/or

(4) a CHO, COS, BHK, myeloma, monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture), mouse sertoli cell; human lung cell; human liver cell, or a mouse mammary tumor cell.

**14.** A method of making the antibody or antibody fragment according to any one of claims 1-4, by expressing nucleic acids which encode for the expression of said antibody or antibody fragment in a recombinant host cell.

**15.** The method of Claim 14 wherein the host cell is selected from:

(1) a bacteria, yeast, fungi, insect cell, plant cell, avian cell, or mammalian cell;

(2) s a yeast or a filamentous fungi, which may optionally be polyploidal;

(3) a yeast or fungi selected from Pichia pastoris, Pichia finlandica, Pichia trehalophila, Pichia koclamae, Pichia membranaefaciens, Pichia minuta (Ogataea minuta, Pichia lindneri), Pichia opuntiae, Pichia thermotolerans, Pichia salictaria, Pichia guercuum, Pichia pijperi, Pichia stiptis, Pichia methanolica, Pichia sp., Saccharomyces cerevisiae, Saccharomyces sp., Hansenula polymorpha, Kluyveromyces sp., Kluyveromyces lactis, Candida albicans, Aspergillus nidulans, Aspergillus niger, Aspergillus oryzae, Trichoderma reesei, Chrysosporium lucknowense, Fusarium sp., Fusarium gramineum, Fusarium venenatum, Physcomitrella patens and Neurospora crassa. Pichia sp., any Saccharomyces sp., Hansenula polymorpha, any Kluyveromyces sp., Candida albicans, any Aspergillus sp., Trichoderma reesei, Chrysosporium lucknowense, any Fusarium sp. and Neurospora crassa;

(4) a mammalian cell;

(5) a CHO, COS, BHK, myeloma, monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture), mouse sertoli cell; human lung cell; human liver cell, or a mouse mammary tumor cell; or

(6) a CHO cell.

**16.** The method of 14, wherein the recombinant host cell is a haploid or polyploid yeast culture that stably expresses and secretes into the culture medium at least 10-25 mg/liter of said antibody or antibody fragment.

**17.** The method of Claim 16, wherein said polyploidal yeast is made by a method that comprises:

(i) introducing at least one expression vector containing one or more heterologous polynucleotides encoding said antibody operably linked to a promoter and a signal sequence into a haploid yeast cell;
(ii) producing by mating or spheroplast fusion a polyploidal yeast from said first and/or second haploid yeast cell;
(iii) selecting polyploidal yeast cells that stably express said antibody; and
(iv) producing stable polyploidal yeast cultures from said polyploidal yeast cells that stably express said antibody into the culture medium.

**18.** The method of claim 17, wherein said yeast genera is Pichia.

**19.** A method of treatment or diagnosis, wherein said method comprises the administration of an anti-HGF antibody or antibody fragment selected from the following:

(1) administering to a patient with a disease or condition associated with HGF expressing cells or the overexpression of HGF a therapeutically or prophylactically or diagnostically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7;

(2) modulating (inhibiting, blocking or promoting) HGF- associated angiogenesis in a subject in need thereof comprising administering a therapeutically or prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7;

(3) modulating (inhibiting, blocking or promoting) HGF- associated cell proliferation in a subject in need thereof comprising administering a therapeutically or prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7;

(4) modulating (inhibiting, blocking or promoting) HGF- associated cell invasion in a subject in need thereof comprising administering a therapeutically or

prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7;

(5) inhibiting or blocking HGF- associated metastasis in a subject in need thereof comprising administering a therapeutically or prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7;

(6) modulating (inhibiting, blocking or promoting) the HGF/HGF-R (c-met) interaction and/or c-met activation in a subject in need thereof comprising administering a therapeutically or prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7;

(7) inhibiting or blocking the mitogenic, motogenic, and/or morphogenic properties of HGF in a subject in need thereof comprising administering a therapeutically or prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7;

(8) promoting HGF-associated fibrosis in a subject in need thereof comprising administering a therapeutically or prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7; and/or

(9) inhibiting HGF-associated cell scattering in a subject in need thereof comprising administering a therapeutically or prophylactically effective amount of at least one anti-human HGF antibody or fragment or composition containing according to one of claims 1-7, or any combination thereof.

**20.** A method according to Claim 19, wherein

(1) said antibody or fragment inhibits or prevents HGF/ c-met binding;

(2) said antibody or fragment does not inhibit or prevent HGF/ c-met binding;

(3) said antibody or fragment inhibits c-met activation;

(4) said antibody or fragment binds to HGF/HGF-R complexes or multimers.

**21**. A method according to claim 19 or 20, wherein said method includes administration of another therapeutic agent.

**22.** The method of 21 wherein the other therapeutic agent is selected from: chemotherapy agents, statins, cytokines, immunosuppressive agents, gene therapy agents, anti-coagulants, anti-cachexia agents, anti-weakness agent, anti-fatigue agent, anti-fever agent, anti-nausea agents, antiemetic agents, IL-6 antagonists, cytotoxic agents, analgesics, antipyretics, anti-inflammatory agents, antibiotics, antiviral agents, anti-cytokine agents, anti-angiogenesis agents, or any combination thereof.

**23**. The method of claim 22 wherein :

(1) the chemotherapy agent is selected from: VEGF antagonists, EGFR antagonists, platins, taxols, irinotecan, 5-fluorouracil, gemcytabine, leucovorine, steroids, cyclophosphamide, melphalan, vinca alkaloids, vinblastine, vincristine, vindesine, vinorelbine, mustines, tyrosine kinase inhibitors, radiotherapy, sex hormone antagonists, selective androgen receptor modulators, selective estrogen receptor modulators, PDGF antagonists, TNF antagonists, IL-I antagonists, interleukins, IL- 12, IL-2, IL-12R antagonists, Toxin conjugated monoclonal antibodies, tumor antigen specific monoclonal antibodies, Erbitux™, Avastin™, Pertuzumab, anti-CD20 antibodies, Rituxan®, ocrelizumab, ofatumumab, DXL625, Herceptin®, or any combination thereof;

(2) the anti-coagulant is selected from abciximab (ReoPro™), acenocoumarol, antithrombin IE, argatroban, aspirin, bivalirudin (Angiomax™), clopidogrel, dabigatran, dabigatran etexilate (Pradaxa™/Pradax™), desirudin (Revasc™/Iprivask™), dipyridamole, eptifibatide (Integrilin™), fondaparinux, heparin, hirudin, idraparinux, lepirudin (Refludan™), low molecular weight heparin, melagatran, phenindione, phenprocoumon, ticlopidine, tirofiban (Aggrastat™), warfarin, ximelagatran, ximelagatran (Exanta™/ Exarta™), or any combination thereof;

(3) the statin is selected from: atorvastatin, cerivastatin, fluvastatin, lovastatin, mevastatin, pravastatin, pravastatin, rosuvastatin, simvastatin, or any combination thereof;

(4) the another therapeutic agent is an antagonist of a factor selected from tumor necrosis factor-alpha, Interferon gamma, Interleukin 1 alpha, Interleukin 1 beta, Interleukin 6, proteolysis inducing factor, leukemia-inhibitory factor, or any combination thereofPichia

(5) the another therapeutic agent is an anti-angiogenesis factor selected from soluble VEGFR-1, NRP-1, Angiopoietin 2, TSP-1 and TSP-2, angiostatin and related molecules, endostatin, vasostatin, calreticulin, platelet factor-4, TIMP, CDAI, Meth-1, Meth-2, IFN-α, -β and -γ, CXCL10, IL-4, -12 and -18, prothrombin (kringle domain-2), antithrombin III fragment, prolactin, VEGI, SPARC, osteopontin, maspin, and canstatin;

(6) the other therapeutic agent is an anti-cachexia agent comprising: cannabis, dronabinol (Marinol™), nabilone (Cesamet), cannabidiol, cannabichromene, tetrahydrocannabinol, Sativex, megestrol acetate, or any combination thereof;

(7) the other therapeutic agent is an anti-nausea agent or antiemetic agent is comprising: 5-HT3 receptor antagonists, ajwain, alizapride, anticholinergics, antihistamines, aprepitant, benzodiazepines, cannabichromene, cannabidiol, cannabinoids, cannabis, casopitant, chlorpromazine, cyclizine, dexamethasone, dexamethasone, dimenhydrinate (Gravol™), diphenhydramine, dolasetron, domperidone, dopamine antagonists, doxylamine, dronabinol (Marinol™), droperidol, emetrol, ginger, granisetron, haloperidol, hydroxyzine, hyoscine, lorazepam, meclizine, metoclopramide, midazolam, muscimol, nabilone (Cesamet), nkl receptor antagonists, ondansetron, palonosetron, peppermint, Phenergan, prochlorperazine, Promacot, promethazine, Pentazine, propofol, sativex, tetrahydrocannabinol, trimethobenzamide, tropisetron, nandrolone, stilbestrol, thalidomide, lenalidomide, ghrelin agonists, myostatin antagonists, anti-myostatin antibodies, selective androgen receptor modulators, selective estrogen receptor modulators, angiotensin All antagonists, beta

two adenergic receptor agonists, beta three adenergic receptor agonists, or any combination thereof;

(8) the other therapeutic agent comprises tamoxifen, BCL-2 antagonists, estrogen, bisphosphonates, teriparatide, strontium ranelate, sodium alendronate (Fosamax), risedronate (Actonel), raloxifene, ibandronate (Boniva), Obatoclax, ABT-263, gossypol, gefitinib, epidermal growth factor receptor tyrosine kinase inhibitors, erlotinib, epidermal growth factor receptor inhibitors, psoralens, trioxysalen, methoxsalen, bergapten, retinoids, etretinate, acitretin, infliximab (Remicade®), adalimumab, infliximab, etanercept, Zenapax™, Cyclosporine, Methotrexate, granulocyte-colony stimulating factor, filgrastim, lenograstim, Neupogen, Neulasta, 2-Arylpropionic acids, Aceclofenac, Acemetacin, Acetylsalicylic acid (Aspirin), Alclofenac, Alminoprofen, Amoxiprin, Ampyrone, Arylalkanoic acids, Azapropazone, Benorylate/Benorilate, Benoxaprofen, Bromfenac, Carprofen, Celecoxib, Choline magnesium salicylate, Clofezone, COX-2 inhibitors, Dexibuprofen, Dexketoprofen, Diclofenac, Diflunisal, Droxicam, Ethenzamide, Etodolac, Etoricoxib, Faislamine, fenamic acids, Fenbufen, Fenoprofen, Flufenamic acid, Flunoxaprofen, Flurbiprofen, Ibuprofen, Ibuproxam, Indometacin, Indoprofen, Kebuzone, Ketoprofen, Ketorolac, Lornoxicam, Loxoprofen, Lumiracoxib, Magnesium salicylate, Meclofenamic acid, Mefenamic acid, Meloxicam, Metamizole, Methyl salicylate, Mofebutazone, Nabumetone, Naproxen, N-Arylanthranilic acids, Oxametacin, Oxaprozin, Oxicams, Oxyphenbutazone, Parecoxib, Phenazone, Phenylbutazone, Phenylbutazone, Piroxicam, Pirprofen, profens, Proglumetacin, Pyrazolidine derivatives, Rofecoxib, Salicyl salicylate, Salicylamide, Salicylates, Sulfinpyrazone, Sulindac, Suprofen, Tenoxicam, Tiaprofenic acid, Tolfenamic acid, Tolmetin, and Valdecoxib, Antibiotics, Amikacin, Aminoglycosides, Amoxicillin, Ampicillin, Ansamycins, Arsphenamine, Azithromycin, Azlocillin, Aztreonam, Bacitracin, Carbacephem, Carbapenems, Carbenicillin, Cefaclor, Cefadroxil, Cefalexin, Cefalothin, Cefalotin, Cefamandole, Cefazolin, Cefdinir, Cefditoren, Cefepime, Cefixime, Cefoperazone, Cefotaxime, Cefoxitin, Cefpodoxime, Cefprozil, Ceftazidime, Ceftibuten, Ceftizoxime, Ceftobiprole, Ceftriaxone, Cefuroxime, Cephalosporins, Chloramphenicol, Cilastatin, Ciprofloxacin, Clarithromycin, Clindamycin, Cloxacillin, Colistin, Co-trimoxazole, Dalfopristin, Demeclocycline, Dicloxacillin, Dirithromycin, Doripenem, Doxycycline, Enoxacin,

Ertapenem, Erythromycin, Ethambutol, Flucloxacillin, Fosfomycin, Furazolidone, Fusidic acid, Gatifloxacin, Geldanamycin, Gentamicin, Glycopeptides, Herbimycin, Imipenem, Isoniazid, Kanamycin, Levofloxacin, Lincomycin, Linezolid, Lomefloxacin, Loracarbef, Macrolides, Mafenide, Meropenem, Meticillin, Metronidazole, Mezlocillin, Minocycline, Monobactams, Moxifloxacin, Mupirocin, Nafcillin, Neomycin, Netilmicin, Nitrofurantoin, Norfloxacin, Ofloxacin, Oxacillin, Oxytetracycline, Paromomycin, Penicillin, Penicillins, Piperacillin, Platensimycin, Polymyxin B, Polypeptides, Prontosil, Pyrazinamide, Quinolones, Quinupristin, Rifampicin, Rifampin, Roxithromycin, Spectinomycin, Streptomycin, Sulfacetamide, Sulfamethizole, Sulfanamide, Sulfasalazine, Sulfisoxazole, Sulfonamides, Teicoplanin, Telithromycin, Tetracycline, Tetracyclines, Ticarcillin, Tinidazole, Tobramycin, Trimethoprim, Trimethoprim-Sulfamethoxazole, Troleandomycin, Trovafloxacin, Vancomycin; Aldosterone, Beclometasone, Betamethasone, Corticosteroids, Cortisol, Cortisone acetate, Deoxycorticosterone acetate, Dexamethasone, Fludrocortisone acetate, Glucocorticoids, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone, Steroids, and Triamcinolone; Antiviral agents including by way of example abacavir, aciclovir, acyclovir, adefovir, amantadine, amprenavir, an antiretroviral fixed dose combination, an antiretroviral synergistic enhancer, arbidol, atazanavir, atripla, brivudine, cidofovir, combivir, darunavir, delavirdine, didanosine, docosanol, edoxudine, efavirenz, emtricitabine, enfuvirtide, entecavir, entry inhibitors, famciclovir, fomivirsen, fosamprenavir, foscarnet, fosfonet, fusion inhibitor, ganciclovir, gardasil, ibacitabine, idoxuridine, imiquimod, imunovir, indinavir, inosine, integrase inhibitor, interferon, interferon type I, interferon type II, interferon type III, lamivudine, lopinavir, loviride, maraviroc, MK-0518, moroxydine, nelfinavir, nevirapine, nexavir, nucleoside analogues, oseltamivir, penciclovir, peramivir, pleconaril, podophyllotoxin, protease inhibitor, reverse transcriptase inhibitor, ribavirin, rimantadine, ritonavir, saquinavir, stavudine, tenofovir, tenofovir disoproxil, tipranavir, trifluridine, trizivir, tromantadine, truvada, valaciclovir, valganciclovir, vicriviroc, vidarabine, viramidine, zalcitabine, zanamivir, zidovudine, or any combination thereof;

(9) the other therapeutic agent is selected from a cytotoxic agent, chemotherapeutic agent, or immunosuppressive agent is comprising: 1-dehydrotestosterone, 1-methylnitrosourea, 5-fluorouracil, 6-mercaptopurine, 6-

mercaptopurine, 6-thioguanine, Abatacept, abraxane, acitretin, aclarubicin, Actinium-225 ($^{225}$Ac), actinomycin, Adalimumab, adenosine deaminase inhibitors, Afelimomab, Aflibercept, Afutuzumab, Alefacept, alitretinoin, alkyl sulfonates, alkylating agents, altretamine, alvocidib, aminolevulinic acid/methyl aminolevulinate, aminopterin, aminopterin, amrubicin, amsacrine, amsacrine, anagrelide, Anakinra, anthracenediones, anthracyclines, anthracyclines, anthracyclines, anthramycin (AMC); antimytotic agents, antibiotics, anti-CD20 antibodies, antifolates, Anti-lymphocyte globulin, Antimetabolites, Anti-thymocyte globulin, arsenic trioxide, Aselizumab, asparaginase, asparagine depleters, Astatine-211 ($^{211}$At), Atlizumab, Atorolimumab, atrasentan, Avastin™, azacitidine, Azathioprine, azelastine, aziridines, Basiliximab, BAYX antibodies, Belatacept, Belimumab, belotecan, bendamustine, Bertilimumab, bexarotene, bisantrene, Bismuth -213 ($^{213}$Bi), Bismuth-212 ($^{212}$Bi), bleomycin, bleomycin, bleomycin, bleomycin, BLyS antibodies, bortezomib, busulfan, busulfan, Calcineurin inhibitors, calicheamicin, camptothecin, camptothecins, capecitabine, carboplatin (paraplatin), carboquone, carminomycin, carmofur, carmustine, carmustine (BSNU), CAT antibodies, CD11a antibodies, CD147/Basigin antibodies, CD154 antibodies, CD18 antibodies, CD20 antibodies, CD23 antibodies, CD3 antibodies, CD4 antibodies, CD40 antibodies, CD62L/L-selectin antibodies, CD80 antibodies, CDK inhibitors, Cedelizumab, celecoxib, Certolizumab pegol, chlorambucil, chlorambucils, Ciclosporin, cis-dichlorodiamine platinum (II) (DDP) cisplatin, cladribine, Clenoliximab, clofarabine, colchicin, Complement component 5 antibodies, Copper-67 (67Cu), corticosteroids, CTLA-4 antibodies, CTLA-4 fusion proteins, Cyclophilin inhibitors, cyclophosphamides, cyclothosphamide, cytarabine, cytarabine, cytochalasin B, cytotoxic ribonucleases, dacarbazine, Daclizumab, dactinomycin, dactinomycin (actinomycin D), daunorubicin, daunorubicin, daunorubicin (formerly daunomycin), decitabine, Deforolimus, demecolcine, detorubicin, dibromomannitol, diethylcarbamazine, dihydrofolate reductase inhibitors, dihydroxy anthracin dione, diphtheria toxin, DNA polymerase inhibitors, docetaxel, Dorlimomab aritox, Dorlixizumab, doxorubicin (adriamycin), DXL625, Eculizumab, Efalizumab, efaproxiral, EGFR antagonists, elesclomol, elsamitrucin, Elsilimomab, emetine, endothelin receptor antagonists, epipodophyllotoxins, epirubicin, epothilones, Erbitux™, Erlizumab, estramustine, Etanercept, ethidium bromide, etoglucid, etoposide, etoposide phosphate, Everolimus, Faralimomab, farnesyltransferase

inhibitors, FKBP inhibitors, floxuridine, fludarabine, fluorouracil, Fontolizumab, fotemustine, Galiximab, Gallium-67 (67Ga), Gantenerumab, Gavilimomab, gemcitabine, glucocorticoids, Golimumab, Gomiliximab, gramicidin D, Gusperimus, Herceptin®, hydrazines, hydroxyurea, hypomethylating agents, idarubicin, Idarubicine, ifosfamide, IL-I antagonists, IL-I receptor antagonists, IL-12, IL-12 antibodies, IL-12R antagonists, IL-13 antibodies, IL-2, IL-2 inhibitors, IL-2 receptor/CD25 antibodies, IL-6 antibodies, imatinib mesylate, Immunoglobulin E antibodies, IMP dehydrogenase inhibitors, Infliximab, Inolimomab, Integrin antibodies, Interferon antibodies, interferons, Interleukin 5 antibodies, Interleukin-6 receptor antibodies, interleukins, Iodine-125 ($^{125}$I), Iodine-131 (131I), Ipilimumab, irinotecan, ixabepilone, Keliximab, larotaxel, Lead-212 ($^{212}$Pb), Lebrilizumab, Leflunomide, Lenalidomide, Lerdelimumab, leucovorine, LFA-I antibodies, lidocaine, lipoxygenase inhibitors, lomustine (CCNU), lonidamine, lucanthone, Lumiliximab, Lutetium-177 ($^{177}$Lu), Macrolides, mannosulfan, Maslimomab, masoprocol, mechlorethamine, melphalan, Mepolizumab, mercaptopurine, Metelimumab, Methotrexate, microtubule assembly inhibitors, microtubule stability enhancers, mithramycin, mitobronitol, mitoguazone, mitomycin, mitomycin C, mitotane, mitoxantrone, Morolimumab, mTOR inhibitors, Muromonab-CD3, mustines, Mycophenolic acid, mytotane (O,P'-(DDD)), Natalizumab, nedaplatin, Nerelimomab, nimustine, nitrogen mustards, nitrosoureas, nordihydroguaiaretic acid, oblimersen, ocrelizumab, Ocrelizumab, Odulimomab, ofatumumab, olaparib, Omalizumab, ortataxel, Otelixizumab, oxaliplatin, oxaliplatin, paclitaxel (taxol), Pascolizumab, PDGF antagonists, pegaspargase, pemetrexed, Pentostatin, Pertuzumab, Pexelizumab, phosphodiesterase inhibitors, Phosphorus-32 ($^{32}$P), Pimecrolimus Abetimus, pirarubicin, pixantrone, platins, plicamycin, poly ADP ribose polymerase inhibitors, porfimer sodium, porphyrin derivatives, prednimustine, procaine, procarbazine, procarbazine, propranolol, proteasome inhibitors, pseudomonas exotoxin, Pseudomonas toxin, purine synthesis inhibitors, puromycin, pyrimidine synthesis inhibitors, radionuclides, radiotherapy, raltitrexed, ranimustine, Reslizumab, retinoid X receptor agonists, retinoids, Rhenium-186 ($^{186}$ Re), Rhenium- 188 ( $^{188}$Re), ribonucleotide reductase inhibitors, ricin, Rilonacept, Rituxan®, Rovelizumab, rubitecan, Ruplizumab, Samarium-153 ($^{153}$Sm), satraplatin, Scandium-47 ($^{47}$Sc), selective androgen receptor modulators, selective estrogen receptor modulators, seliciclib, semustine, sex hormone antagonists, Siplizumab, Sirolimus, steroid

aromatase inhibitors, steroids, streptozocin, streptozotocin, Tacrolimus, talaporfin, Talizumab, taxanes, taxols, tegafur, Telimomab aritox, temoporfin, temozolomide, temsirolimus, Temsirolimus, Teneliximab, teniposide, Teplizumab, Teriflunomide, tesetaxel, testolactone, tetracaine, Thalidomide, thioepa chlorambucil, thiopurines thioguanine, ThioTEPA, thymidylate synthase inhibitors, tiazofurin, tipifarnib, T-lymphocyte antibodies, TNF antagonists, TNF antibodies, TNF fusion proteins, TNF receptor fusion proteins, TNF-alpha inhibitors, Tocilizumab, topoisomerase inhibitors, topotecan, Toralizumab, trabectedin, Tremelimumab, treosulfan, tretinoin, triazenes, triaziquone, triethylenemelamine, triplatin tetranitrate, trofosfamide, tumor antigen specific monoclonal antibodies, tyrosine kinase inhibitors, uramustine, Ustekinumab, valrubicin, Valrubicine, Vapaliximab, VEGF antagonists, Vepalimomab, verteporfin, vinblastine, vinca alkaloids, vincristine, vindesine, vinflunine, vinorelbine, Visilizumab, vorinostat, Yttrium-88 ($^{88}Y$), Yttrium-90 ($^{90}Y$), Zanolimumab, zileuton, Ziralimumab, Zolimomab aritox, zorubicin, Zotarolimus, or any combination thereof; and/or

(10) the another active agent is one or more agonist, antagonist, or modulator of a factor comprising: TNF-alpha, IL-2, IL-4, IL-6, IL-10, IL-12, IL-13, IL-18, ÏFN-alpha, WN-gamma, BAFF, CXCL13, IP-10, VEGF, EPO, EGF, HRG, Hepatocyte Growth Factor (HGF), Hepcidin, or any combination of (1) through (10).

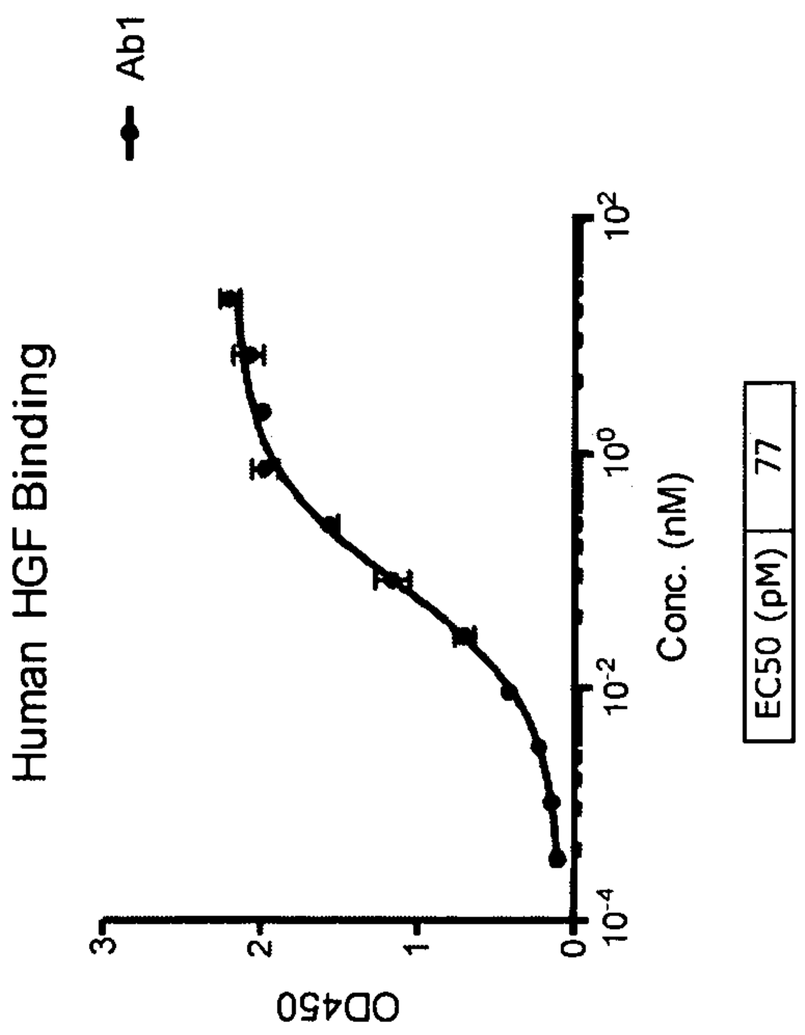

Ab1
Human HGF Binding
OD450
3
2
1
0
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 77

FIGURE 1

FIGURE 2

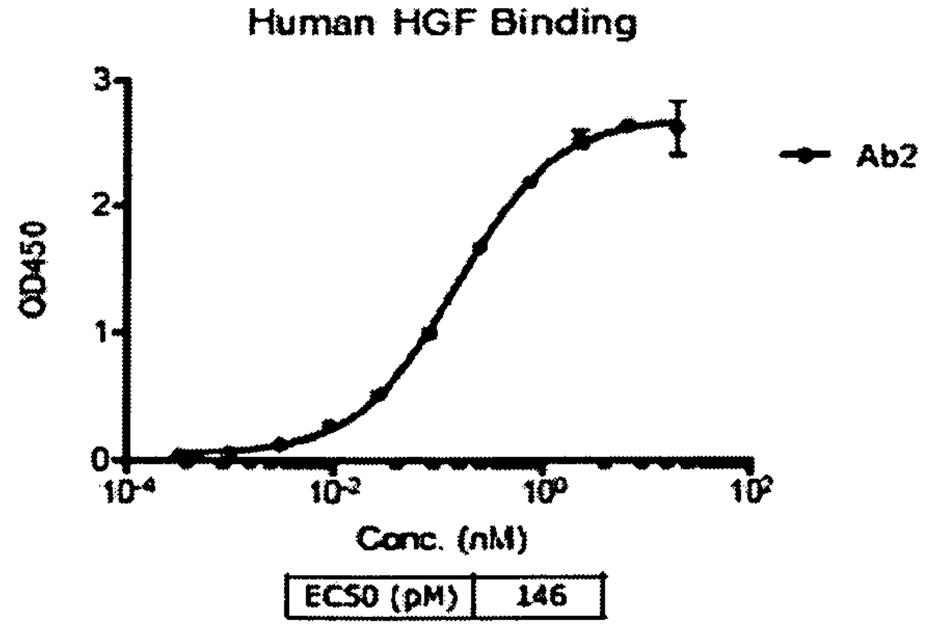

Human HGF Binding
OD450
3
2
1
0
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
Ab2
EC50 (pM) 146

FIGURE 3

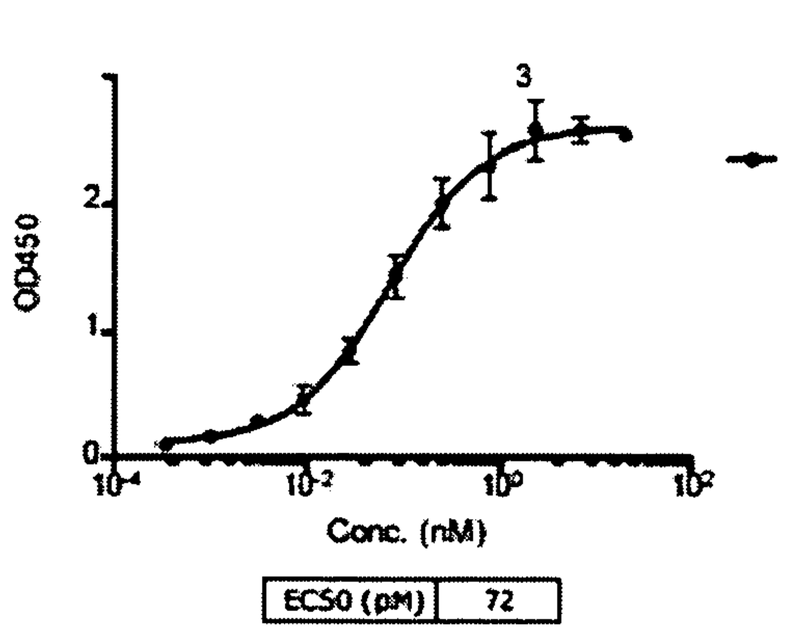

Human HGF Binding
Ab3
OD450
0
1
2
3
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 72

FIGURE 4

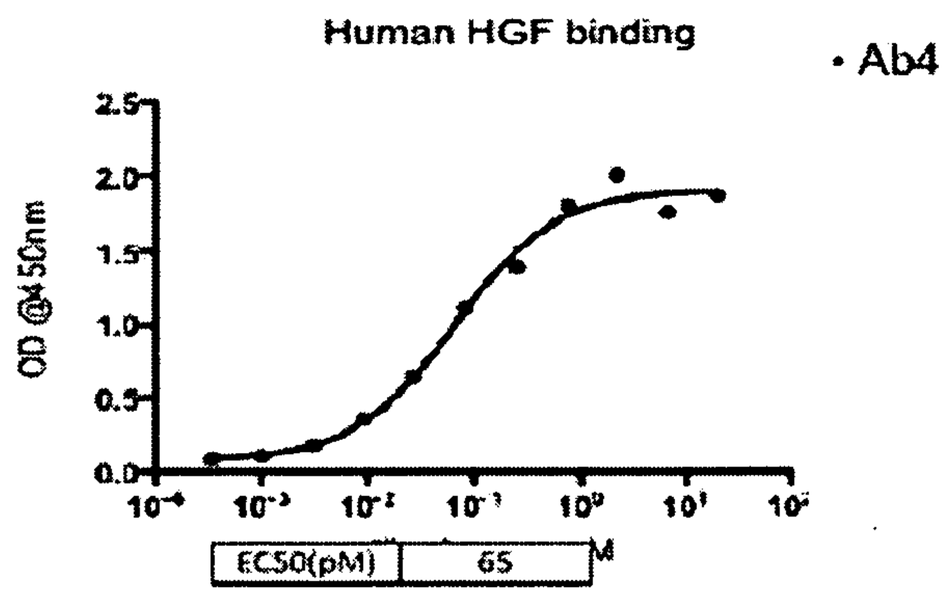


FIGURE 5

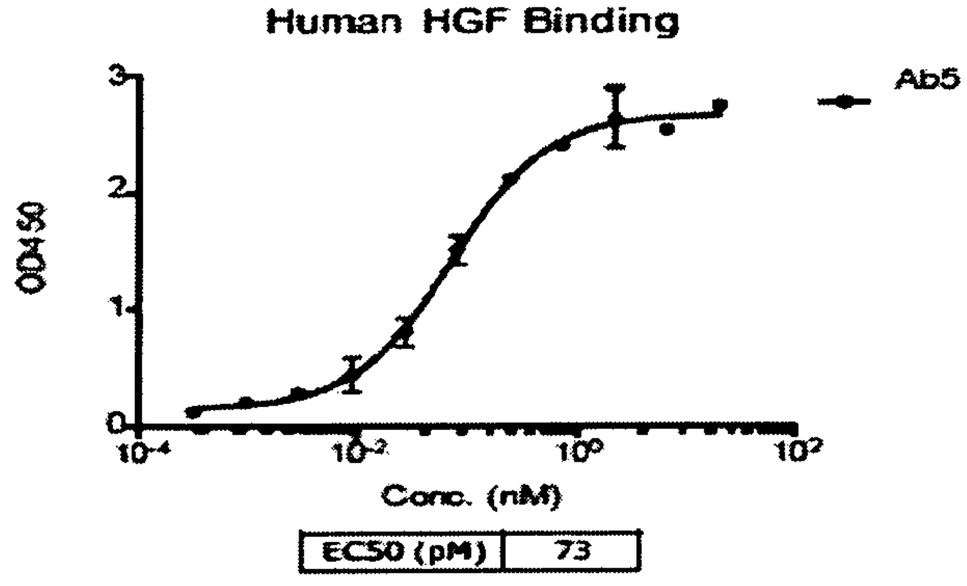

Human HGF Binding
Ab5
OD450
3
2
1
0
10-4
10-2
100
102
Conc. (nM)
EC50 (pM) 73

FIGURE 6

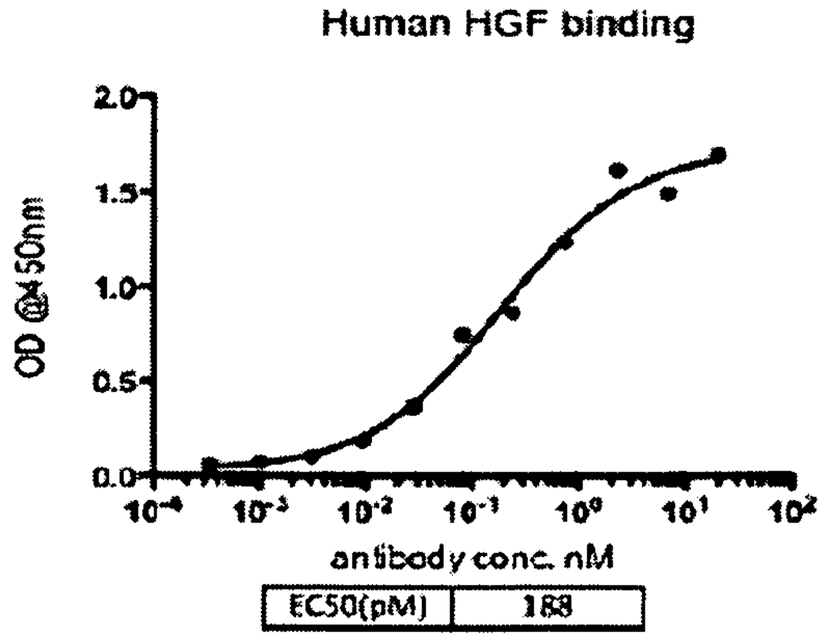

Human HGF binding
• Ab6
OD @450nm
2.0
1.5
1.0
0.5
0.0
10⁻⁴
10⁻³
10⁻²
10⁻¹
10⁰
10¹
10²
antibody conc. nM
EC50(pM)
188

FIGURE 7

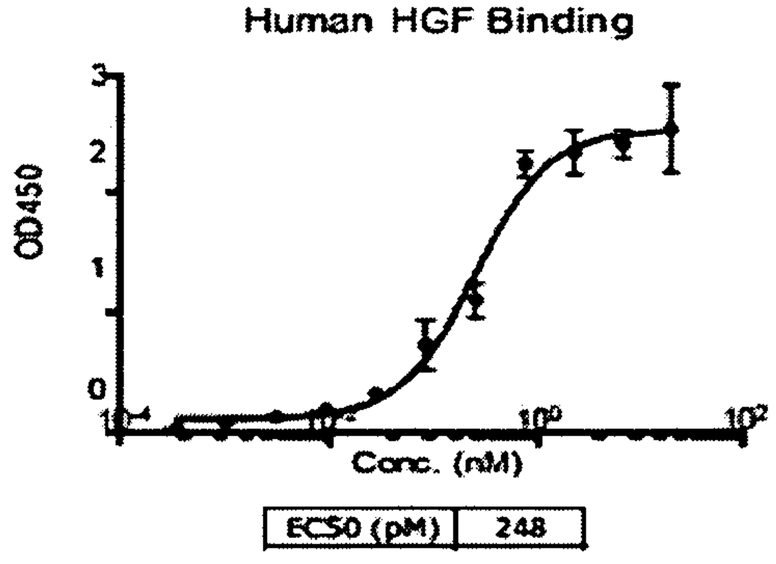

Human HGF Binding
Ab7
OD450
0
1
2
3
$10^{-1}$
$10^{0}$
$10^{1}$
$10^{2}$
Conc. (nM)
EC50 (pM) 248

FIGURE 8

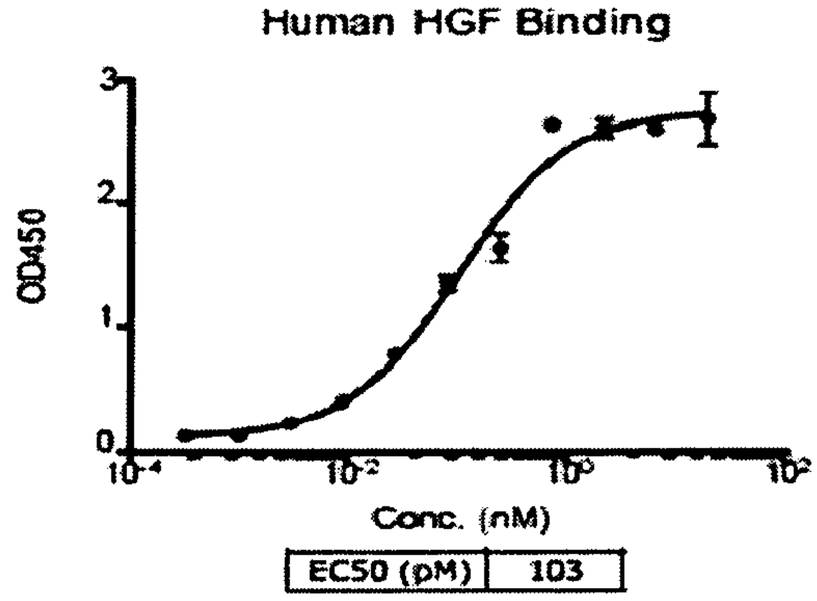

Human HGF Binding
Ab8
OD450
3
2
1
0
10-4
10-2
10⁰
10²
Conc. (nM)
EC50 (pM) 103

FIGURE 9

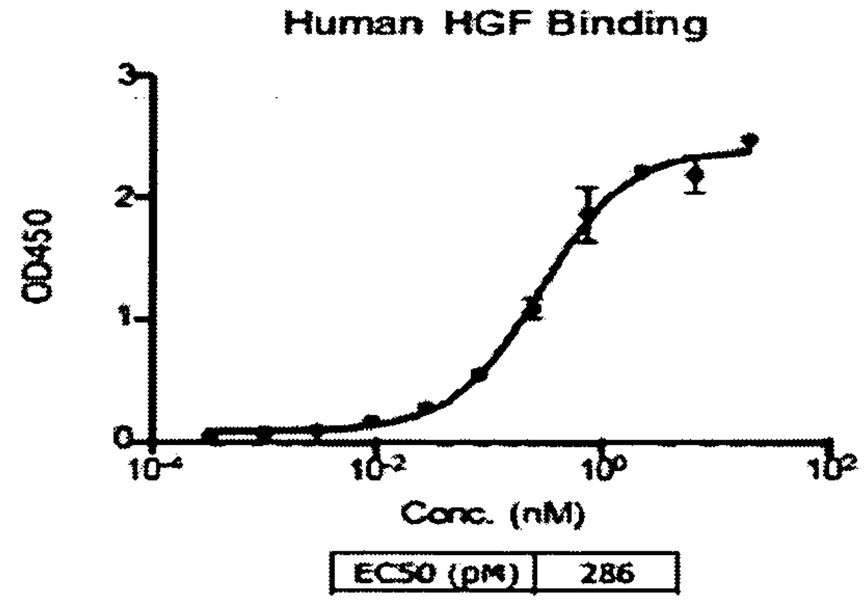

Human HGF Binding
Ab9
OD450
0
1
2
3
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 286

FIGURE 10

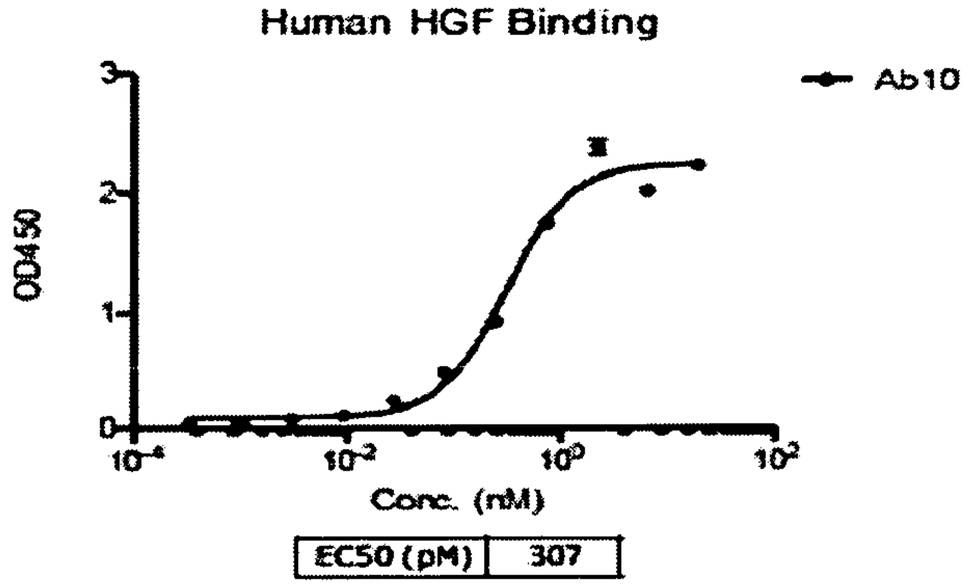

Human HGF Binding
Ab10
OD450
3
2
1
0
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 307

FIGURE 11

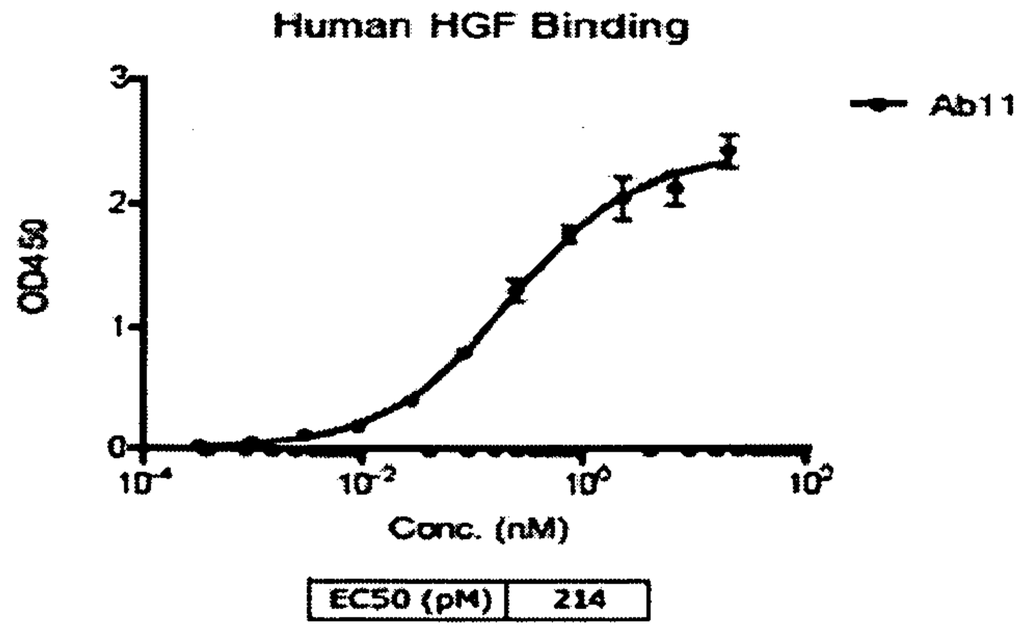


FIGURE 12

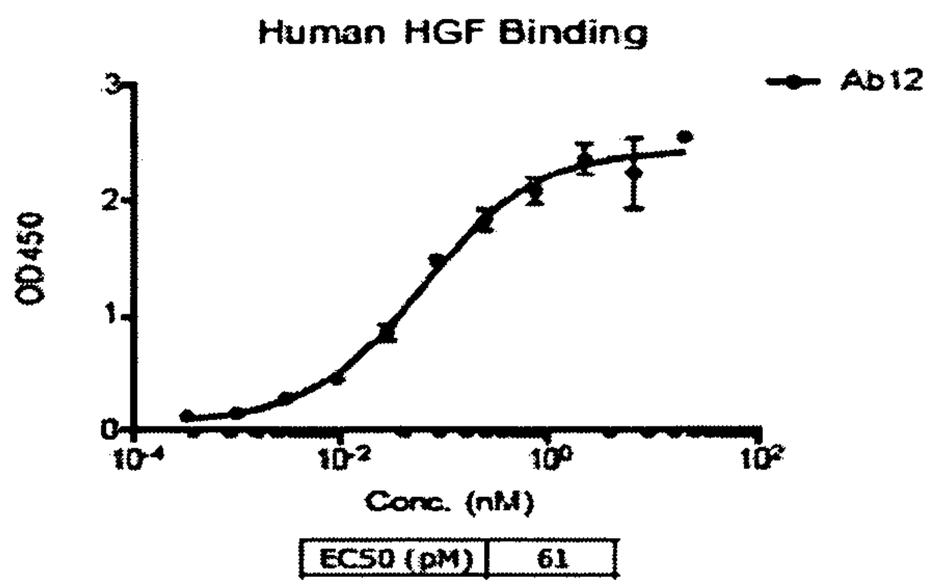

Human HGF Binding
Ab12
OD450
0
1
2
3
10-4
10-2
100
102
Conc. (nM)
EC50 (pM) 61

FIGURE 13

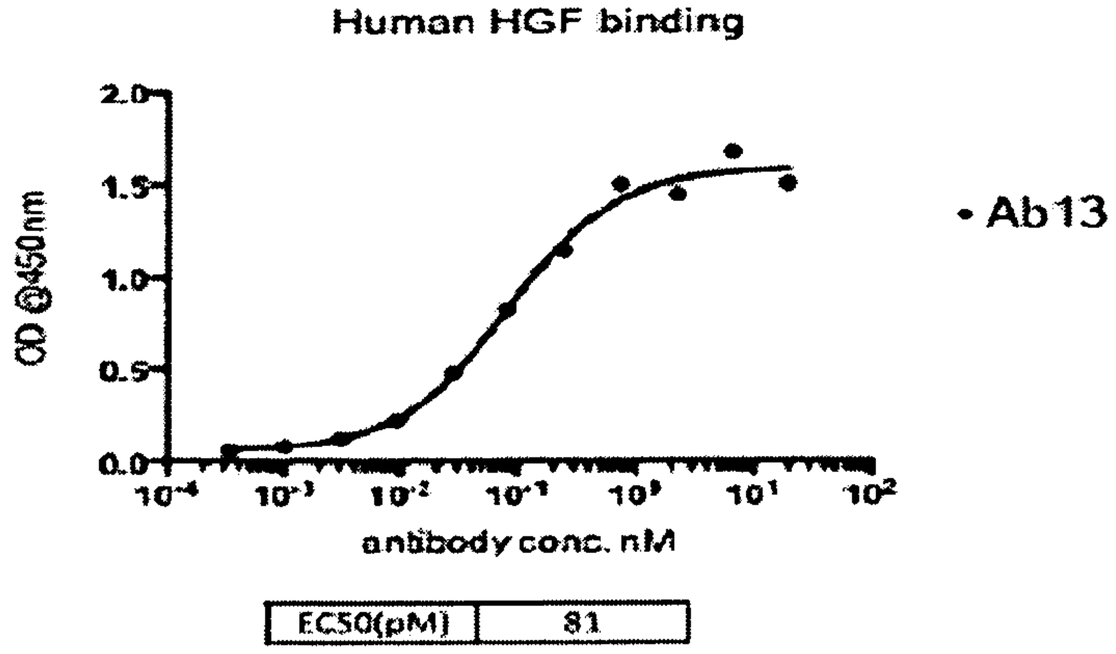

Human HGF binding
OD @450nm
2.0
1.5
1.0
0.5
0.0
$10^{-4}$
$10^{-3}$
$10^{-2}$
$10^{-1}$
$10^{0}$
$10^{1}$
$10^{2}$
antibody conc. nM
• Ab13
EC50(pM)
81

FIGURE 14

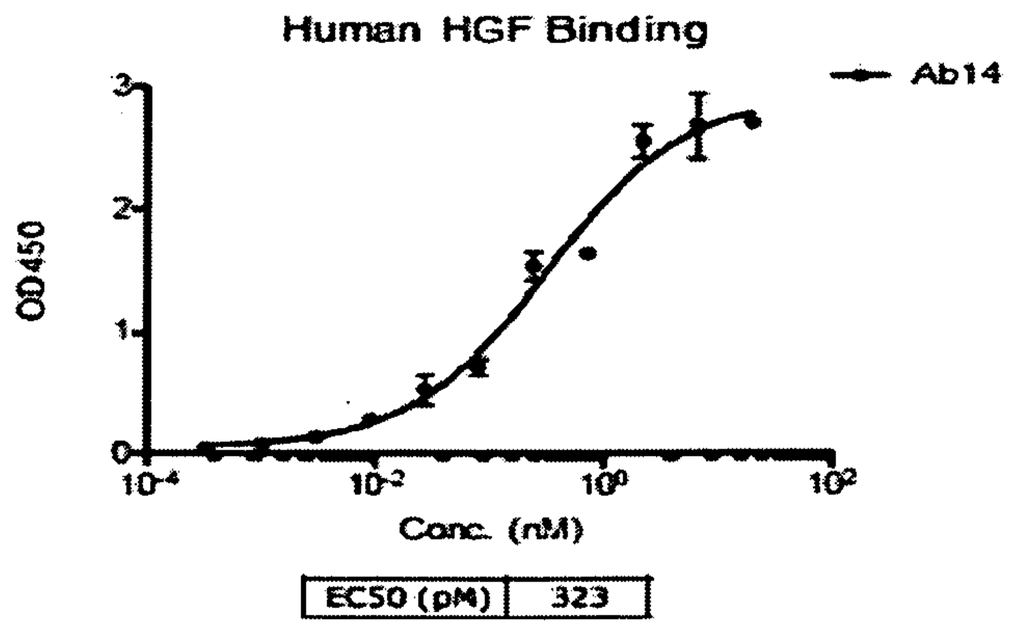

Human HGF Binding
Ab14
OD450
0
1
2
3
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 323

FIGURE 15

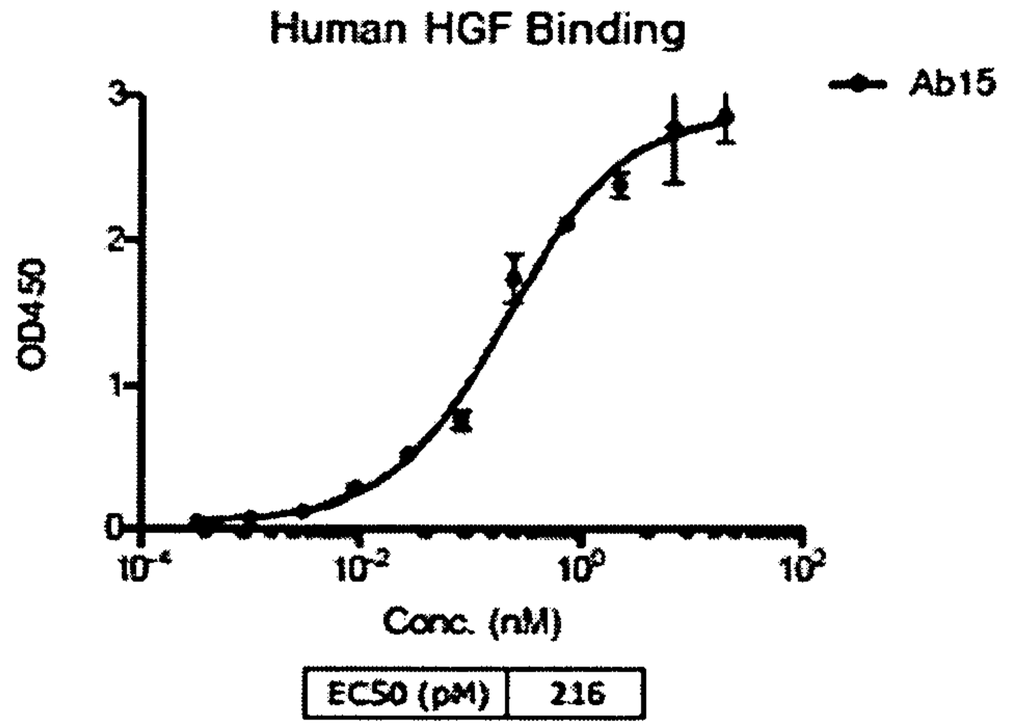

Human HGF Binding
Ab15
OD450
0
1
2
3
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 216

FIGURE 16

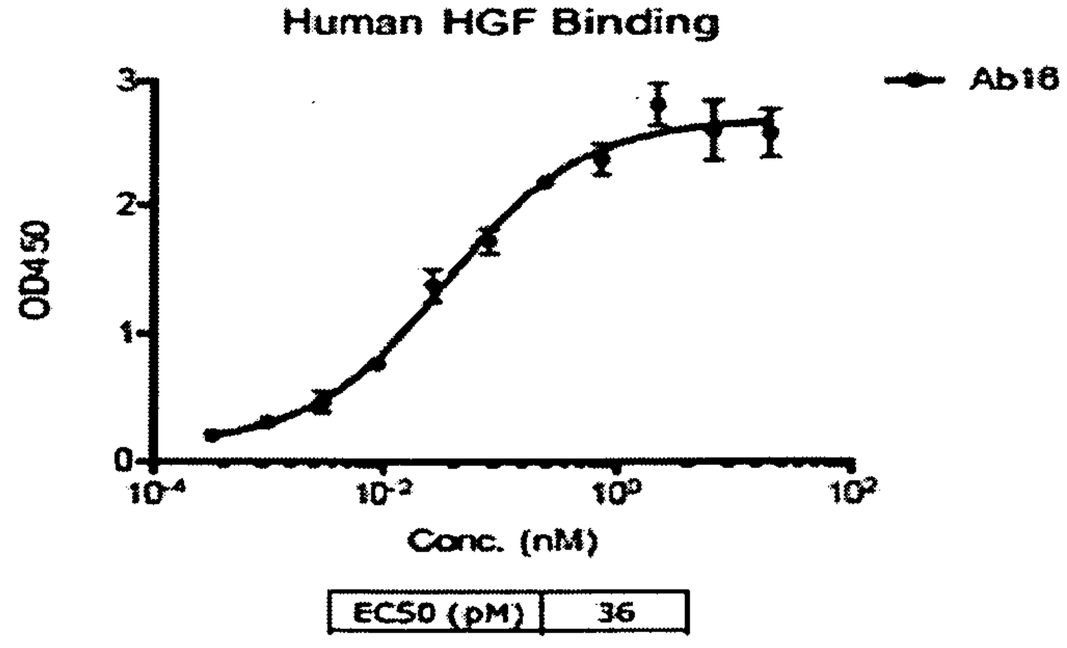

Human HGF Binding
Ab16
OD450
3
2
1
0
10-4
10-2
100
102
Conc. (nM)
EC50 (pM) 36

FIGURE 17

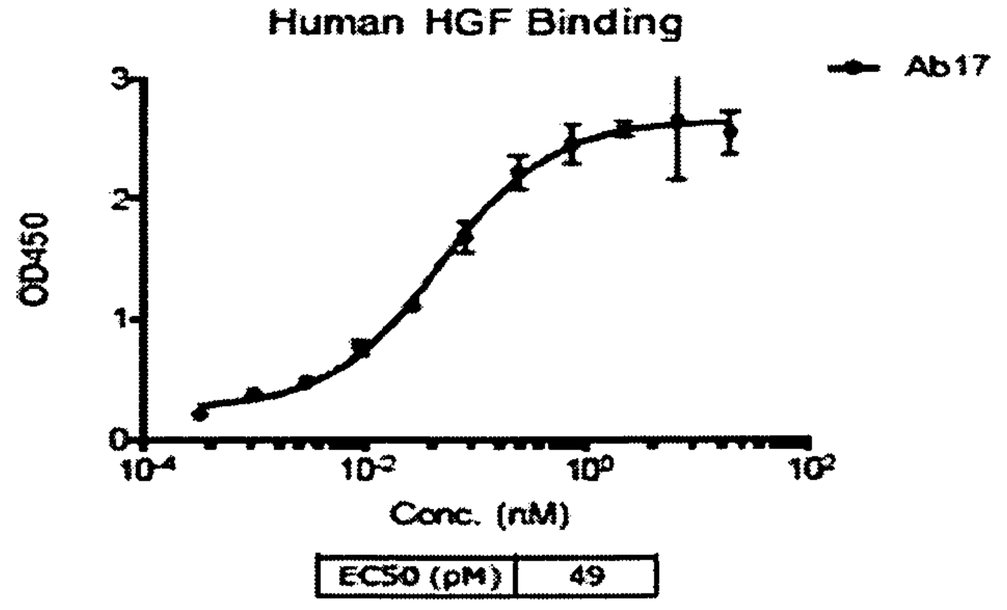

Human HGF Binding
Ab17
OD450
0
1
2
3
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 49

FIGURE 18

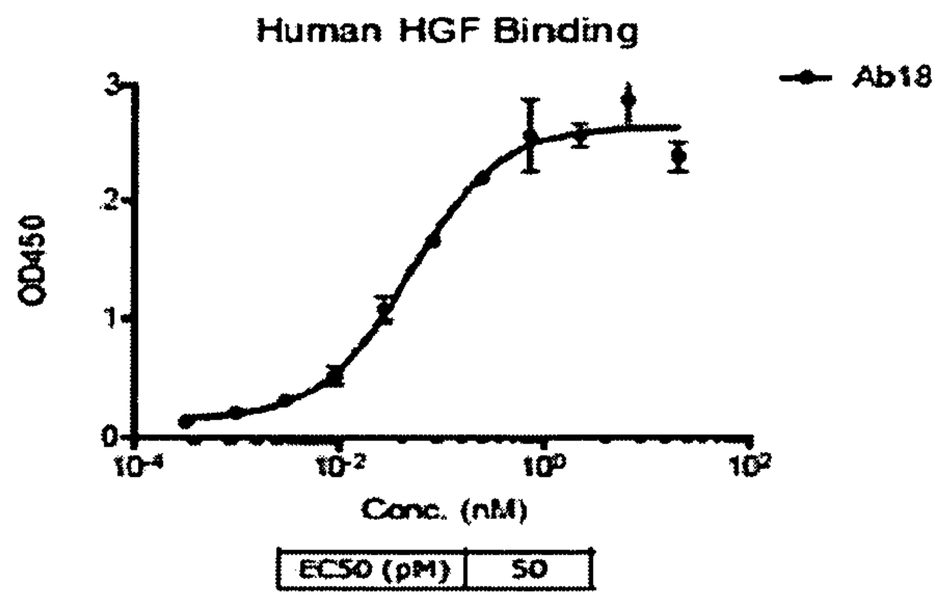

Human HGF Binding
Ab18
OD450
3
2
1
0
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 50

FIGURE 19

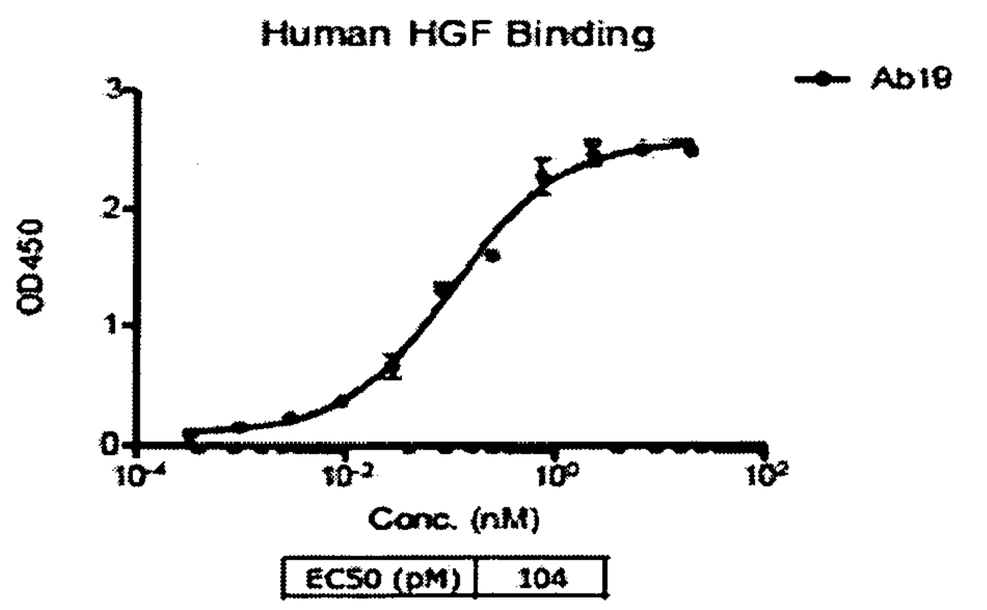

Human HGF Binding
Ab19
OD450
0
1
2
3
10-4
10-2
100
102
Conc. (nM)
EC50 (pM) 104

FIGURE 20

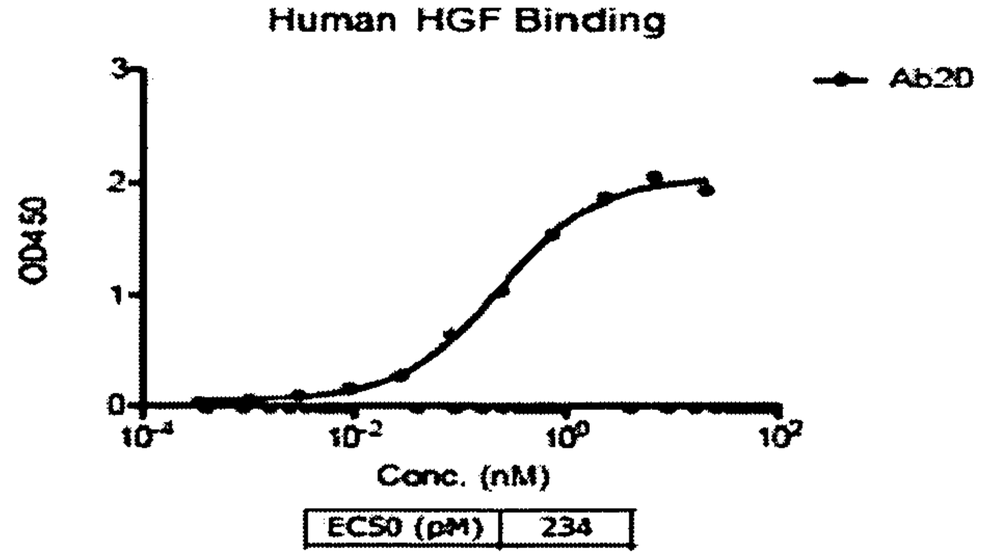

Human HGF Binding
Ab20
OD450
3
2
1
0
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM)
234

FIGURE 21

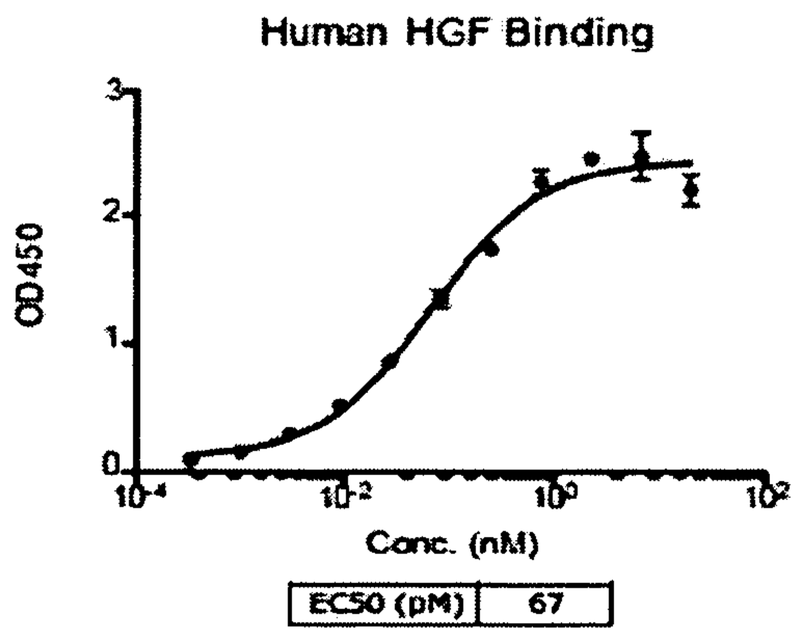


FIGURE 22

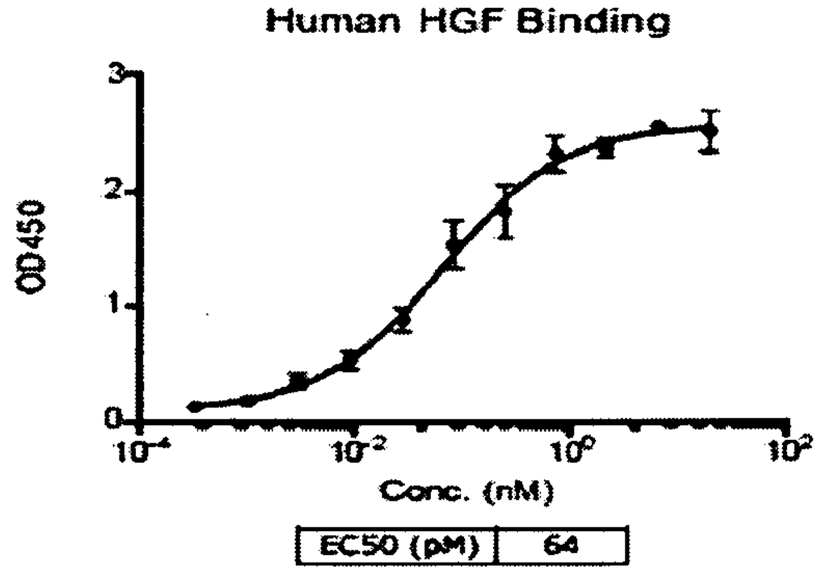

Human HGF Binding
Ab23
OD450
3
2
1
0
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 64

FIGURE 23

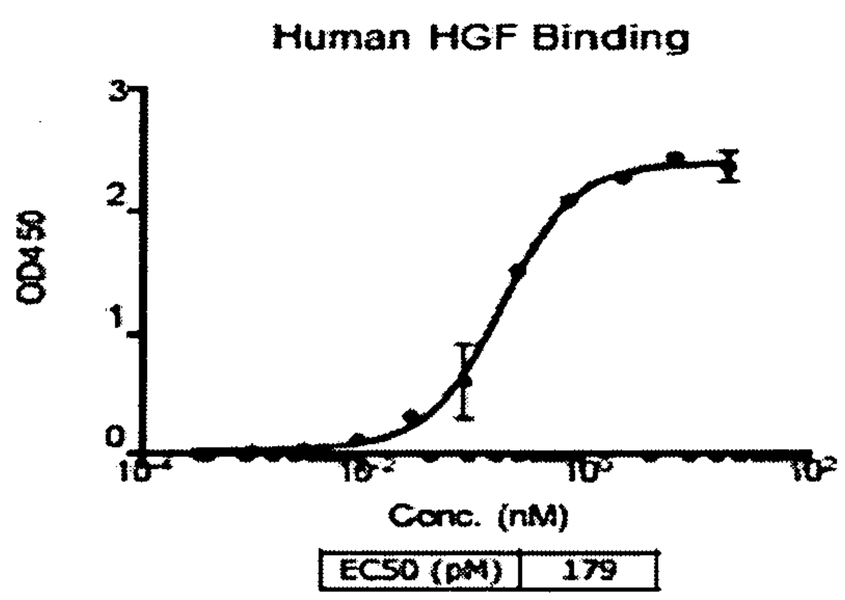

Human HGF Binding
Ab24
OD450
3
2
1
0
10⁻¹
10¹
10³
10⁵
Conc. (nM)
EC50 (pM) 179

FIGURE 24

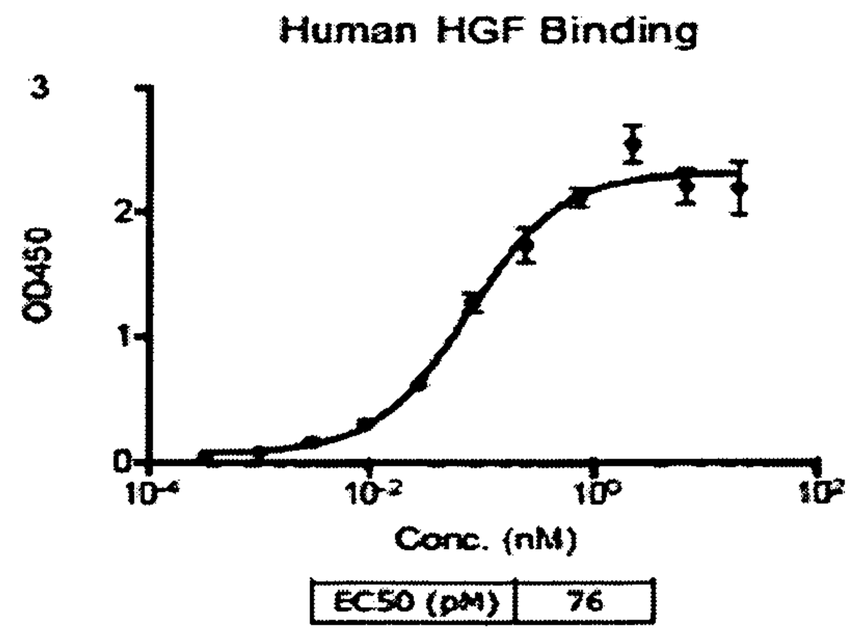

Human HGF Binding
Ab25
OD450
3
2
1
0
10⁻⁴
10⁻²
10⁰
10²
Conc. (nM)
EC50 (pM)
76

FIGURE 25

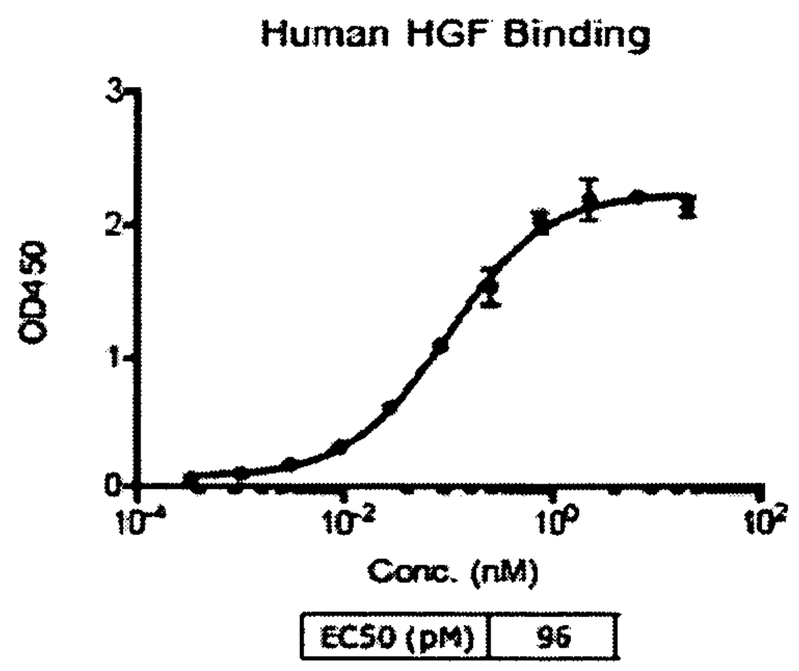

Human HGF Binding
Ab26
OD450
3
2
1
0
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 96

FIGURE 26

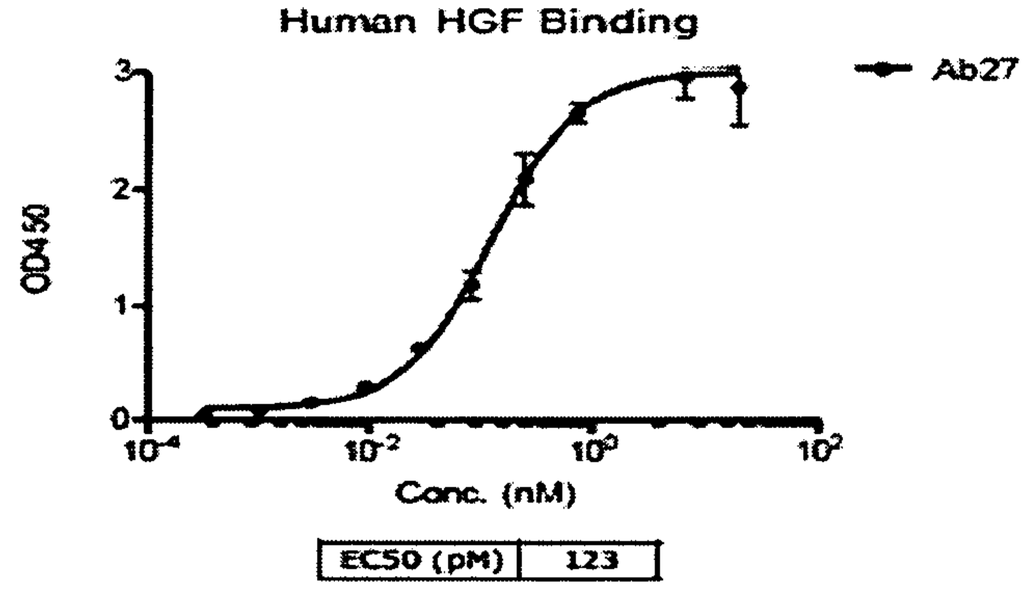

Human HGF Binding
Ab27
OD450
0
1
2
3
$10^{-4}$
$10^{-2}$
$10^{0}$
$10^{2}$
Conc. (nM)
EC50 (pM) 123

FIGURE 27

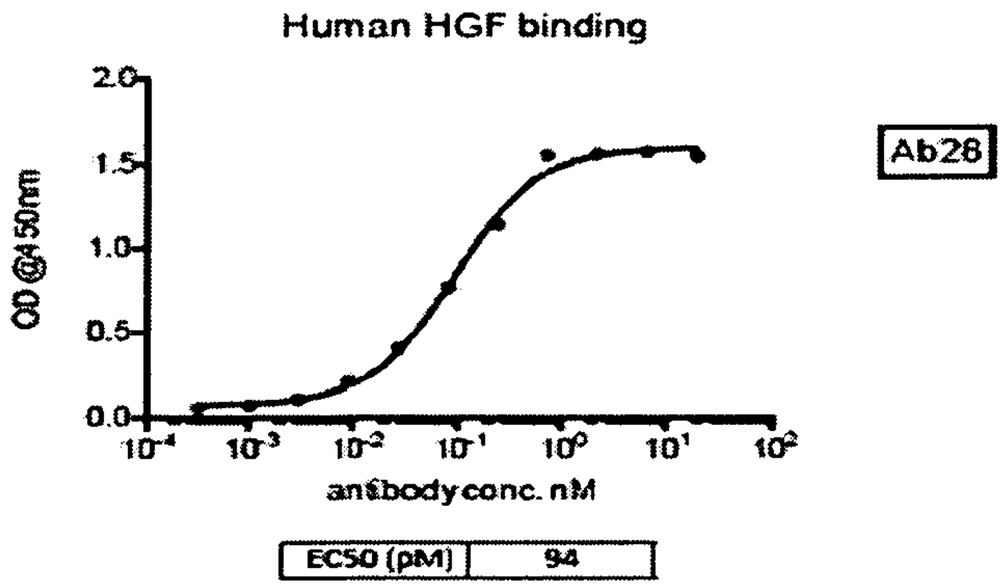
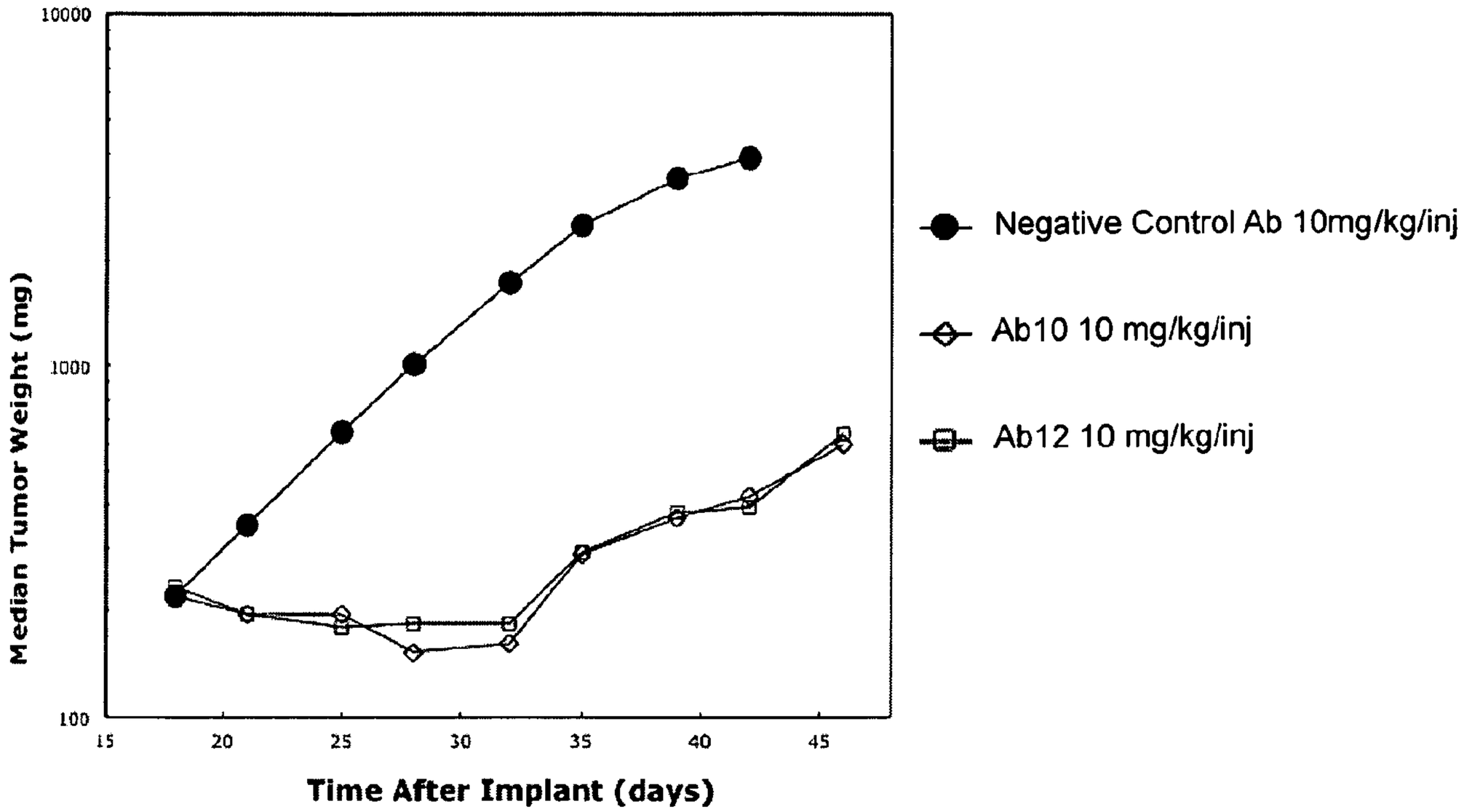

Human HGF binding
OD @450nm
2.0
1.5
1.0
0.5
0.0
$10^{-4}$
$10^{-3}$
$10^{-2}$
$10^{-1}$
$10^{0}$
$10^{1}$
$10^{2}$
antibody conc. nM
Ab28
EC50 (pM)
94

Figure 28


Response of SC U-87MG Glioma to Treatment
Median Tumor Weight (mg)
10000
1000
100
15
20
25
30
35
40
45
Time After Implant (days)
Negative Control Ab 10mg/kg/inj
Ab10 10 mg/kg/inj
Ab12 10 mg/kg/inj

# Figure 29

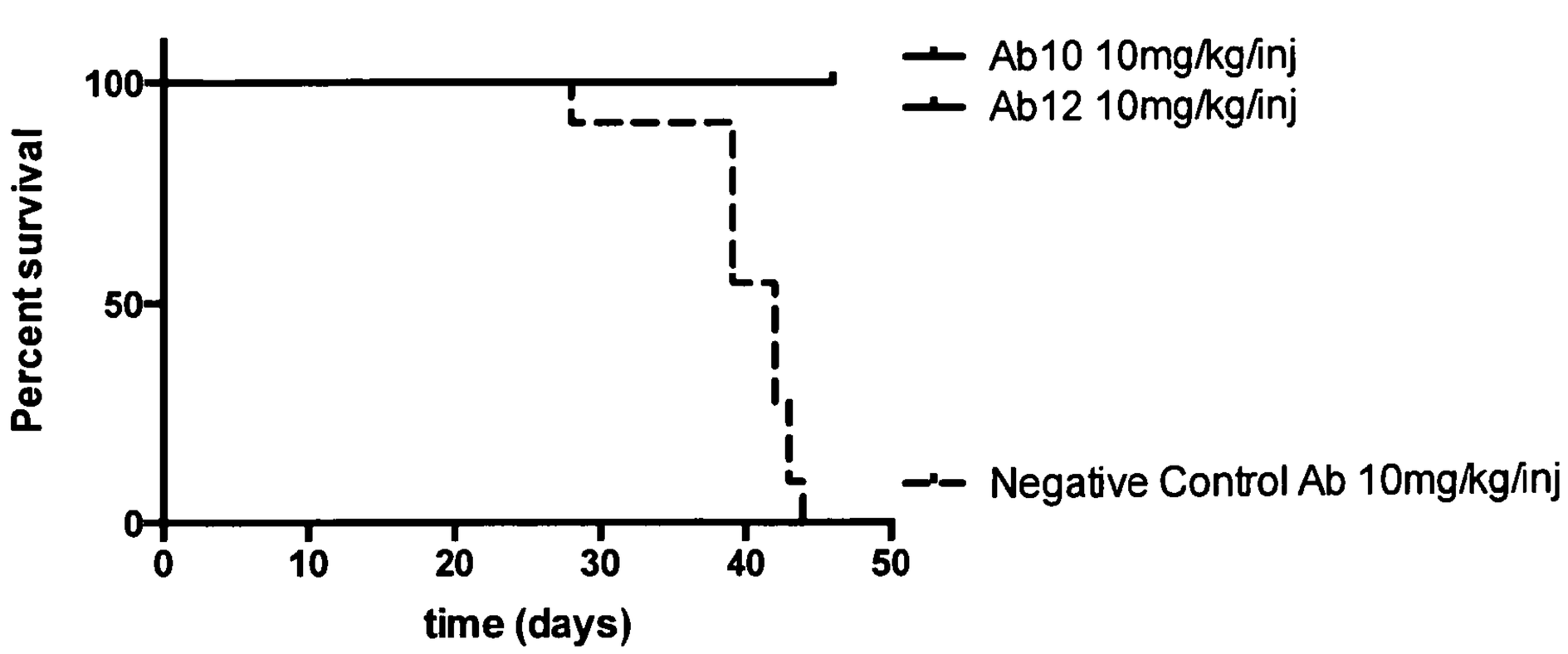
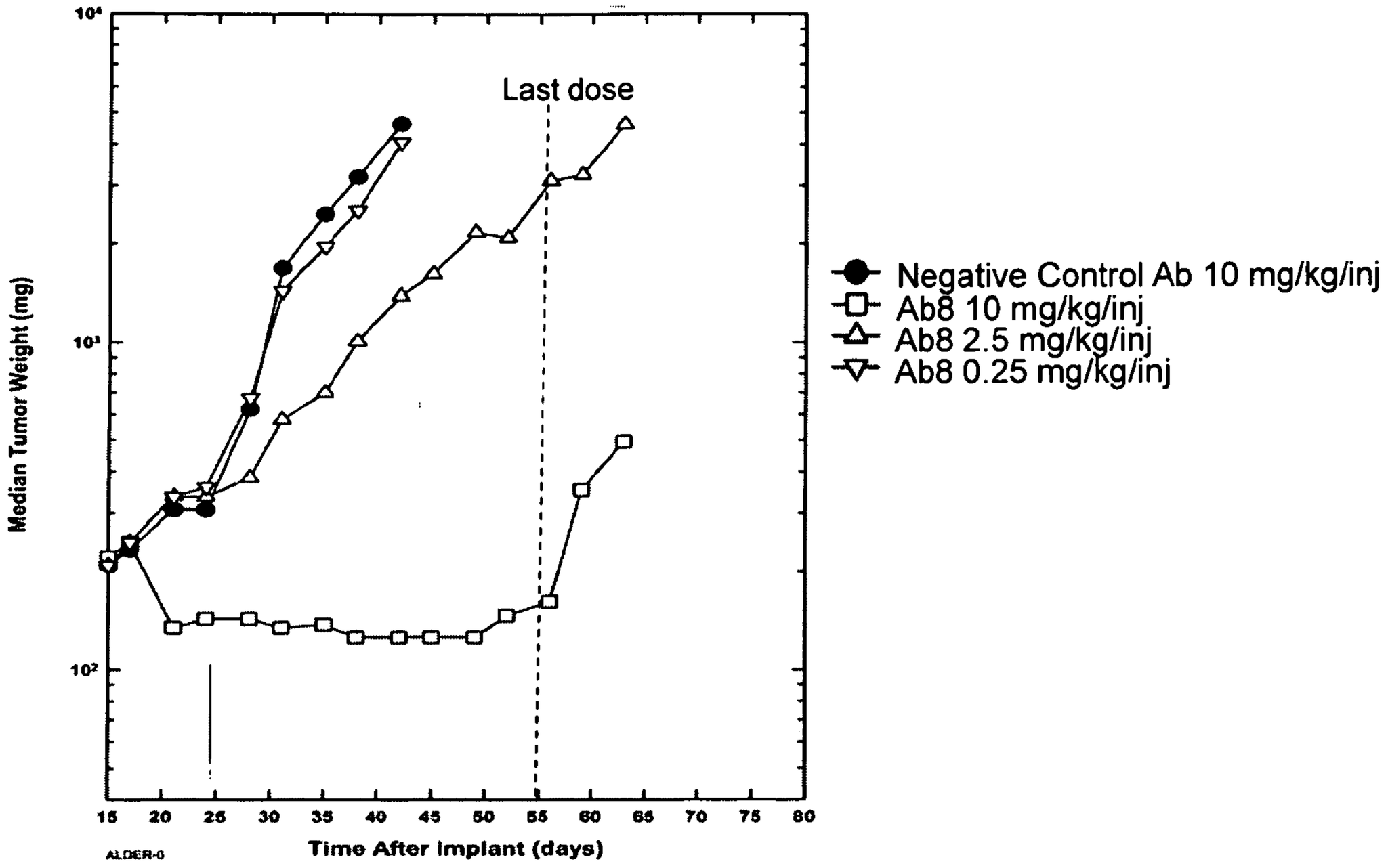
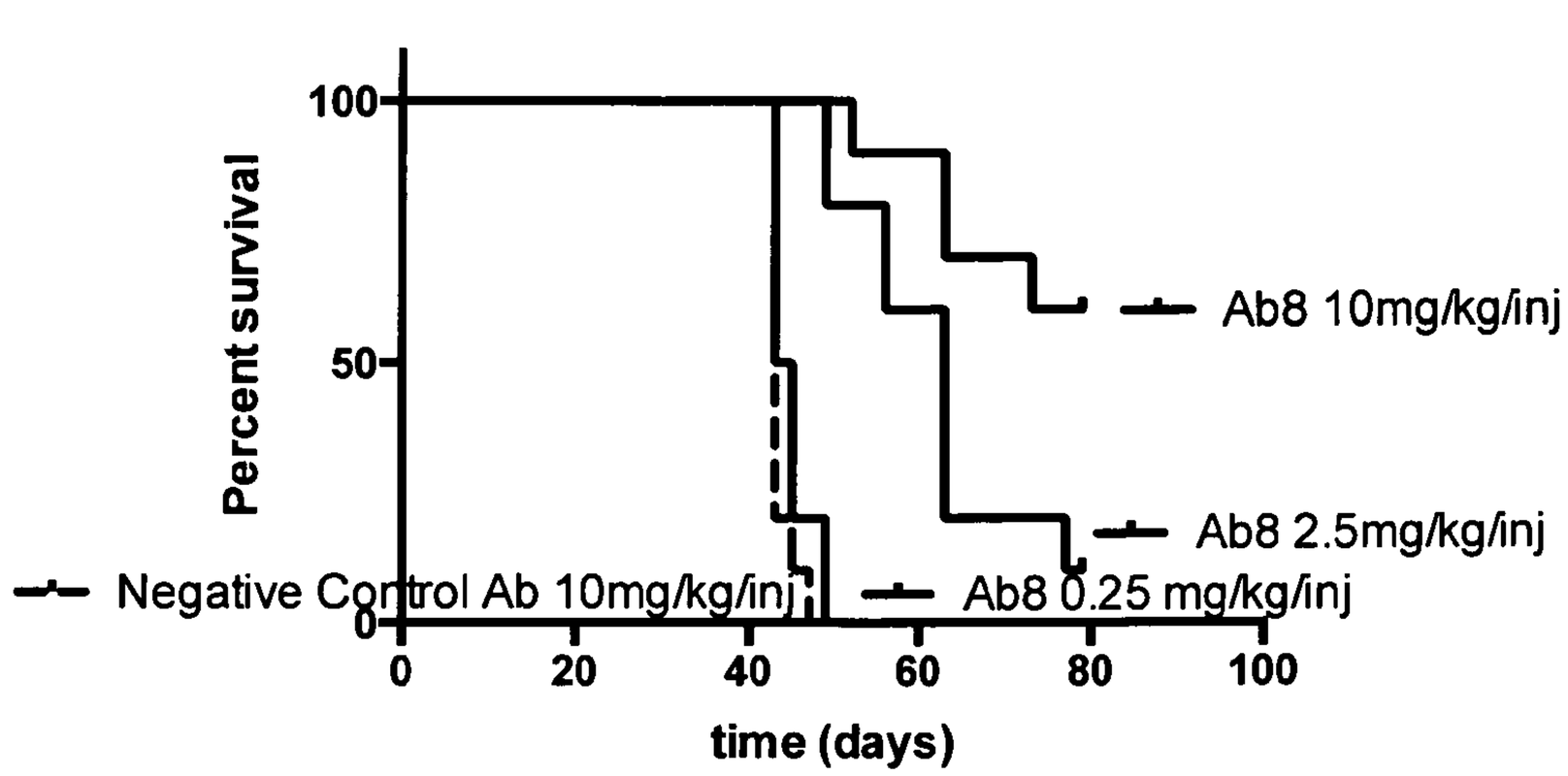

Survival proportions: SC U-87MG Glioma
Percent survival
100
50
0
0
10
20
30
40
50
time (days)
Ab10 10mg/kg/inj
Ab12 10mg/kg/inj
Negative Control Ab 10mg/kg/inj

**Figure 30**


Last dose
Median Tumor Weight (mg)
$10^4$
$10^3$
$10^2$
15
20
25
30
35
40
45
50
55
60
65
70
75
80
Time After Implant (days)
ALDER-6
Negative Control Ab 10 mg/kg/inj
Ab8 10 mg/kg/inj
Ab8 2.5 mg/kg/inj
Ab8 0.25 mg/kg/inj

# Figure 31


Survival proportions: SC U-87MG Glioma
Percent survival
100
50
0
0
20
40
60
80
100
time (days)
Ab8 10mg/kg/inj
Ab8 2.5mg/kg/inj
Ab8 0.25 mg/kg/inj
Negative Control Ab 10mg/kg/inj

# Figure 32

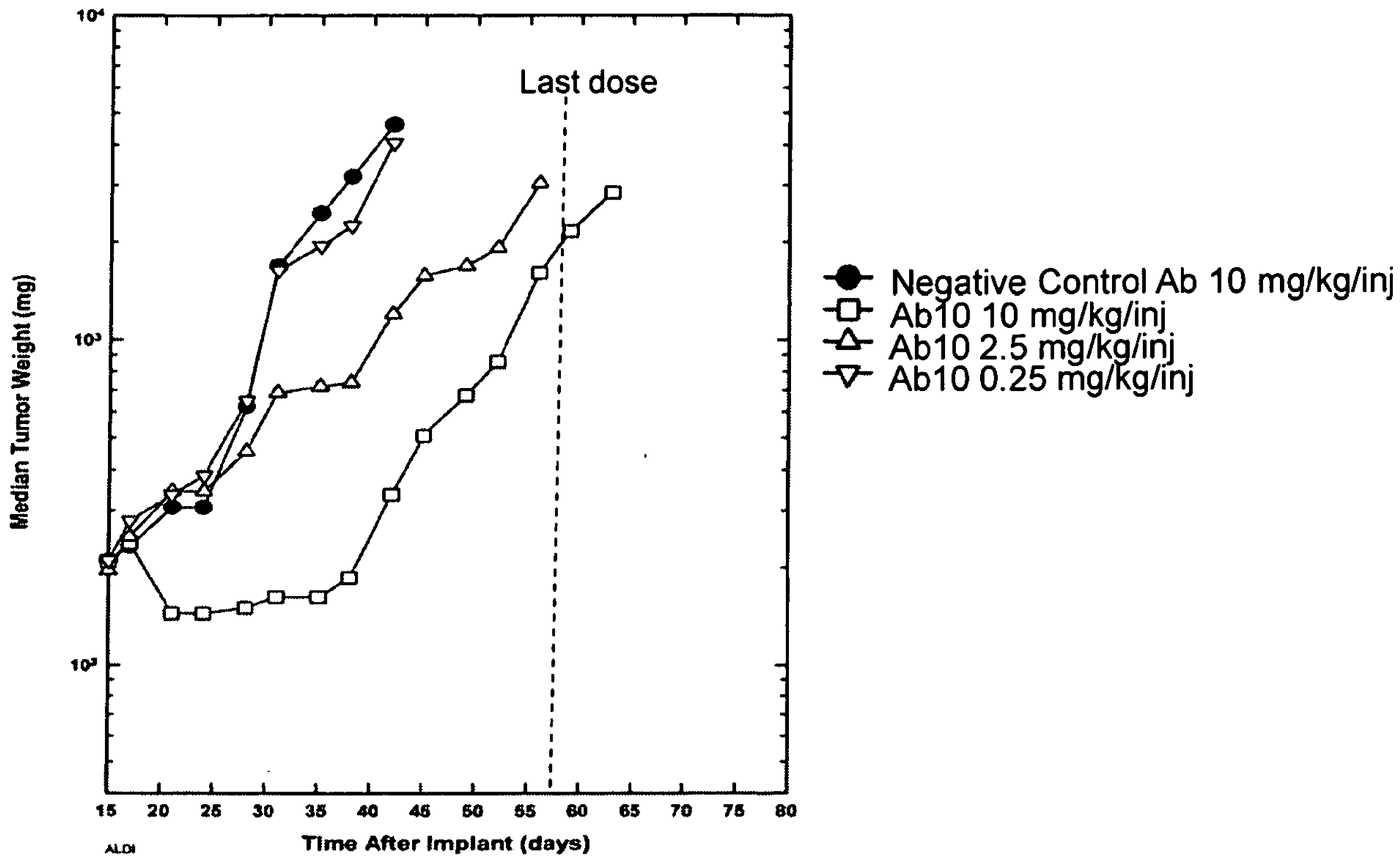

Last dose
Median Tumor Weight (mg)
Time After Implant (days)
Negative Control Ab 10 mg/kg/inj
Ab10 10 mg/kg/inj
Ab10 2.5 mg/kg/inj
Ab10 0.25 mg/kg/inj

**Figure 33**

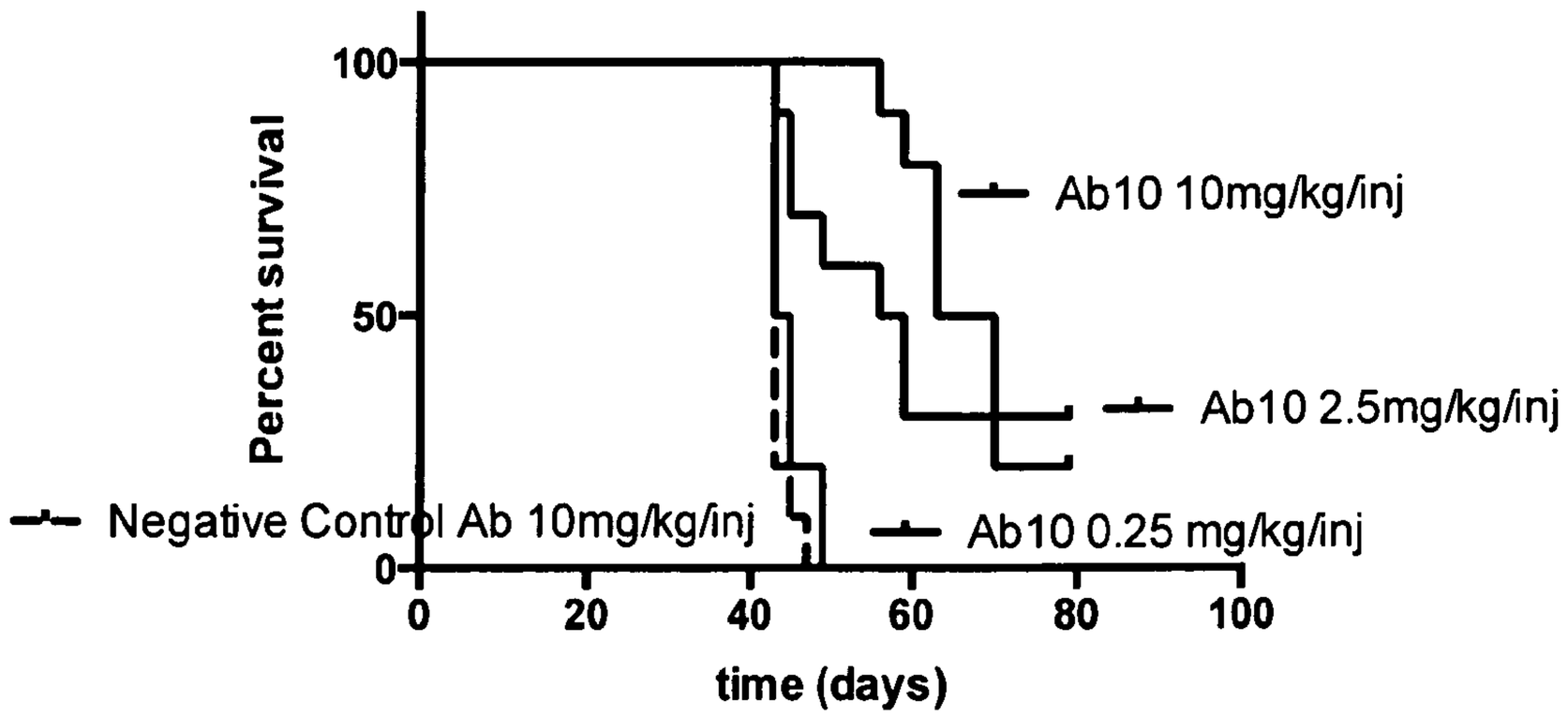
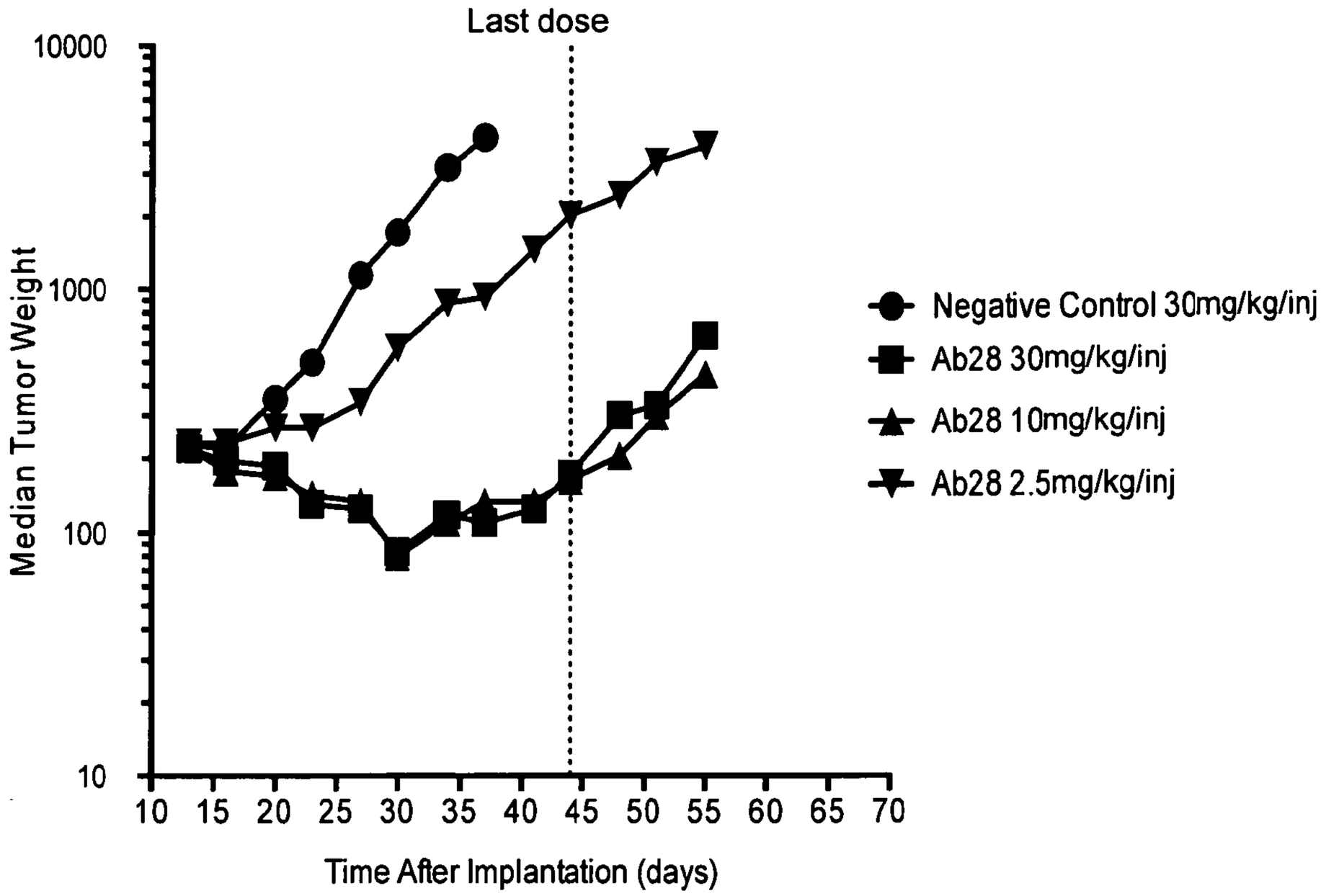

Survival proportions: Survival of Ab10
Percent survival
100
50
0
0
20
40
60
80
100
time (days)
Ab10 10mg/kg/inj
Ab10 2.5mg/kg/inj
Ab10 0.25 mg/kg/inj
Negative Control Ab 10mg/kg/inj

**Figure 34**


Last dose
10000
1000
100
10
Median Tumor Weight
10 15 20 25 30 35 40 45 50 55 60 65 70
Time After Implantation (days)
Negative Control 30mg/kg/inj
Ab28 30mg/kg/inj
Ab28 10mg/kg/inj
Ab28 2.5mg/kg/inj

# Figure 35

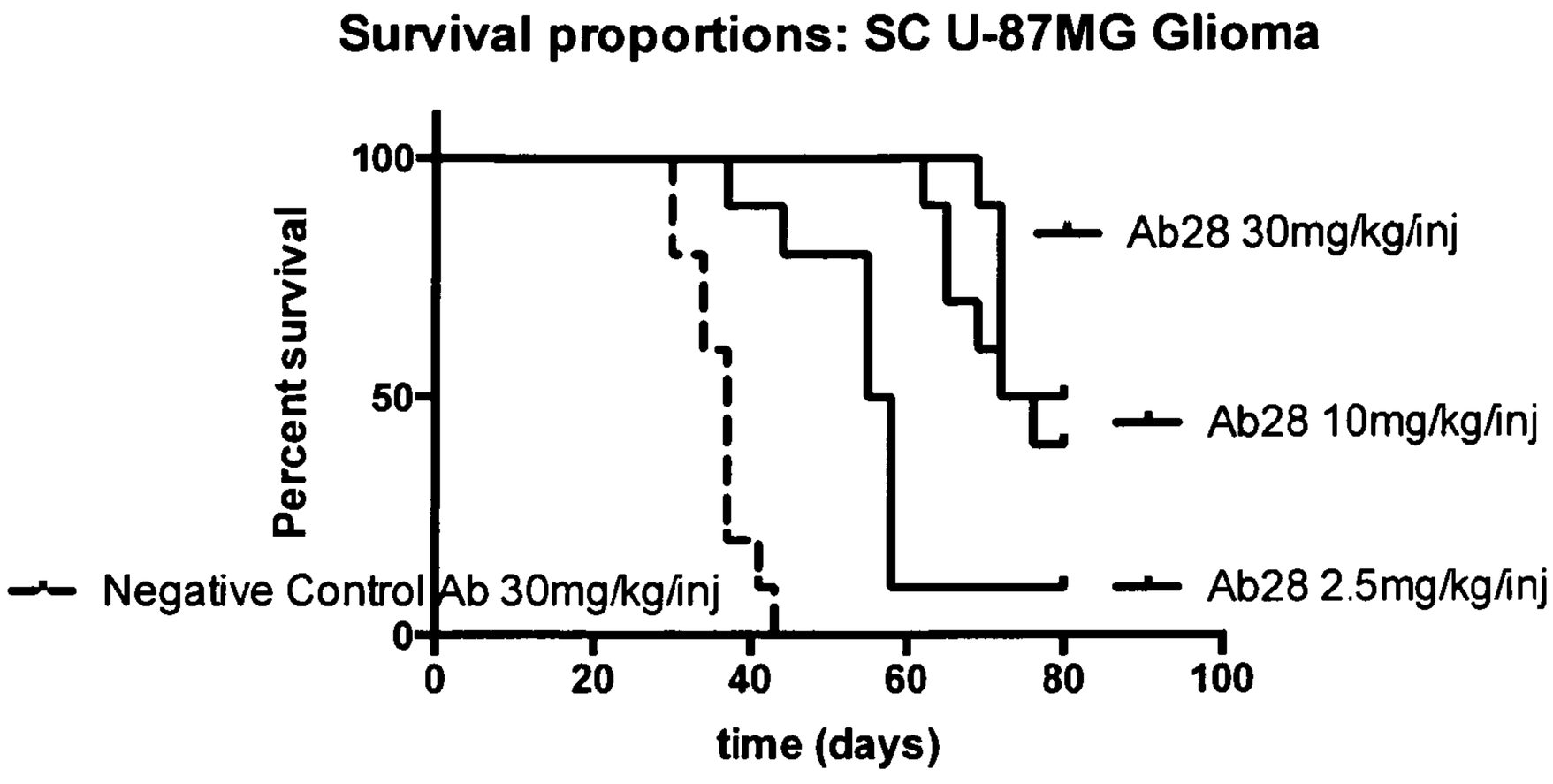
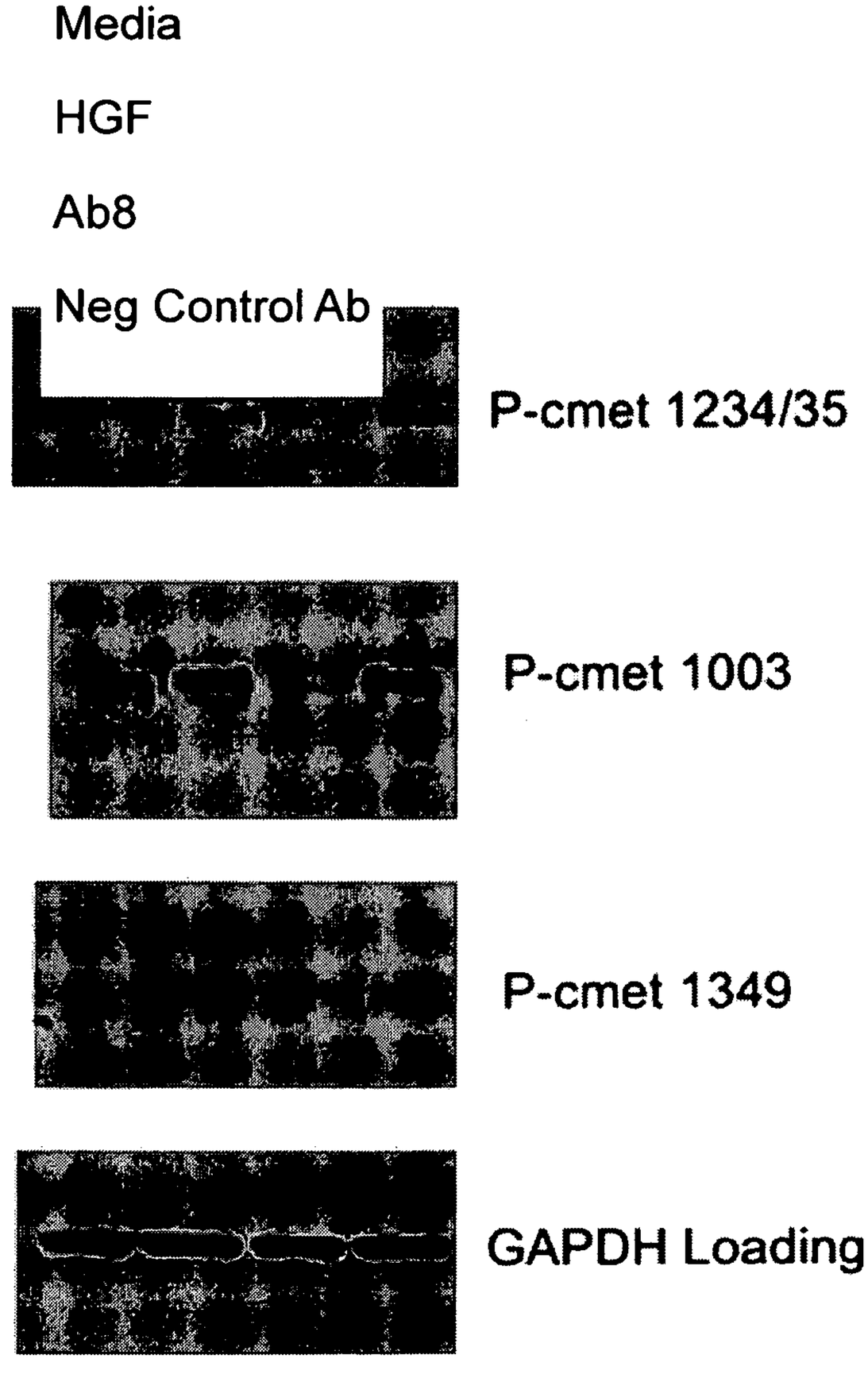
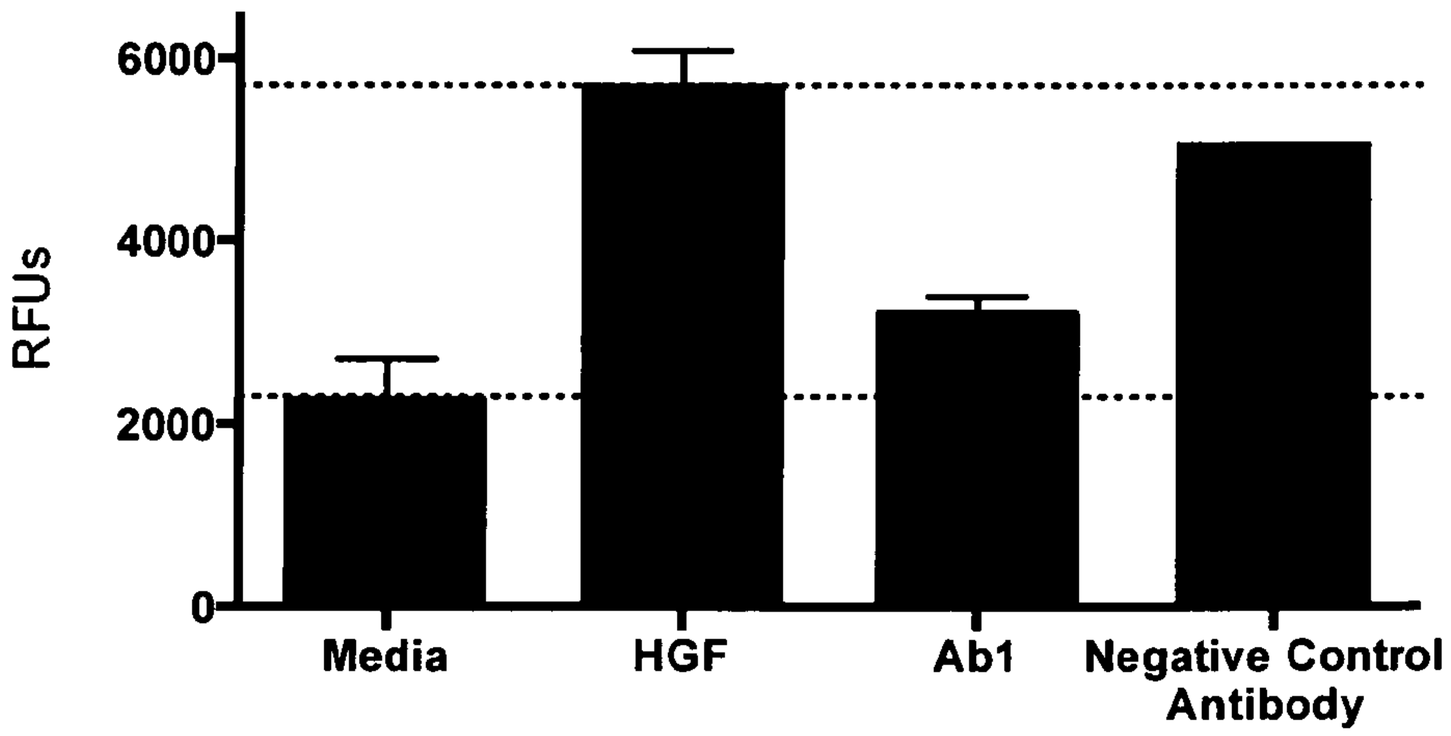

Survival proportions: SC U-87MG Glioma
Percent survival
100
50
0
0
20
40
60
80
100
time (days)
Negative Control Ab 30mg/kg/inj
Ab28 30mg/kg/inj
Ab28 10mg/kg/inj
Ab28 2.5mg/kg/inj

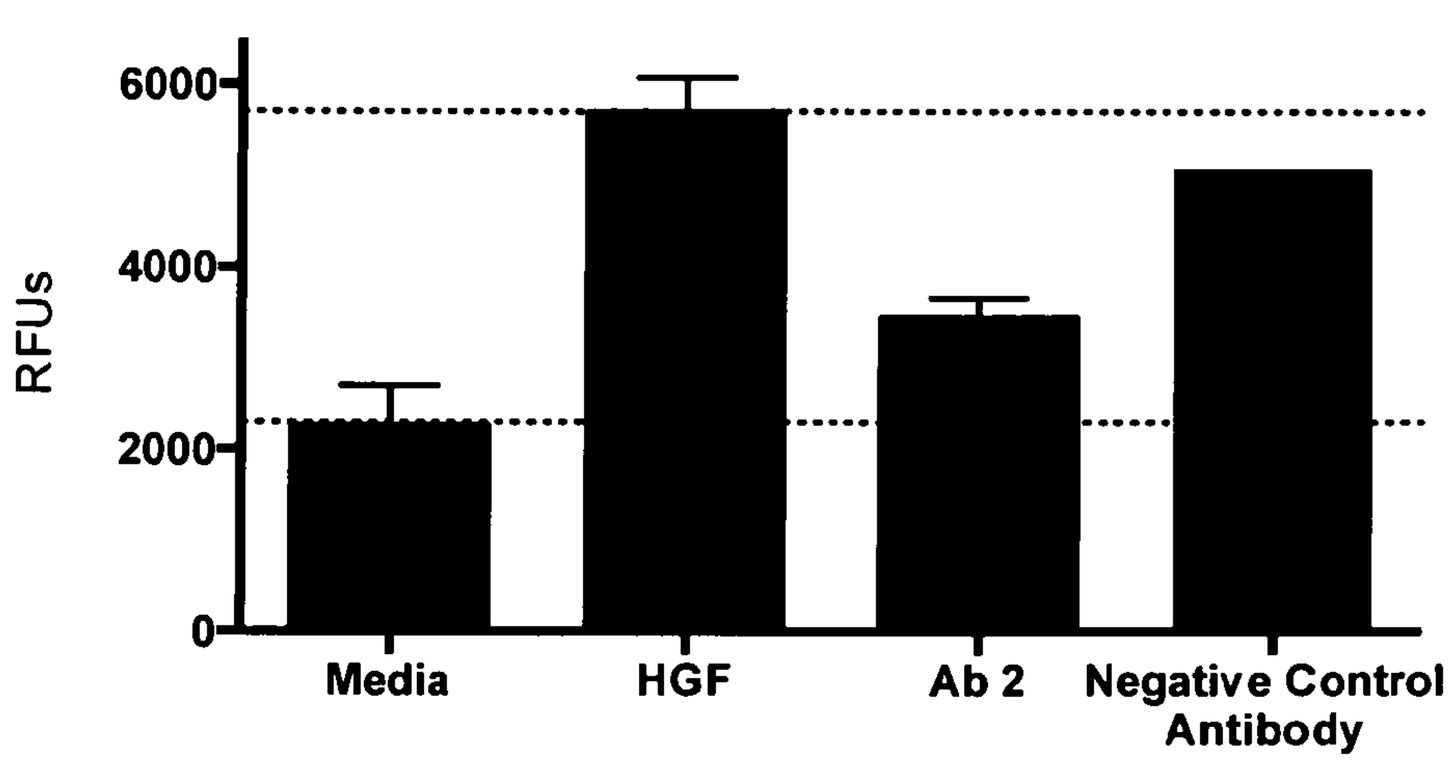
**Figure 36**


Media
HGF
Ab8
Neg Control Ab
P-cmet 1234/35
P-cmet 1003
P-cmet 1349
GAPDH Loading

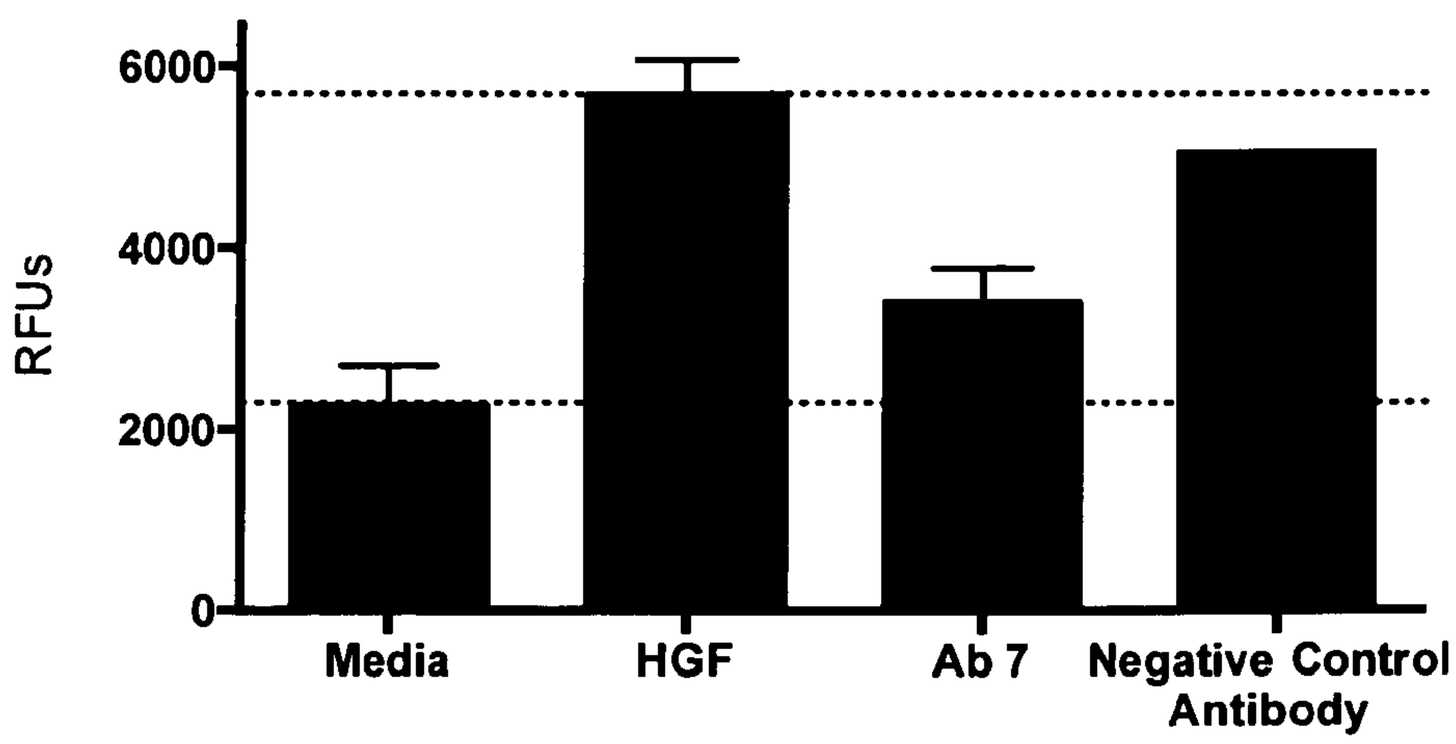
# Figure 37


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab1
Negative Control Antibody

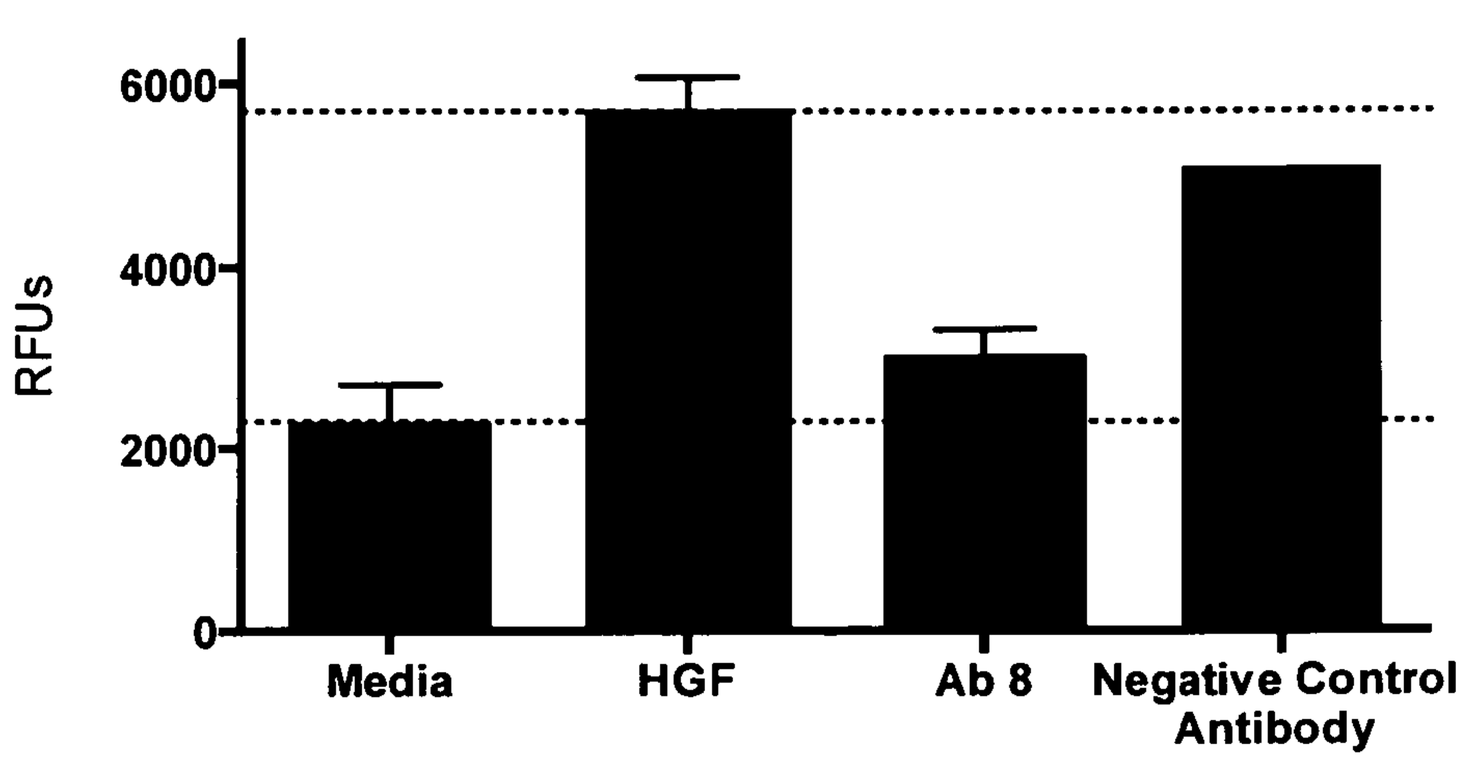
# Figure 38


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 2
Negative Control Antibody

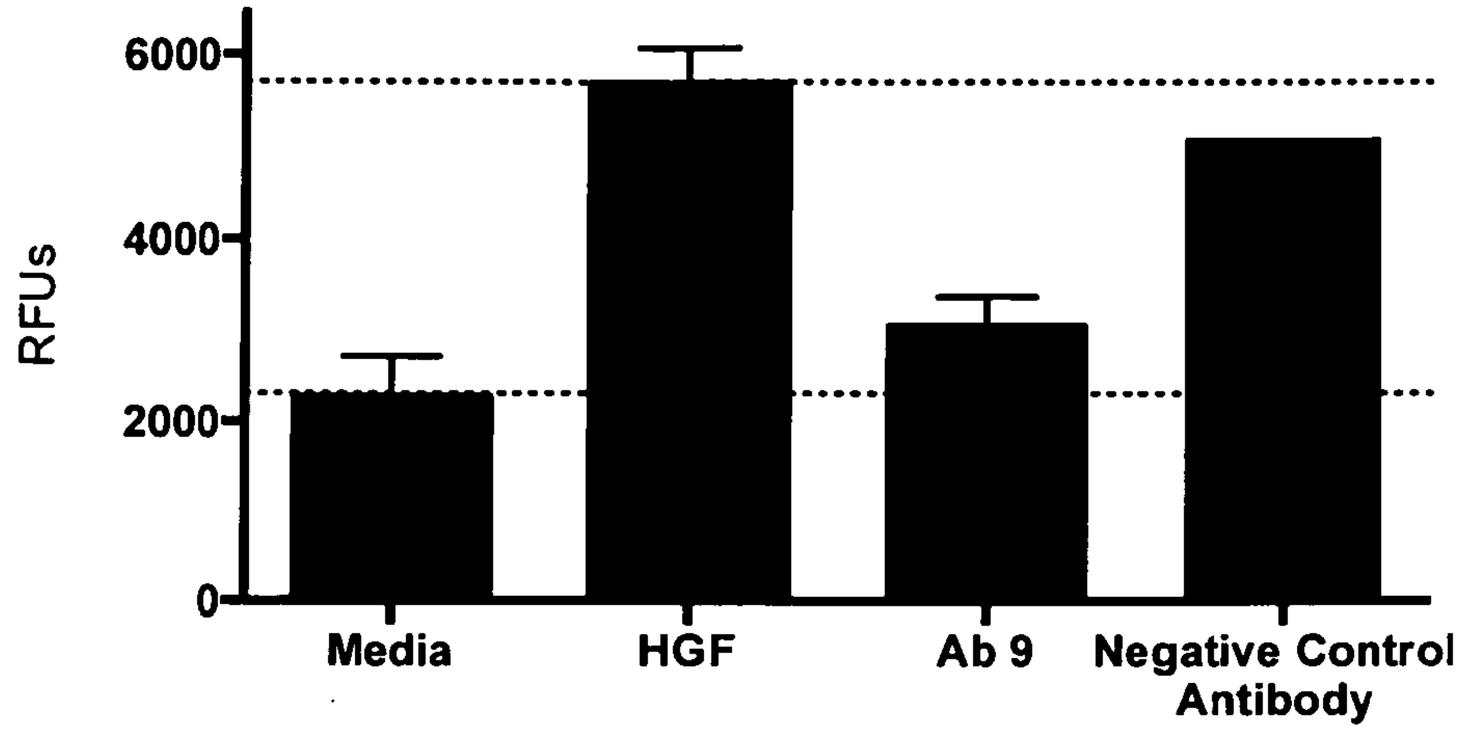
# Figure 39


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 7
Negative Control Antibody

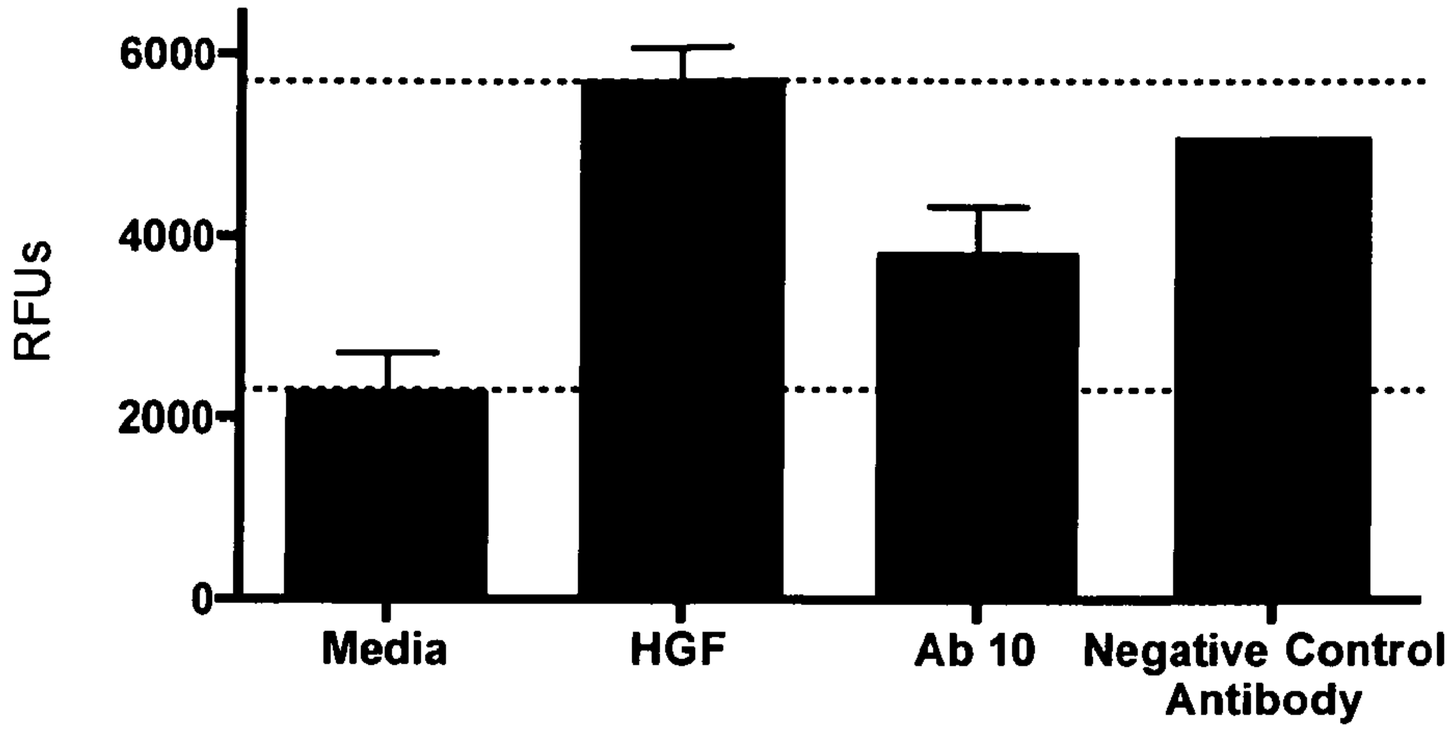
# Figure 40


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 8
Negative Control Antibody

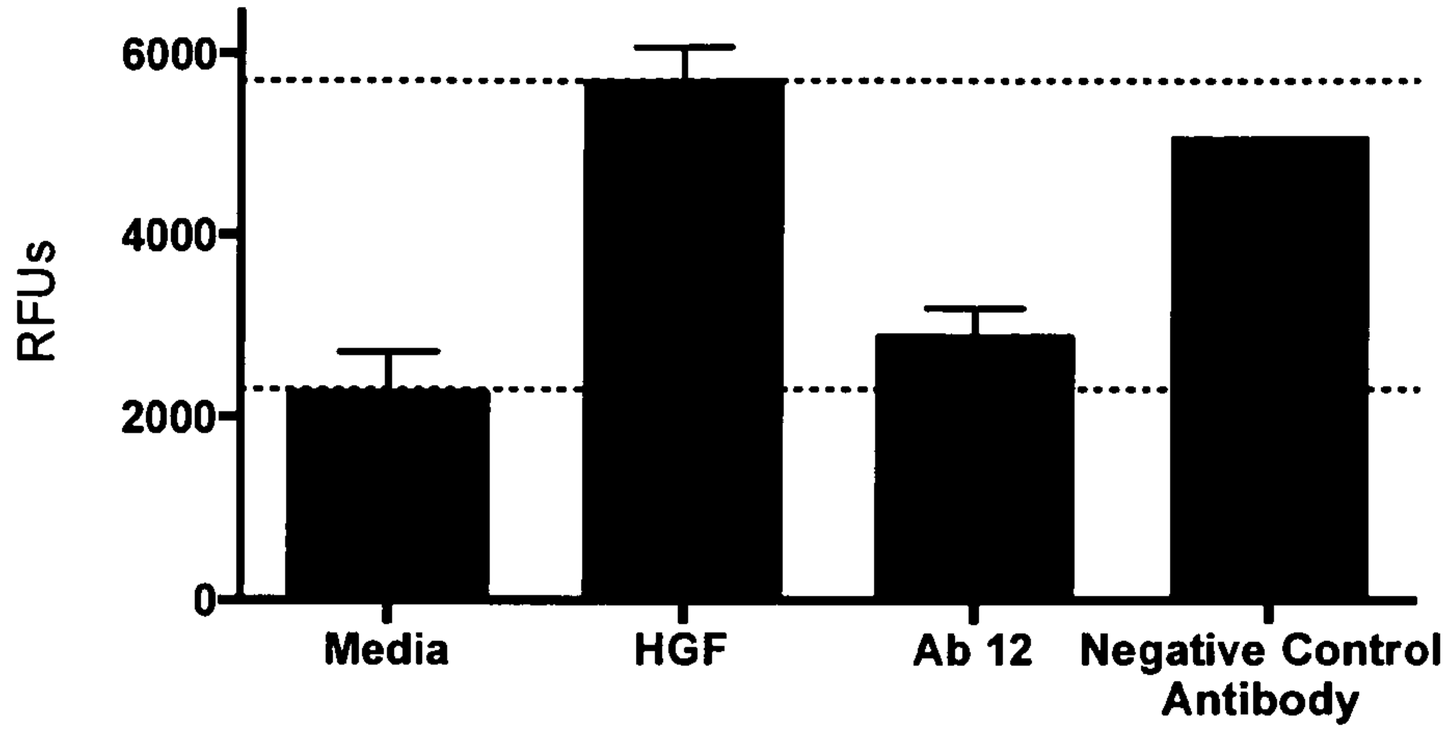
# Figure 41


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 9
Negative Control Antibody

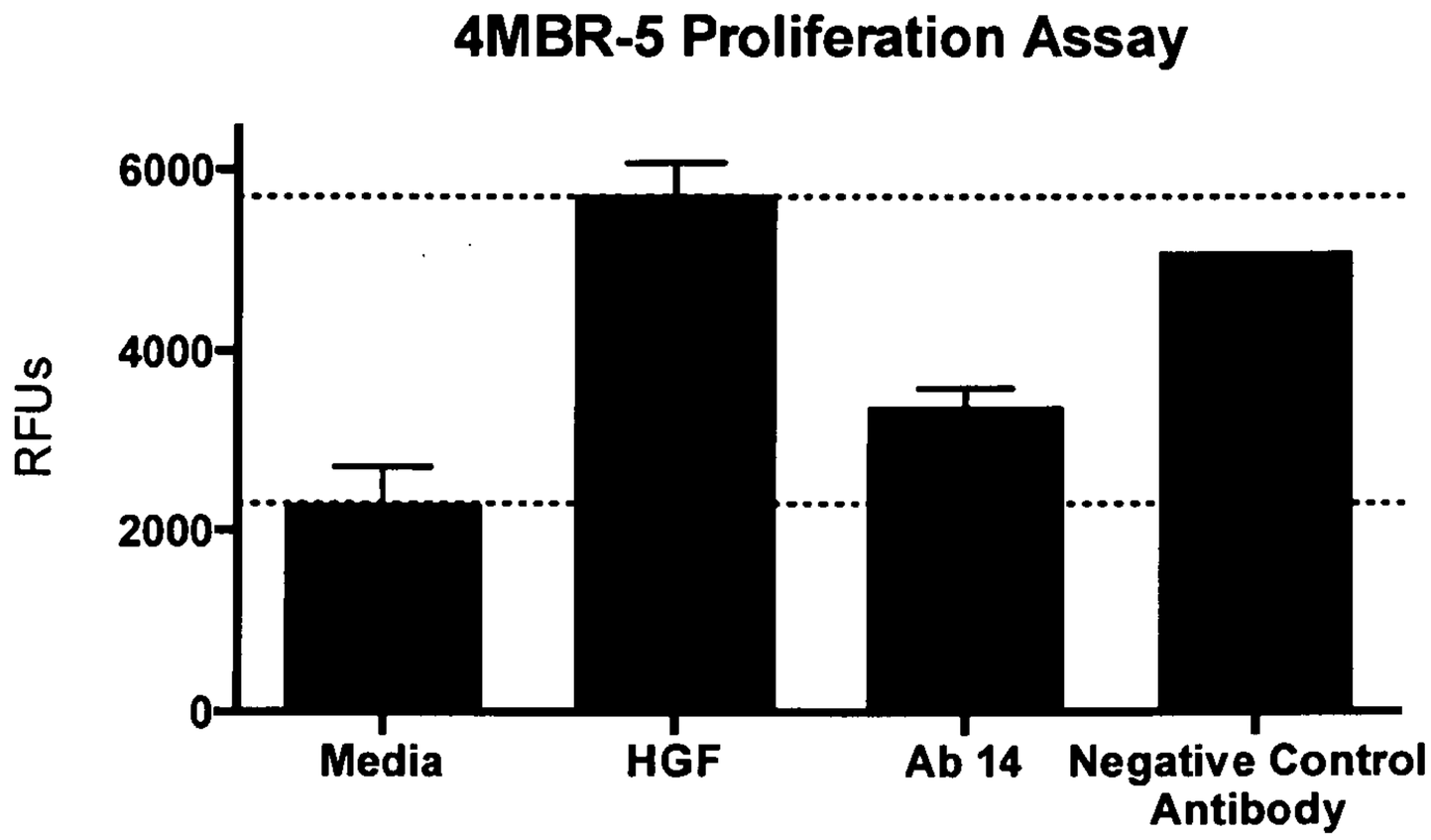
# Figure 42


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 10
Negative Control Antibody

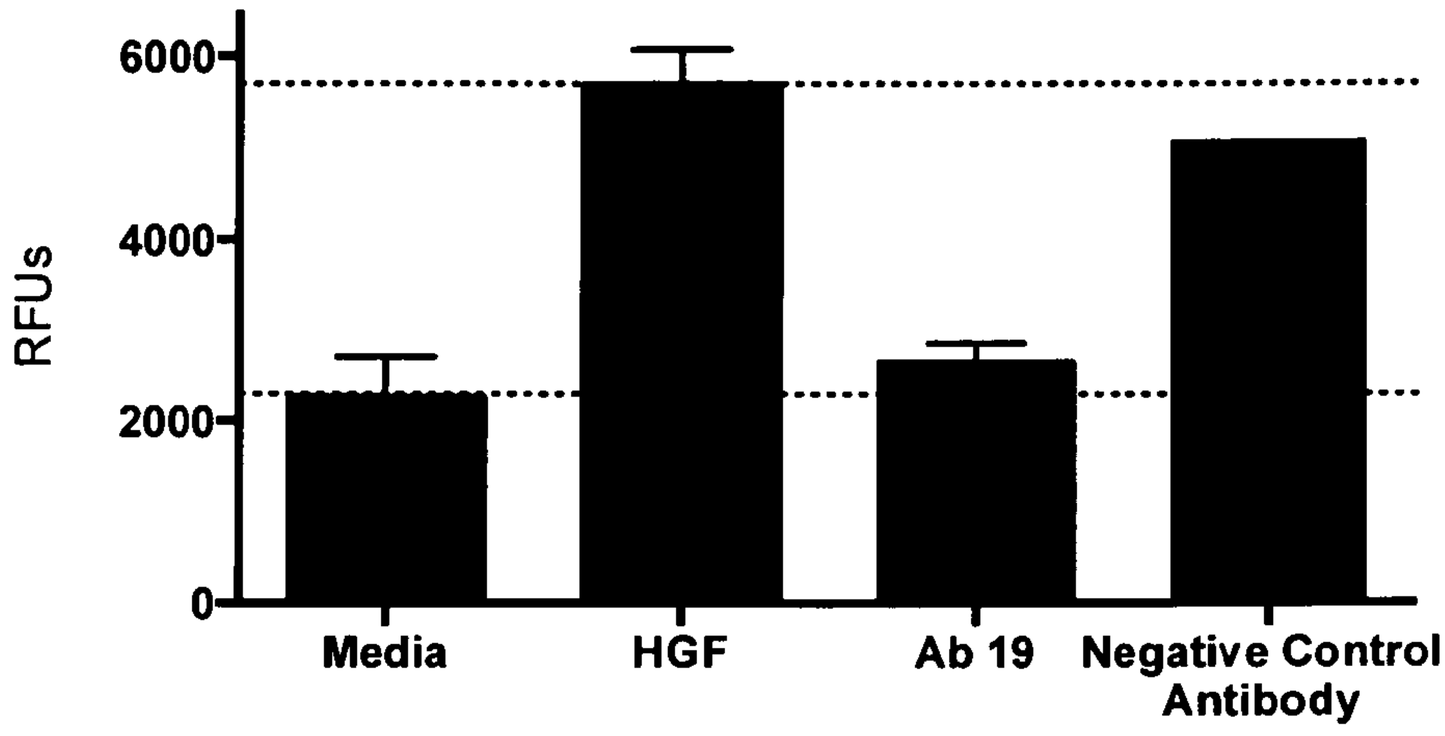
# Figure 43


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 12
Negative Control Antibody

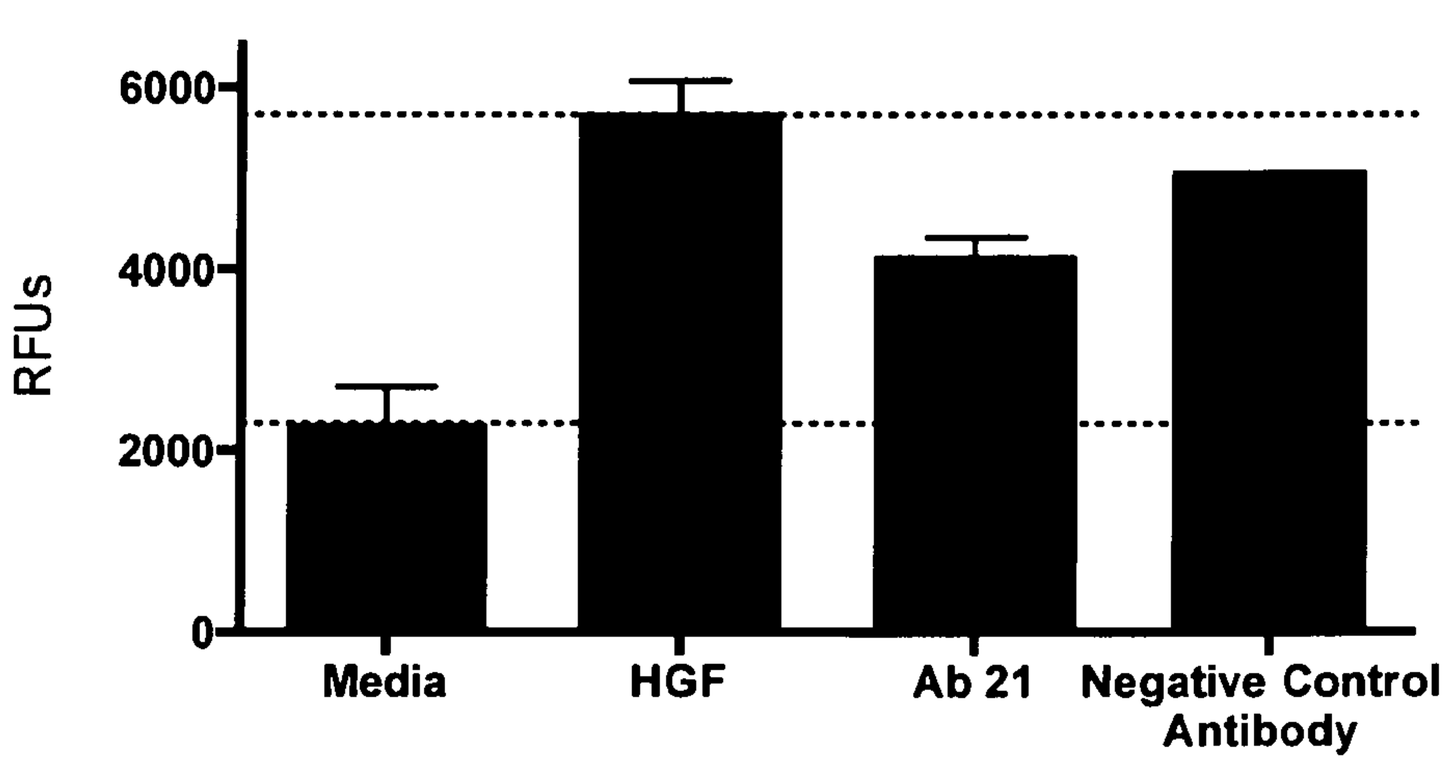
## Figure 44


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 14
Negative Control Antibody

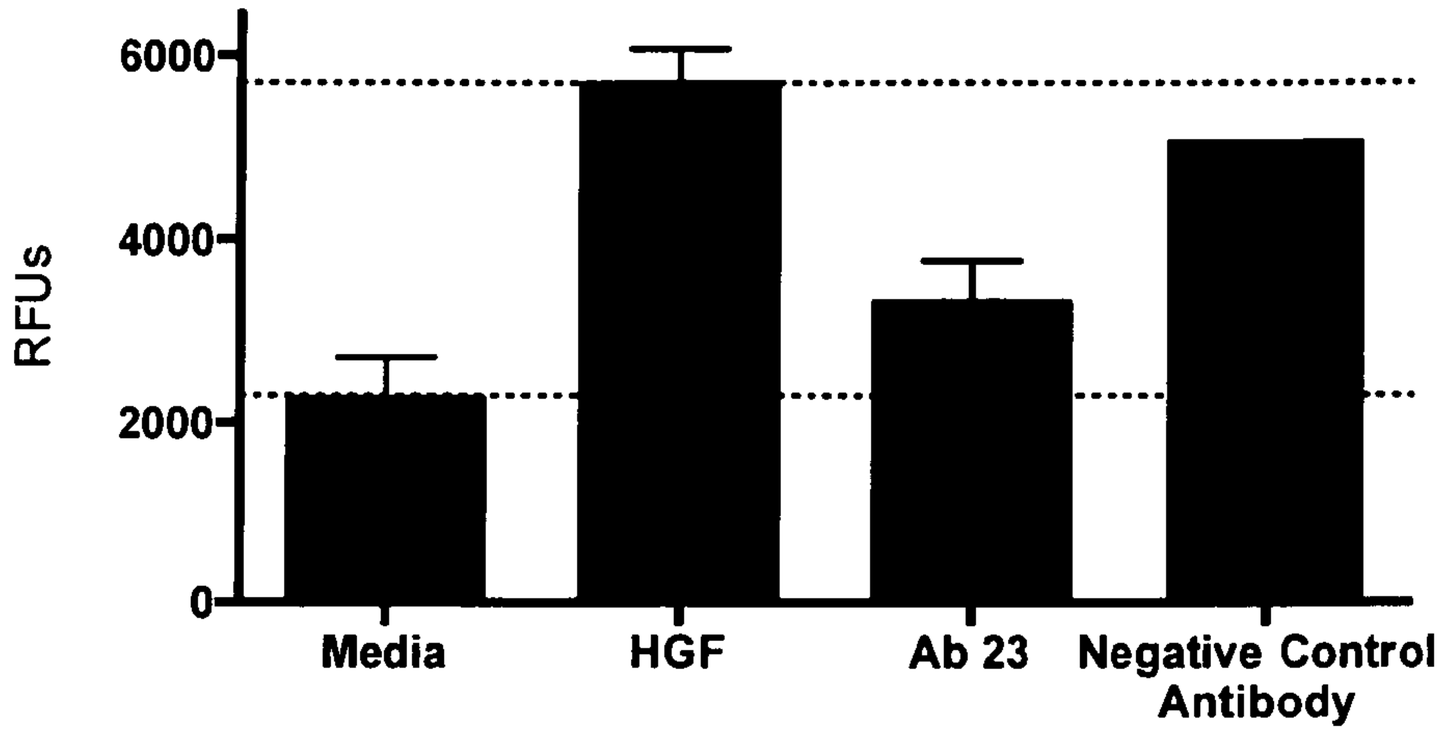
# Figure 45


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 19
Negative Control Antibody

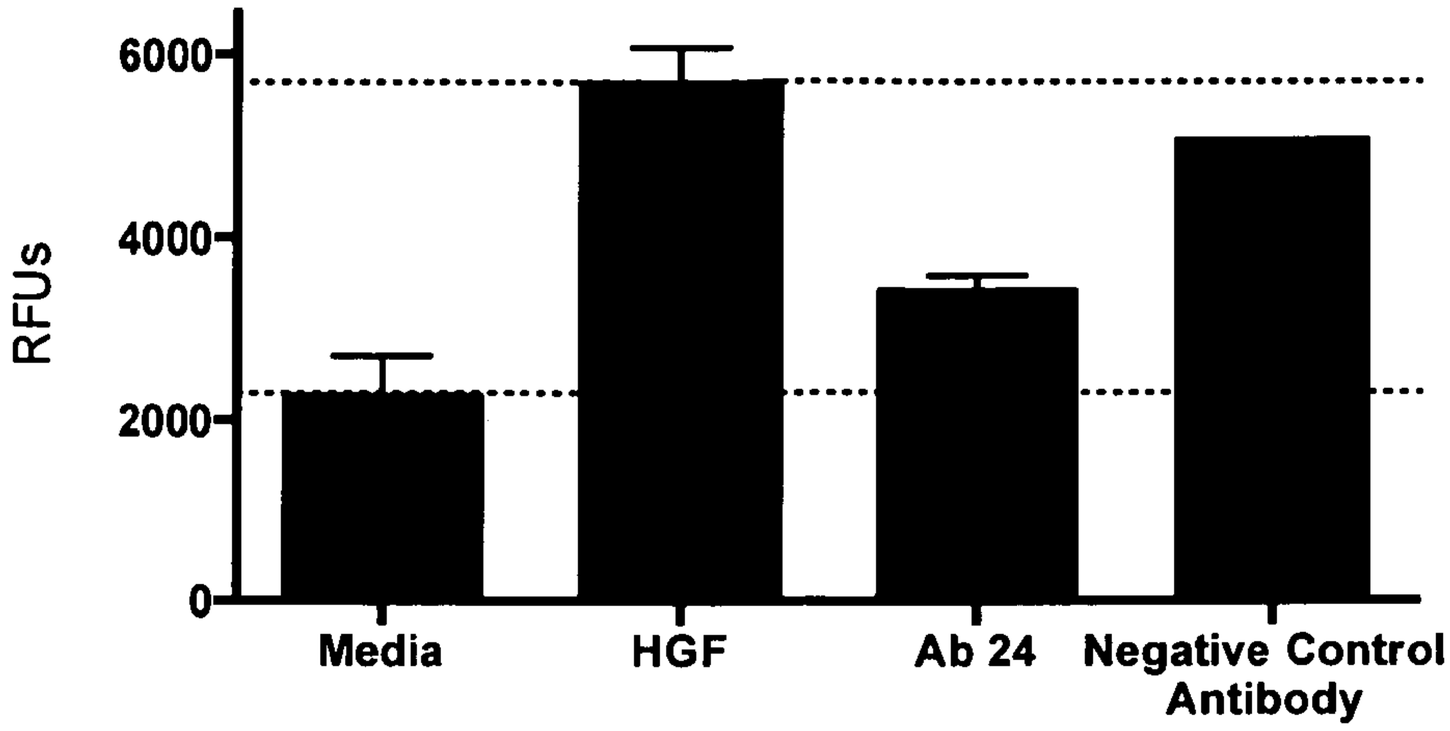
# Figure 46


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 21
Negative Control Antibody

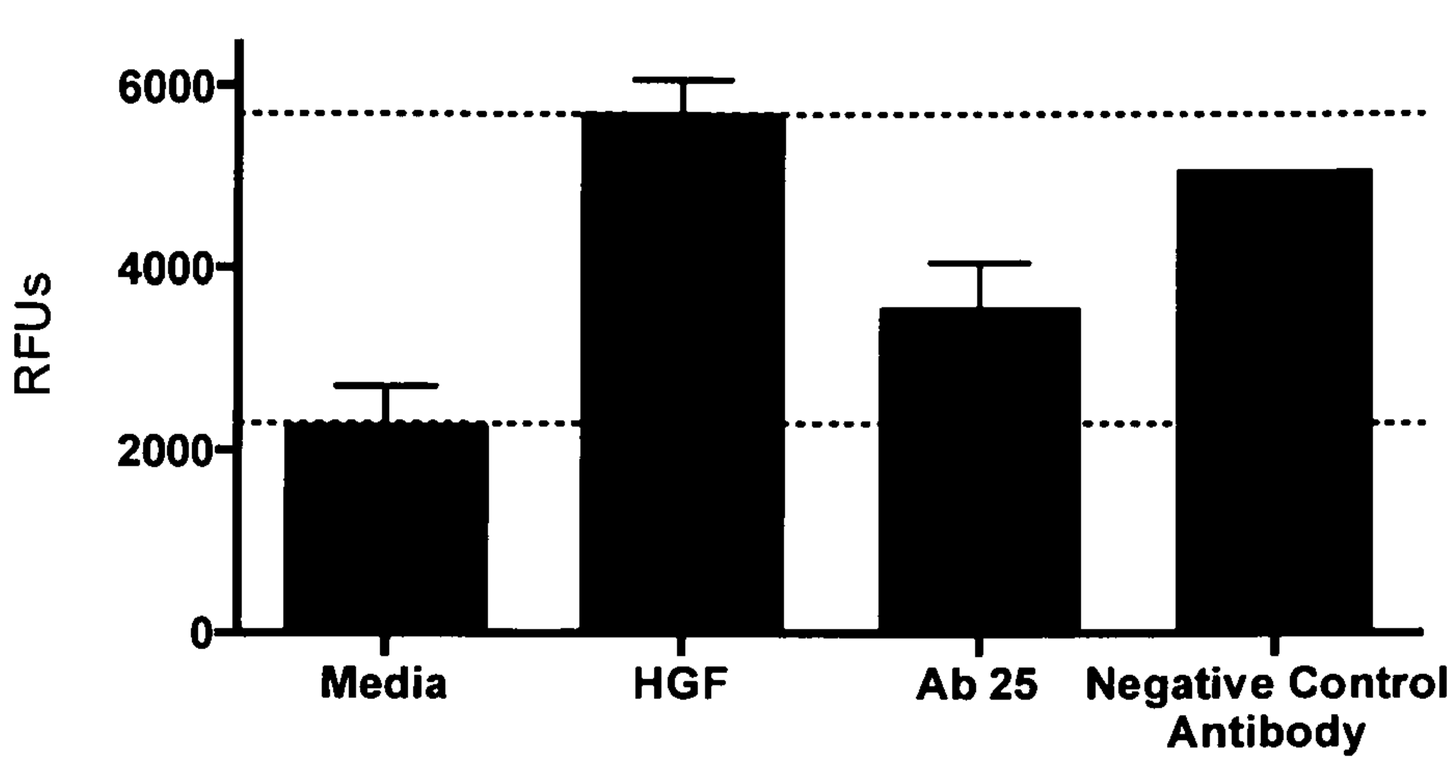
# Figure 47


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 23
Negative Control Antibody

# Figure 48


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 24
Negative Control Antibody

# Figure 49


4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab 25
Negative Control Antibody

# Figure 50

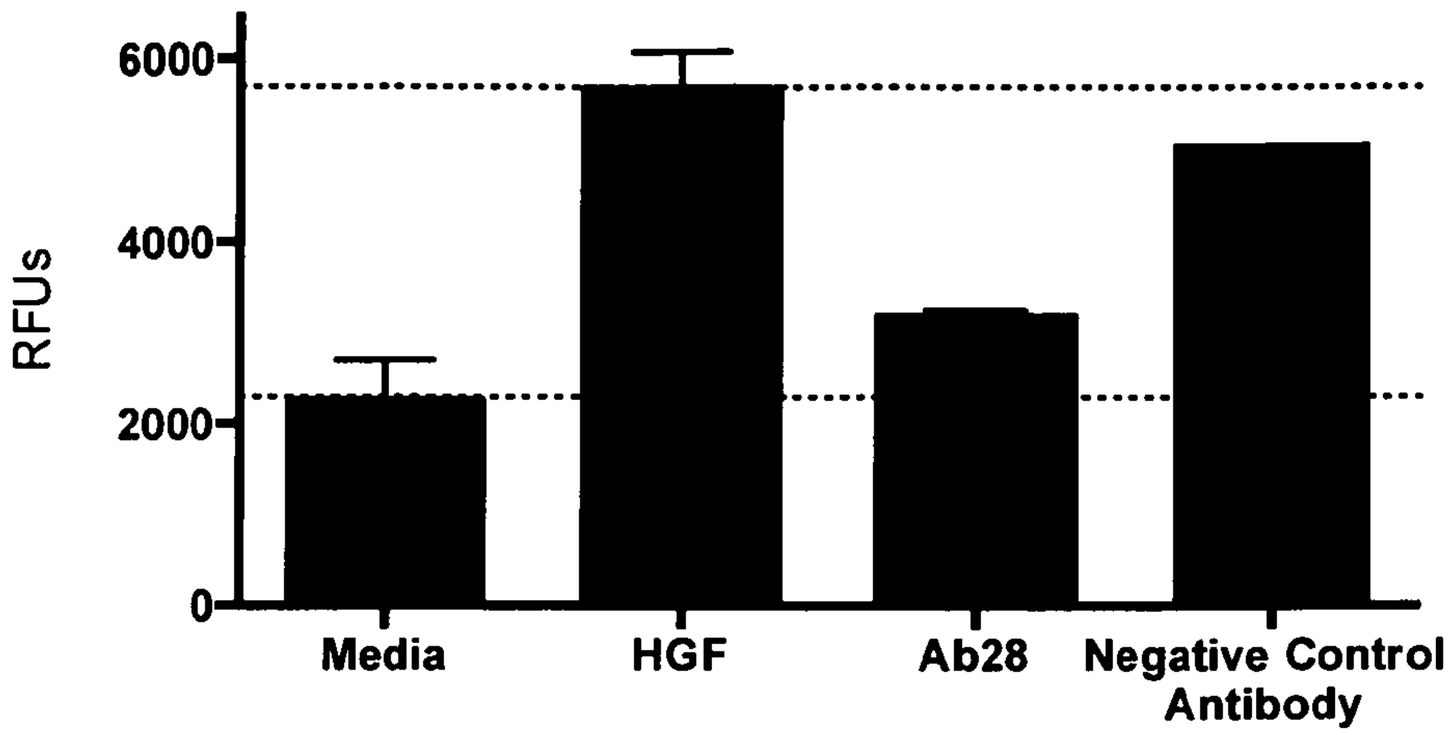

4MBR-5 Proliferation Assay
RFUs
6000
4000
2000
0
Media
HGF
Ab28
Negative Control Antibody

**Figure 51**

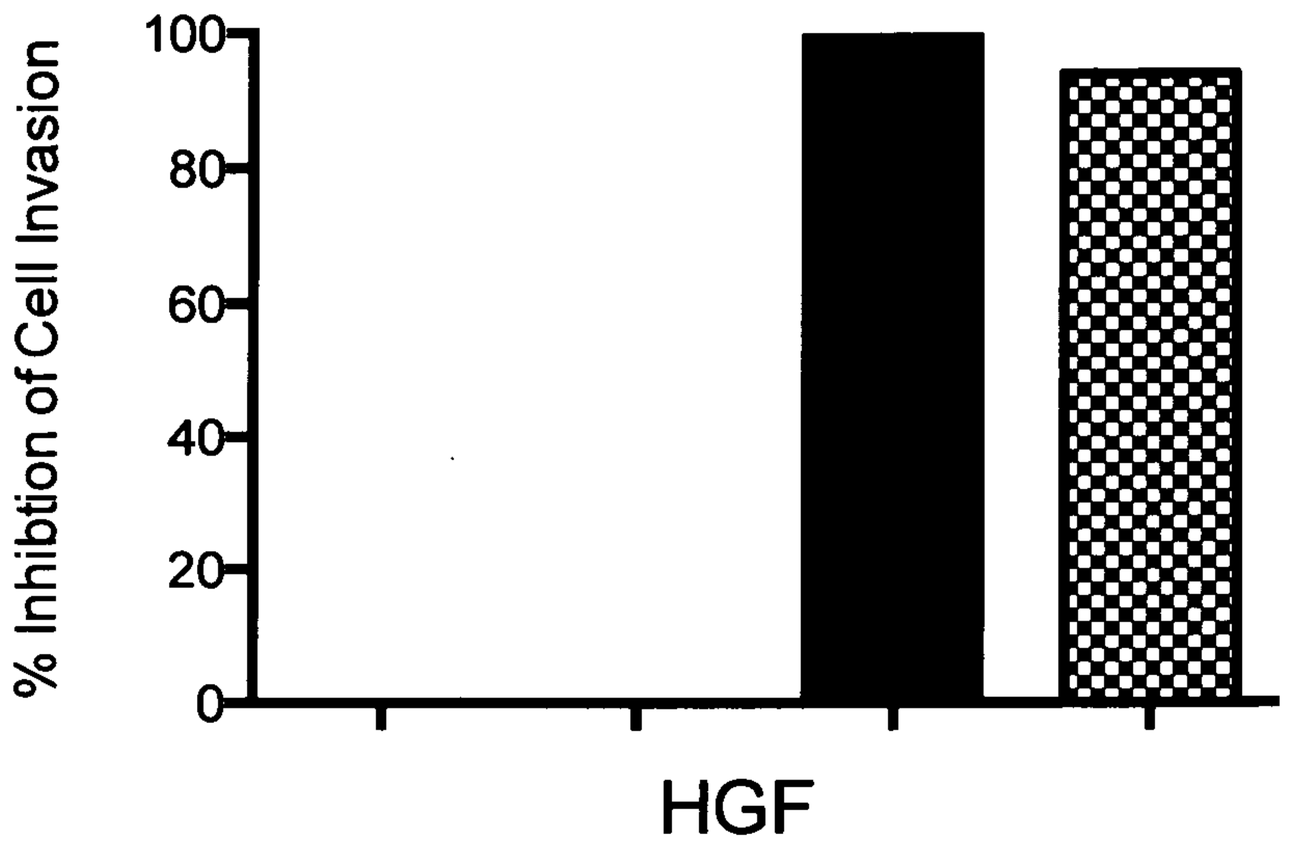

% Inhibtion of Cell Invasion
100
80
60
40
20
0
HGF
Negative Control Ab
Ab8 10 μg/mL
Ab8 2 μg/mL

Figure 52A

Antibody Heavy chain Protein features

| Sequence Name | FR1 | CDR1 | FR2 | CDR2 |
|---|---|---|---|---|
| Ab1 | QSVEESGGRLVTPGTPLTLTCTVSGFSLS | AYAMS | WVRQAPEKGLEWIA | VIYVIGATDYASWAKG |
| Ab2 | EVQLVESGGGLVQPGGSLRLSCAASGFTVS | AYAMS | WVRQAPGKGLEWVA | VIYVIGATDYASSAKG |
| Ab3 | QSVEESGGRLVTPGTPLTLTCTVSGLTIS | SYYMS | WVRQAPGKGLEWIG | TINPGANTYFASWAKG |
| Ab4 | QSLEESGGRLVQPGTPLTLSCTASGLTIS | SYYMS | WVRQAPGKGLEWVG | TINPGANTYFASSAKG |
| Ab5 | QSLEESGGRLVTPGTPLTLTCTVSGFSLN | NYAVG | WVRQAPGKGLEWIG | IIYLSGNTDYANWAKG |
| Ab6 | QSVEESGGRLVMPGTPLTLTCTVSGFSLS | SNAIS | WVRQAPEKGLEWIG | VIYVIGVTDYASWAQG |
| Ab7 | QSVEESGGRLVMPGTPLTLTCTVSGFSLS | SNAIS | WVRQAPEKGLEWIG | VIYVIGVTDYASWAQG |
| Ab8 | EVQLVESGGGLVQPGGSLRLSCAASGFTVS | SNAIS | WVRQAPGKGLEWVG | VIYVIGVTDYASSAQG |
| Ab9 | QSVEESGGRLVTPGTPLTLTCTVSGIDLN | SNGMS | WVRQAPGEGLEWIG | ASSIDGTTYYTNWAKG |
| Ab10 | EVQLVESGGGLVQPGGSLRLSCAASGFTVS | SNGMS | WVRQAPGKGLEWVG | ASSIDGTTYYTNSAKG |
| Ab11 | QSMEESGGRLVTPGTPLTLTCTVSGFSLS | DYALS | WVRQAPGKGLEWIG | MISSGDNTYYASWAKG |
| Ab12 | QSLEESGGRLVTPGGSLTLTCTVSGIDLS | SNAIS | WVRQAPEKGLEWIA | VIYVVGATDYASWAKG |
| Ab13 | EVQLVESGGGLVQPGGSLRLSCAASGFTVS | SNAIS | WVRQAPGKGLEWVA | VIYVVGATDYASSAKG |
| Ab14 | QSVEESGGRLVTPGTPLTLTCTVSGFSLS | NYAMT | WVRQAPGKGLEWIG | VISFGGNTYYANWAKG |
| Ab15 | QSVEESGGRLVTPGTPLTLTCTVSGFSLS | NYAMT | WVRQAPGKGLEWIG | VISFGGNTYYANWAKG |
| Ab16 | QSVEESGGRLVTPGTPLTLTCTVSGIDLS | NYAMG | WVRQAPGKGLEYIG | MIGVNGRAWYATWAKG |
| Ab17 | QSVEESGGRLVPPGTPLTLTCTVSGIDLS | SYAMG | WVRQAPGKGLEYIG | MIDVSGSTYYADWAKG |
| Ab18 | QSLEESGGRLVTPGTPLTLTCTASGFSLS | SYDMS | WVRQAPGKGLEWIG | IIYAGSASTWFASWVKG |
| Ab19 | QSVEESGGRLVTPGTPLTLTCTASGFSLS | NYWMG | WVRQAPGEGLEWIG | TISYDGNTYYASWAKG |
| Ab20 | EVQLVESGGGLVQPGGSLRLSCAASGFTVS | NYWMG | WVRQAPGKGLEWIG | TISYDGNTYYASSAKG |
| Ab21 | QSVEESGGRLVTPGTPLTLTCTVSGFSLS | TYYMS | WVRQAPGKGLEWIG | IIYVSGITDYARWAKG |
| Ab23 | QSLEESGGRLVTPGTPLTLTCTASGFTIG | RYYMS | WVRQAPGKGLEWIG | IIYTHGVNPDYASWAKG |
| Ab24 | EVQLVESGGGLVQPGGSLRLSCAASGFTVG | RYYMS | WVRQAPGKGLEWIG | IIYTHGVNPDYASSAKG |
| Ab25 | QSLEESGGRLVTPGTPLTLTCTASGFSLS | SYAMG | WFRQAPGKGLEWIA | YIFASGSTYYASWAKG |
| Ab26 | QSVEESGGRLVTPGTPLTLTCTVSGFSLS | TYTMN | WVRQAPGKGLEYIG | FISSSSSIDYVSWAKG |
| Ab27 | QSLEESGGDLVKPGGTLTLTCTASGFSFS | DDHYMC | WVRQAPGKGLQWIA | CMYVGSSGATYYASWAKG |
| Ab28 | EVQLVESGGGLVQPGGSLRLSCAASGFTVS | SNAIS | WVRQAPGKGLEWVG | VIYVIGVTDYASSAQG |

Figure 52B

Antibody Heavy chain Protein features

| Sequence Name | FR3 | CDR3 | FR4 |
|---|---|---|---|
| Ab1 | RFTISRTSTTVDLRIPSPTTEDTATYFCAR | VYDSVWNHFNL | WGPGTLVTVSS |
| Ab2 | RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR | VYDSVWNHFNL | WGQGTLVTVSS |
| Ab3 | RFTISRTSTTVDLKITSPTTEDTATYFCAR | EGDSNDWGVFDL | WGQGTLVTVSS |
| Ab4 | RFTISRSSTTLDLKMTSPTAEDTATYYCAR | EGDSNDWGVFDL | WGQGTLVTVSS |
| Ab5 | RFTISKTSTTVDLKITSPTTEDTATYFCAR | KFDTGYDI | WGPGTLVTVSS |
| Ab6 | RFTISKTSTTVDLKIPSPTTEDTATYFCAR | VYDSGWNHFNL | WGPGTLVTVSS |
| Ab7 | RFTISKTSTTVDLKIPSPTTEDTATYFCAR | VYDSGWNHFNL | WGPGTLVTVSS |
| Ab8 | RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR | VYDSGWNHFNL | WGQGTLVTVSS |
| Ab9 | RFTISKTSSTTVDLKITSPTTEDTATYFCTR | GEYAGVVGSNYFDL | WGQGTLVTVSS |
| Ab10 | RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR | GEYAGVVGSNYFDL | WGQGTLVTVSS |
| Ab11 | RFTISKASTTVDLKITSPTTEDTATYFCAR | DKDASSGGYLVLDLLDVPDGMDL | WGPGTLVTVSS |
| Ab12 | RFTISRTSTTVDLKMTSLTTEDTATYFCAR | VYDSGWNHFNL | WGPGTLVTVSS |
| Ab13 | RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR | VYDSGWNHFNL | WGQGTLVTVSS |
| Ab14 | RFTISKTSTTVDLKITSPTTEDTATYFCAR | WDAENNEILNL | WGQGTLVTVSS |
| Ab15 | RFTISKTSTTVDLKITSPTTEDTATYFCAR | WDAENNEILNL | WGPGTLVTVSS |
| Ab16 | RFTISKTSPTVDLKITSPTTEDTATYFCAR | LIDERSTYSYVFDL | WGQGTLVTVSS |
| Ab17 | RLTISKTPTTVDLEITSPTTEDTATYFCAR | LIDERSTYSYAFDL | WGQGTLVTVSS |
| Ab18 | RFTISKTSTTVDLKMTSLTTEDTATYFCAR | VGYSGYGYDDNLDM | WGQGTLVTVSS |
| Ab19 | RFTISRTSTTVDLKMTSLTTEDTAIYFCAT | VNYPDYSTGAFNI | WGPGTLVTVSS |
| Ab20 | RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAT | VNYPDYSTGAFNI | WGQGTLVTVSS |
| Ab21 | RFTISKTSTTVDLKMTSLTTEDTATYFCAR | HIDSSGWDGLGI | WGQGTLVTVSS |
| Ab23 | RFTISRPSTTVDLKITSPTTEDTATYFCAR | VGGFNDYSDI | WGPGTLVTVSS |
| Ab24 | RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR | VGGFNDYSDI | WGQGTLVTVSS |
| Ab25 | RFTISKTSTTVELKITSLTTEDTATYFCAR | GSGARFFPNYFAI | WGPGTLVTVSS |
| Ab26 | RFTISKTSTTVDLKITSPTTEDTATYFCAR | DFYADYIGGGYPYI | WGPGTLVTVSS |
| Ab27 | RFTISKTSSTTVTLQMTSLTAADTATYFCAR | DDWTSYYAWGYWAL | WGPGTLVTVSS |
| Ab28 | RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR | VYDSGWNHFNL | WGQGTLVTVSS |

Figure 52C

Antibody Heavy chain Protein features

| Sequence Name | Constant region |
|---|---|
| Ab1 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab2 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab3 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab4 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab5 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab6 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab7 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab8 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab9 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab10 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab11 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab12 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab13 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab14 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab15 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab16 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab17 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab18 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab19 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab20 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab21 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab23 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab24 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab25 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab26 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab27 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |
| Ab28 | ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL |

Figure 52D

Antibody Heavy chain Protein features

| Sequence Name | Constant region |
|---|---|
| Ab1 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab2 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab3 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab4 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab5 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab6 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab7 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab8 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab9 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab10 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab11 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab12 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab13 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab14 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab15 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab16 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab17 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab18 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab19 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab20 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab21 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab23 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab24 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab25 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab26 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab27 | GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |
| Ab28 | GTQTYICNVNHKPSNTKVDARVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH |

Figure 52E

Antibody Heavy chain Protein features

| Sequence Name | Constant region |
|---|---|
| Ab1 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab2 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab3 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab4 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab5 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab6 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab7 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab8 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab9 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab10 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab11 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab12 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab13 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab14 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab15 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab16 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab17 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab18 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab19 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab20 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab21 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab23 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab24 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab25 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab26 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab27 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |
| Ab28 | EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP |

Figure 52F

Antibody Heavy chain Protein features

| Sequence Name | Constant region |
|---|---|
| Ab1 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab2 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab3 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab4 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab5 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab6 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab7 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab8 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab9 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab10 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab11 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab12 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab13 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab14 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab15 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab16 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab17 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab18 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab19 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab20 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab21 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab23 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab24 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab25 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab26 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab27 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |
| Ab28 | REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ |

Figure 52G

Antibody Heavy chain Protein features

| Sequence Name | Constant region | |
|---|---|---|
| Ab1 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:1) |
| Ab2 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:41) |
| Ab3 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:81) |
| Ab4 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:121) |
| Ab5 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:161) |
| Ab6 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:201) |
| Ab7 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:241) |
| Ab8 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:281) |
| Ab9 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:321) |
| Ab10 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:361) |
| Ab11 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:401) |
| Ab12 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:441) |
| Ab13 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:481) |
| Ab14 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:521) |
| Ab15 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:561) |
| Ab16 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:601) |
| Ab17 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:641) |
| Ab18 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:681) |
| Ab19 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:721) |
| Ab20 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:761) |
| Ab21 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:801) |
| Ab23 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:841) |
| Ab24 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:881) |
| Ab25 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:921) |
| Ab26 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:961) |
| Ab27 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:1001) |
| Ab28 | QGNVFSCSVMHEALHNHYTQKSLSLSPGK | (SEQ_ID_NO:1041) |

Figure 53A

Antibody Light chain Protein features

| Sequence Name | FR1 | CDR1 | FR2 | | CDR2 |
|---|---|---|---|---|---|
| Ab1 | AYDMTQTPASVEVAVGGTVTIKC | QASQSISSWLA | WYQQKPGQPPKLLIY | QASKLAS | |
| Ab2 | DIQMTQSPSTLSASVGDRVTITC | QASQSISSWLA | WYQQKPGKAPKLLIY | QASKLAS | |
| Ab3 | AYDMTQTPASVEIAVGGTVTIRC | QASEDIESYLA | WYQQKPGQPPKLLIY | RASDLAS | |
| Ab4 | AYDMTQSPASVEAAVGGTVTIRC | QASEDIESYLA | WYQQKPGQPPKLLIY | RASDLAS | |
| Ab5 | AYDMTQTPASMEVAVGGTVTIKC | QASQSISTYLA | WYQQKPGQPPKLLIY | DASDLAS | |
| Ab6 | ADIVMTQTPSSVEAAVGGTVTIKC | QASENIYRLLA | WYQQKPGQRPKLLIY | SASTLAS | |
| Ab7 | AYDMTQTPASVEVAVGGTVTIKC | QASQSISSWLA | WYQQKPGQPPKLLIY | EASKLAS | |
| Ab8 | DIQMTQSPSTLSASVGDRVTITC | QASQSISSWLA | WYQQKPGKAPKLLIY | EASKLAS | |
| Ab9 | QVLTQTPPSVSAVVGGTVTINC | QSSQRIYSNWLS | WYQQKPGQTPKPLIY | AASSLAS | |
| Ab10 | DIQMTQSPSSVSASVGDRVTITC | QSSQRIYSNWLS | WYQQKPGKAPKLLIY | AASSLAS | |
| Ab11 | AVLTQTPSPVSAAVGGTVTIKC | QSSQSVYNNNLLS | WYQQKPGQPPKLLIW | GASYLPS | |
| Ab12 | AYDMTQTPASVEVAVGGTVTIKC | QVSQSISSWLS | WYQKKPGQRPKLLIY | RASTLAS | |
| Ab13 | DYQMTQSPSTLSASVGDRVTITC | QVSQSISSWLS | WYQQKPGKAPKLLIY | RASTLAS | |
| Ab14 | AYDMTQTPASVEVAVGGTVTIKC | QASESIESYLA | WYQQKSGQPPKLLIY | RASTLAS | |
| Ab15 | AYDMTQTPASVEVAVGGTVTIKC | QASESISSYLA | WYQQKSGQPPKLLIY | RASTLAS | |
| Ab16 | QVLTQTPSPVSAAVGGTVTINC | QGSQSLYNNNAFS | WYQQKPGQPPKLLIY | DASTLAS | |
| Ab17 | QVLTQTPSPVSAAVGGTVTINC | QASQSFYNNGAFS | WYQQKPGQPPKLLIY | DASTLAS | |
| Ab18 | AYDMTQTPASVEVAVGGTVTIKC | QASQSISTALA | WYQQKPGQRPKLLIY | DASKLAS | |
| Ab19 | DVVMTQTPASVSEPVGGTVTIKC | QASQSIDNYLA | WYQQKPGQRPRLLIY | YTSTLAS | |
| Ab20 | DIQMTQSPSSLSASVGDRVTITC | QASQSIDNYLA | WYQQKPGKVPKLLIY | YTSTLAS | |
| Ab21 | AYDMTQTPASVEVAVGGTVTIKC | QASESISSYLN | WYQQKLGQPPKLLIY | RASTLTS | |
| Ab23 | AYDMTQTPASVEVAVGGTVTIKC | QASESISTYLA | WYQQKPGQPPKLLIY | RASTLAS | |
| Ab24 | DIQMTQSPSSLSASVGDRVTITC | QASESISTYLA | WYQQKPGKVPKLLIY | RASTLAS | |
| Ab25 | QVLTQTASSVSAAVGGTVTISC | QSSQSVTNNNDLA | WYQQKPGQPPKLLIY | QASKLAS | |
| Ab26 | ADVVMTQTPASVSEPVGGTVTIKC | QASQSISSYLS | WYQQKPGQPPKLLIY | GASKLTS | |
| Ab27 | ADIVMTQNPASVSEPVGGTVTIKC | QASQSVNSWLS | WYQQKPGQPPKFLIY | KASTLAS | |
| Ab28 | DIQMTQSPSTLSASVGDRVTITC | QASQSISSWLA | WYQQKPGKAPKLLIY | EASKLAS | |

Figure 53B

Antibody Light chain Protein features

| Sequence Name | FR3 | CDR3 | FR4 |
|---|---|---|---|
| Ab1 | GVPSRFKGSGSGTEFTLTISGVECADAATYYC | QQAYSVSNVDNA | FGGGTEVVVKR |
| Ab2 | GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC | QQAYSVSNVDNA | FGGGTKVEIKR |
| Ab3 | GVSSRFKGSGSGTDYTLTISGVECDDAATYYC | QQGYTIDNVDNT | FGGGTEVVVKR |
| Ab4 | GVSSRFKGSGSGTDYTLTISGLEPEDAATYYC | QQGYTIDNVDNT | FGGGTKVEIKR |
| Ab5 | GVSSRFKGSGSGTQFTLTISGVECDDAATYYC | QQDWSDSNVDNA | FGGGTEVVVKR |
| Ab6 | GVPSRFKGSGSGTQFTLTISDLECADAATYYC | QNYYYSSRSSYDTYNV | FGGGTEVVVKR |
| Ab7 | GVPSRFSGSGSGTQFTLTISGVECADAATYYC | QQAYSVANVDNA | FGGGTEVVVKR |
| Ab8 | GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC | QQAYSVANVDNA | FGGGTKVEIKR |
| Ab9 | GVPSRFKGSGSGTQFTLTISDLECDDAASYYC | AGYYSGHIYS | FGGGTEVVVKR |
| Ab10 | GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC | AGYYSGHIYS | FGGGTKVEIKR |
| Ab11 | GVPDRFSGSGSGTQFTLTISGVQCDDAATYYC | LGGYDGDADTYNT | FGGGTEVVVKR |
| Ab12 | GVSSRFKGSGSGTEFTLTISGVECADAATYYC | QQAYSVSNVDNA | FGGGTEVVVKR |
| Ab13 | GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC | QQAYSVSNVDNA | FGGGTKVEIKR |
| Ab14 | GVSSRFKGSGSGTQFTLTISGVECADAATYYC | QQGDAWSNVDNV | FGGGTEVVVKR |
| Ab15 | GVSSRFKGSGSGTQFTLTISGVECADAATYYC | QQGDAWSNVDNV | FGGGTEVVVKR |
| Ab16 | GVPSRFKGSGSGTQFTLTISGVQCADAATYYC | QGEFSCGDVDCIA | FGGGTEVVVKR |
| Ab17 | GVPSRFKGSGSGTQFTLTISGVQCGDAATYYC | QGEFSCGSADCVA | FGGGTEVVVKR |
| Ab18 | GVSSRFKGSGSGAQFTLTISGVECADAATYYC | HQGYSSSNVDNT | FGGGTEVVVKR |
| Ab19 | GVPSRFKGSGSGTEYTLTISDLECADAATYYC | QFTAYYSTYIGA | FGGGTEVVVKR |
| Ab20 | GVPSRFSGSGSGTDFTLTISSLQPEDVATYYC | QFTAYYSTYIGA | FGGGTKVEIKR |
| Ab21 | GVSSRFKGSGSGTEYTLTISDLECADAATYYC | QQTYGYSDTDNS | FGGGTEVVVKR |
| Ab23 | GVSSRFKGSGSGTQFTLTISGVECADAATYYC | QQGYSYSNVDNA | FGGGTEVVVKR |
| Ab24 | GVPSRFSGSGSGTDFTLTISSLQPEDVATYYC | QQGYSYSNVDNA | FGGGTKVEIKR |
| Ab25 | GVPSRFKGSGSGTQFTLTISDLECDDAATYYC | QGSYSGGICA | FGGGTEVVVKR |
| Ab26 | GVPSRFKGSGSGTEYTLTISDLECADAATYYC | QSNYDIYSYA | FGGGTEVVVKR |
| Ab27 | GVSSRFKGSGIGTEFTLTISDLECADAATYYC | QFSNSGTIYGSG | FGGGTEVVVKR |
| Ab28 | GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC | QQAYSVANVDNA | FGGGTKVEIKR |

Figure 53C

Antibody Light chain Protein features

| Sequence Name | Constant region |
|---|---|
| Ab1 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab2 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab3 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab4 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab5 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab6 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab7 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab8 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab9 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab10 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab11 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab12 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab13 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab14 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab15 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab16 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab17 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab18 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab19 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab20 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab21 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab23 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab24 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab25 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab26 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab27 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |
| Ab28 | TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA |

Figure 53D

Antibody Light chain Protein features

| Sequence Name | Constant region | |
|---|---|---|
| Ab1 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:21) |
| Ab2 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:61) |
| Ab3 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:101) |
| Ab4 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:141) |
| Ab5 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:181) |
| Ab6 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:221) |
| Ab7 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:261) |
| Ab8 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:301) |
| Ab9 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:341) |
| Ab10 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:381) |
| Ab11 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:421) |
| Ab12 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:461) |
| Ab13 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:501) |
| Ab14 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:541) |
| Ab15 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:581) |
| Ab16 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:621) |
| Ab17 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:661) |
| Ab18 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:701) |
| Ab19 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:741) |
| Ab20 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:781) |
| Ab21 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:821) |
| Ab23 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:861) |
| Ab24 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:901) |
| Ab25 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:941) |
| Ab26 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:981) |
| Ab27 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:1021) |
| Ab28 | DYEKHKVYACEVTHQGLSSPVTKSFNRGEC | (SEQ_ID_NO:1061) |

Figure 54A

Antibody Heavy chain DNA features

| Sequence Name | FR1 |
|---|---|
| Ab1 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggat |
| Ab2 | gaggtgcagctggtggagtctgggggaggcttggtccagcctgggggtccctgagactctcctgtgcagcctctg |
| Ab3 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacaccttgacactcacctgcacagtctctggac |
| Ab4 | cagtcgctggaggagtctgggggacgcttggtccagcctgggacacccctgacactctcctgtacagcctctggac |
| Ab5 | cagtcgctggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggat |
| Ab6 | cagtcggtggaggagtccgggggtcgcctggtcatgcctgggacacccctgacactcacctgcaccgtctctggat |
| Ab7 | cagtcggtggaggagtccgggggtcgcctggtcatgcctgggacacccctgacactcacctgcaccgtctctggat |
| Ab8 | gaggtgcagctggtggagtctgggggaggcttggtccagcctgggggtccctgagactctcctgtgcagcctctg |
| Ab9 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtgtctggaa |
| Ab10 | gaggtgcagctggtggagtctgggggaggcttggtccagcctgggggtccctgagactctcctgtgcagcctctg |
| Ab11 | cagtcaatggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggat |
| Ab12 | cagtcgctggaggagtccgggggtcgcctggtaacgcctggaggatccctgacactcacctgcacagtctctggaa |
| Ab13 | gaggtgcagctggtggagtctgggggaggcttggtccagcctgggggtccctgagactctcctgtgcagcctctg |
| Ab14 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggat |
| Ab15 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggat |
| Ab16 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggaa |
| Ab17 | cagtcggtggaggagtccgggggtcgcctggtcccgcctgggacacccctgacactcacctgcacagtctctggaa |
| Ab18 | cagtcgctggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagcctctggat |
| Ab19 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagcctctggat |
| Ab20 | gaggtgcagctggtggagtctgggggaggcttggtccagcctgggggtccctgagactctcctgtgcagcctctg |
| Ab21 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat |
| Ab23 | cagtcgctggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagcctctggat |
| Ab24 | gaggtgcagctggtggagtctgggggaggcttggtccagcctgggggtccctgagactctcctgtgcagcctctg |
| Ab25 | cagtcgctggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagcctctggat |
| Ab26 | cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggat |
| Ab27 | cagtcgttggaggagtccgggggagacctggtcaagcctggaggaaccctgacactcacctgcacagcctctggat |
| Ab28 | gaggtgcagctggtggagtctgggggaggcttggtccagcctgggggtccctgagactctcctgtgcagcctctg |

Figure 54B

Antibody Heavy chain DNA features

| Sequence Name | FR1 | CDR1 | FR2 |
|---|---|---|---|
| Ab1 | tctccctcagt | gcctatgcaatgagc | tgggtccgccaggctccagagaaggggctggagtggatcgca |
| Ab2 | gattcaccgtcagt | gcctatgcaatgagc | tgggtccgtcaggctccagggaaggggctggagtgggtcgca |
| Ab3 | tcaccattagt | agctactacatgagc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab4 | tcaccattagt | agctactacatgagc | tgggtccgtcaggctccagggaaggggctggagtgggtcgga |
| Ab5 | tctccctcaat | aattatgcagtgggc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab6 | tctccctcagt | agcaatgcaataagc | tgggtccgccaggctccagagaaggggctggaatggatcgga |
| Ab7 | tctccctcagt | agcaatgcaataagc | tgggtccgccaggctccagagaaggggctggaatggatcgga |
| Ab8 | gattcaccgtcagt | agcaatgcaataagc | tgggtccgtcaggctccagggaaggggctggagtgggtcgga |
| Ab9 | tcgacctcaat | agcaatggaatgagc | tgggtccgccaggctccaggggaggggctggaatggatcgga |
| Ab10 | gattcaccgtcagt | agcaatggaatgagc | tgggtccgtcaggctccagggaaggggctggagtgggtcgga |
| Ab11 | tctccctcagt | gactatgcgttgagc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab12 | tcgacctcagt | agcaatgcaataagc | tgggtccgccaggctccagagaaggggctggagtggatcgca |
| Ab13 | gattcaccgtcagt | agcaatgcaataagc | tgggtccgtcaggctccagggaaggggctggagtgggtcgca |
| Ab14 | tctccctcagt | aactacgcaatgacc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab15 | tctccctcagt | aactacgcaatgacc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab16 | tcgacctcagt | aattatgcaatgggc | tgggtccgccaggctccagggaaggggctggaatacatcgga |
| Ab17 | tcgacctcagt | agctatgcaatgggc | tgggtccgccaggctccagggaaggggctggaatacatcgga |
| Ab18 | tctccctcagc | agctacgacatgagc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab19 | tctccctcagt | aattattggatgggc | tgggtccgccaggctccaggggaggggctggaatggatcgga |
| Ab20 | gattcaccgtcagt | aactattggatgggc | tgggtccgtcaggctccagggaaggggctggagtggatcgga |
| Ab21 | tctccctcagt | acctactacatgagc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab23 | tcactatcggt | cgctactacatgagc | tgggtccgccaggctccagggaaggggctggaatggatcgga |
| Ab24 | gattcaccgtcggt | cgctactacatgagc | tgggtccgtcaggctccagggaaggggctggagtggatcgga |
| Ab25 | tctccctcagt | agctatgcaatgggc | tggttccgccaggctccagggaaggggctggagtggatcgca |
| Ab26 | tctccctcagt | acctatacaatgaac | tgggtccgccaggctccagggaaggggctggaatacatcgga |
| Ab27 | tctccttcagt | gacgaccactacatgtgc | tgggtccgccaggctccagggaaggggctgcagtggatcgca |
| Ab28 | gattcaccgtcagt | agcaatgcaataagc | tgggtccgtcaggctccagggaaggggctggagtgggtcgga |

Figure 54C

Antibody Heavy chain DNA features

| Sequence Name | CDR2 | FR3 |
|---|---|---|
| Ab1 | gtcatttatgttattggtgccactgactacgcgagctgggcgaaaggc | cgattcaccatctccagaacct |
| Ab2 | gtcatctatgttattggtgccactgactacgcgagcagtgcgaaaggc | cgattcaccatctccagagaca |
| Ab3 | accattaatcctggtgctaacacatacttcgcgagctgggcaaaaggc | cgattcaccatctccagaacct |
| Ab4 | accatcaatcctggtgctaacacatacttcgcgagctctgcaaaaggc | cgattcaccatctccagatcct |
| Ab5 | atcatttaccttagtggtaacacagactacgcgaactgggcgaaaggc | cgattcaccatctccaaaacct |
| Ab6 | gtcatttatgttattggtgtcactgactacgcgagctgggcgcaaggc | cgattcaccatctccaaaacct |
| Ab7 | gtcatttatgttattggtgtcactgactacgcgagctgggcgcaaggc | cgattcaccatctccaaaacct |
| Ab8 | gtcatttatgttattggtgtcactgactacgcgagctctgcgcaaggc | cgattcaccatctccagagaca |
| Ab9 | gccagtagtattgatgggaccacatactacaccaattgggcgaagggc | cgattcaccatctccaaaacct |
| Ab10 | gccagtagtattgatgggaccacatactacaccaattctgcgaagggc | cgattcaccatctccagagaca |
| Ab11 | atgattagtagtggtgacaacacatactacgcgagctgggcgaaaggc | cgattcaccatctccaaagcct |
| Ab12 | gtcatttatgttgttggtgccactgactacgcgagctgggcgaaaggc | cgattcaccatctccagaacct |
| Ab13 | gtcatctatgttgttggtgccactgactacgcgagcagtgcgaaaggc | cgattcaccatctccagagaca |
| Ab14 | gtcattagttttggtggtaacacatactacgcgaactgggcgaaaggc | cgattcaccatctccaaaacct |
| Ab15 | gtcattagttttggtggtaacacatactacgcgaactgggcgaaaggc | cgattcaccatctccaaaacct |
| Ab16 | atgattggtgttaatggtagggcatggtacgcgacttgggcgaaaggc | cgattcaccatctccaagacct |
| Ab17 | atgattgatgttagtggtagcacgtactacgcggactgggcgaaaggc | cgactcaccatctccaaaaccc |
| Ab18 | atcatttatgctggtagtgctagcacatggttcgcgagctgggtgaaaggc | cgattcaccatctccaaaacct |
| Ab19 | accattagttatgatggtaacacatactacgcgagctgggcaaaaggc | cgcttcaccatctcccgaacct |
| Ab20 | accattagttatgatggtaacacatactacgcgagcagcgcaaaaggc | cgattcaccatctccagagaca |
| Ab21 | atcatttatgttagtggtatcacggactacgcgaggtgggcgaaaggc | cgattcaccatctccaaaacct |
| Ab23 | atcatttatactcatggtgttaacccagactacgcgagctgggcgaaaggc | cgattcaccatctccagaccct |
| Ab24 | atcatctatactcatggtgttaacccagactacgcgagcagcgcgaaaggc | cgattcaccatctccagagaca |
| Ab25 | tacatttttgctagtggtagcacatactacgcgagctgggcgaaaggc | cgattcaccatctccaaaacct |
| Ab26 | ttcattagtagtagtagtagcatagattatgtgagttgggcgaaaggc | cgattcaccatctccaaaacct |
| Ab27 | tgcatgtatgttggtagtagtggtgccacttattacgcgagctgggcgaaaggc | cgattcaccatctccaaaacct |
| Ab28 | gtcatttatgttattggtgtcactgactacgcgagctctgcgcaaggc | cgattcaccatctccagagaca |

Figure 54D

Antibody Heavy chain DNA features

| Sequence Name | FR3 |
|---|---|
| Ab1 | cgaccacggtggatctgagaatccccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab2 | attccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactgctgtgtattactgtgctaga |
| Ab3 | cgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacatatttctgtgccaga |
| Ab4 | cgaccaccctggatcttaagatgaccagcccgacagctgaggacactgctacatattactgtgctaga |
| Ab5 | cgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccagg |
| Ab6 | cgaccacggtggatctgaaaatccccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab7 | cgaccacggtggatctgaaaatccccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab8 | attccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactgctgtgtattactgtgctaga |
| Ab9 | cgtcgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtaccaga |
| Ab10 | attccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactgctgtgtattactgtgctaga |
| Ab11 | cgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab12 | cgaccacggtggatctgaaaatgaccagtctgacaaccgaggacacggccacctatttctgtgccaga |
| Ab13 | attccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactgctgtgtattactgtgctaga |
| Ab14 | cgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab15 | cgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab16 | cgcccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab17 | cgaccacggtggatctggaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab18 | cgaccacggtggatctgaaaatgaccagtctgacaaccgaggacacggccacctatttctgtgccaga |
| Ab19 | cgaccacggtggatctgaaaatgaccagtctgacgaccgaggacacggccatctatttctgtgccaca |
| Ab20 | attccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactgctgtgtattactgtgctaca |
| Ab21 | cgaccacggtggatctgaaaatgaccagtctgacaaccgaggacacggccacctatttctgtgccaga |
| Ab23 | cgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab24 | attccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactgctgtgtattactgtgctaga |
| Ab25 | cgaccacggtggagctgaaaatcaccagtctgacaaccgaggacacggccacctatttctgtgccaga |
| Ab26 | cgaccacggtggatctgaaaatcaccagtccgacaaccgaggacacggccacctatttctgtgccaga |
| Ab27 | cgtcgaccacggtgactctgcaaatgaccagtctgacagccgcggacacggccacctatttctgtgcgaga |
| Ab28 | attccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactgctgtgtattactgtgctaga |

Figure 54E

Antibody Heavy chain DNA features

| Sequence Name | | CDR3 |
|---|---|---|
| Ab1 | gtttatgattctgtctggaatcactttaacttg | |
| Ab2 | gtttatgattctgtctggaatcacttcaacttg | |
| Ab3 | gaggggatagtaatgactggggtgtctttgacttg | |
| Ab4 | gaggggatagtaatgactggggtgtctttgacttg | |
| Ab5 | aaatttgatacgggatatgacatc | |
| Ab6 | gtttatgattctggctggaatcactttaacttg | |
| Ab7 | gtttatgattctggctggaatcactttaacttg | |
| Ab8 | gtttatgattctggctggaatcactttaacttg | |
| Ab9 | ggggagtatgctggtgttgttggttcgaactactttgacttg | |
| Ab10 | ggggagtatgctggtgttgttggttcgaactactttgacttg | |
| Ab11 | gataaagatgctagtagtggtggttatttggtccttgacctattggatgtccccgacggcatggacctc | |
| Ab12 | gtttatgattctggctggaatcactttaacttg | |
| Ab13 | gtttatgattctggctggaatcactttaacttg | |
| Ab14 | tgggatgctgaaaacaatgagattcttaacttg | |
| Ab15 | tgggatgctgaaaacaatgagattcttaacttg | |
| Ab16 | ttgattgacgagcgttcaacttatagttatgttttgacttg | |
| Ab17 | ttgattgacgagcgttcaacttatagttatgcttttgacttg | |
| Ab18 | gtgggttatagtggttatggttatgatgataatttggacatg | |
| Ab19 | gtcaattatcctgattatagtactggtgcctttaacatc | |
| Ab20 | gtcaattatcctgattatagtactggtgcctttaacatc | |
| Ab21 | catattgatagtagtggctgggatggactgggcatc | |
| Ab23 | gtgggtggttttaatgactactctgacatt | |
| Ab24 | gtgggtggtttcaatgactactctgacatt | |
| Ab25 | ggtagtggtgctcgtttttttccccaactactttgccatc | |
| Ab26 | gatttttatgctgattatattggtggtggttatccttacatc | |
| Ab27 | gatgattggactagttattatgcgtgggggtattgggccttg | |
| Ab28 | gtttatgattctggctggaatcactttaacttg | |

Figure 54F

Antibody Heavy chain DNA features

| Sequence Name | FR4 | Constant region |
|---|---|---|
| Ab1 | tggggcccgggcaccctggtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab2 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab3 | tggggccagggcaccctggtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab4 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab5 | tggggcccaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab6 | tggggcccgggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab7 | tggggcccagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab8 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab9 | tggggccagggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab10 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab11 | tggggcccaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab12 | tggggcccaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab13 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab14 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab15 | tggggcccagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab16 | tggggccaaggcaccctggtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab17 | tggggccaaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab18 | tggggccaaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab19 | tggggcccaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab20 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab21 | tggggccaaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab23 | tggggcccaggcaccctggtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab24 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab25 | tggggcccaggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab26 | tggggcccgggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab27 | tggggcccgggcaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |
| Ab28 | tggggccaagggaccctcgtcaccgtctcgagc | gcctccaccaagggcccatcggtcttcccccctggcaccctcct |

Figure 54G

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab2 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab3 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab4 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab5 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab6 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab7 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab8 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab9 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab10 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab11 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab12 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab13 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab14 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab15 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab16 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab17 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab18 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab19 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab20 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab21 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab23 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab24 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab25 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab26 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab27 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |
| Ab28 | ccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgt |

Figure 54H

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab2 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab3 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab4 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab5 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab6 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab7 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab8 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab9 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab10 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab11 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab12 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab13 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab14 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab15 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab16 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab17 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab18 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab19 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab20 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab21 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab23 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab24 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab25 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab26 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab27 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |
| Ab28 | cgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccc |

Figure 54I

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab2 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab3 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab4 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab5 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab6 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab7 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab8 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab9 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab10 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab11 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab12 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab13 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab14 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab15 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab16 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab17 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab18 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab19 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab20 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab21 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab23 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab24 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab25 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab26 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab27 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |
| Ab28 | tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagccca |

Figure 54J

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab2 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab3 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab4 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab5 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab6 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab7 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab8 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab9 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab10 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab11 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab12 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab13 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab14 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab15 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab16 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab17 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab18 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab19 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab20 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab21 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab23 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab24 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab25 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab26 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab27 | gcaacaccaaggtggacaagagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |
| Ab28 | gcaacaccaaggtggacgcgagagttgagcccaaatcttgtgacaaaactcacacatgcccaccgtgcccagcac |

Figure 54K

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab2 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab3 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab4 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab5 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab6 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab7 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab8 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab9 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab10 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab11 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab12 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab13 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab14 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab15 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab16 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab17 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab18 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab19 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab20 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab21 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab23 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab24 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab25 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab26 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab27 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |
| Ab28 | ctgaactcctgggggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggaccc |

Figure 54L

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab2 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab3 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab4 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab5 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab6 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab7 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab8 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab9 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab10 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab11 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab12 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab13 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab14 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab15 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab16 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab17 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab18 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab19 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab20 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab21 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab23 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab24 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab25 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab26 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab27 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |
| Ab28 | ctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg |

Figure 54M

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab2 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab3 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab4 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab5 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab6 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab7 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab8 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab9 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab10 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab11 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab12 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab13 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab14 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab15 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab16 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab17 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab18 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab19 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab20 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab21 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab23 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab24 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab25 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab26 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab27 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |
| Ab28 | tggaggtgcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtaccgtgtggtcagcgtcctca |

Figure 54N

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab2 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab3 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab4 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab5 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab6 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab7 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab8 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab9 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab10 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab11 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab12 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab13 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab14 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab15 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab16 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab17 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab18 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab19 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab20 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab21 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab23 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab24 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab25 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab26 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab27 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |
| Ab28 | ccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccccca |

Figure 540

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab2 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab3 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab4 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab5 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab6 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab7 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab8 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab9 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab10 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab11 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab12 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab13 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab14 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab15 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab16 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab17 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab18 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab19 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab20 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab21 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab23 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab24 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab25 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab26 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab27 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |
| Ab28 | tcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgcccccatcccgggagg |

Figure 54P

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab2 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab3 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab4 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab5 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab6 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab7 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab8 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab9 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab10 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab11 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab12 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab13 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab14 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab15 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab16 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab17 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab18 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab19 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab20 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab21 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab23 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab24 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab25 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab26 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab27 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |
| Ab28 | agatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggg |

Figure 54Q

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab2 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab3 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab4 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab5 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab6 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab7 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab8 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab9 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab10 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab11 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab12 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab13 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab14 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab15 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab16 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab17 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab18 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab19 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab20 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab21 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab23 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab24 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab25 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab26 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab27 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |
| Ab28 | agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctct |

Figure 54R

Antibody Heavy chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab2 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab3 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab4 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab5 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab6 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab7 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab8 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab9 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab10 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab11 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab12 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab13 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab14 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab15 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab16 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab17 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab18 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab19 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab20 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab21 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab23 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab24 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab25 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab26 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab27 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |
| Ab28 | acagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctc |

Figure 54S

Antibody Heavy chain DNA features

| Sequence Name | Constant region | |
|---|---|---|
| Ab1 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:11) |
| Ab2 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:51) |
| Ab3 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:91) |
| Ab4 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:131) |
| Ab5 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:171) |
| Ab6 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:211) |
| Ab7 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:251) |
| Ab8 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:291) |
| Ab9 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:331) |
| Ab10 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:371) |
| Ab11 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:411) |
| Ab12 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:451) |
| Ab13 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:491) |
| Ab14 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:531) |
| Ab15 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:571) |
| Ab16 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:611) |
| Ab17 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:651) |
| Ab18 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:691) |
| Ab19 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:731) |
| Ab20 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:771) |
| Ab21 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:811) |
| Ab23 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:851) |
| Ab24 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:891) |
| Ab25 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:931) |
| Ab26 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:971) |
| Ab27 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:1011) |
| Ab28 | tgcacaaccactacacgcagaagagcctctccctgtctccgggtaaa | (SEQ_ID_NO:1051) |

Figure 55A

Antibody Light chain DNA features

| Sequence Name | FR1 |
|---|---|
| Ab1 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggggcacagtcaccatcaagtgc |
| Ab2 | gacatccagatgacccagtctccttccaccctgtctgcatctgtaggagacagagtcaccatcacttgc |
| Ab3 | gcctatgatatgacccagactccagcctctgtagagatagctgtgggaggcacagtcaccatcaggtgc |
| Ab4 | gcctatgatatgacccagtctccagcctccgtggaggcagccgtaggaggcacagtcaccatcaggtgt |
| Ab5 | gcctatgatatgacccagactccagcctctatggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab6 | gctgacattgtgatgacccagactccatcctccgtggaggcagctgtgggaggcacagtcaccatcaagtgc |
| Ab7 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab8 | gacatccagatgacccagtctccttccaccctgtctgcatctgtaggagacagagtcaccatcacttgc |
| Ab9 | caagtgctgacccagactccaccctccgtgtctgcagttgtgggaggcacagtcaccatcaattgc |
| Ab10 | gacatccagatgacccagtctccatcttccgtgtctgcatctgtaggagacagagtcaccatcacttgt |
| Ab11 | gccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggaggcacagtcaccatcaagtgc |
| Ab12 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab13 | gactatcagatgacccagtctccttccaccctgtctgcatctgtaggagacagagtcaccatcacttgc |
| Ab14 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab15 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab16 | caagtgctgacccagactccatcccctgtgtctgcagctgtgggaggcacagtcaccatcaactgc |
| Ab17 | caagtgctgacccagactccatcccctgtgtctgcagctgtgggaggcacagtcaccatcaactgc |
| Ab18 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab19 | gatgttgtgatgacccagactccagcctccgtgtctgaacctgtgggaggcacagtcaccatcaagtgc |
| Ab20 | gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgc |
| Ab21 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab23 | gcctatgatatgacccagactccagcctctgtggaggtagctgtgggaggcacagtcaccatcaagtgc |
| Ab24 | gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgc |
| Ab25 | caagtgctgacccagactgcatcgtccgtgtctgcagctgtgggaggcacagtcaccatcagttgc |
| Ab26 | gccgatgttgtgatgacccagactccagcctccgtgtctgaacctgtgggaggcacagtcaccatcaagtgc |
| Ab27 | gctgacattgtgatgacccagaatccagcctccgtgtctgaacctgtgggaggcacagtcaccatcaagtgc |
| Ab28 | gacatccagatgacccagtctccttccaccctgtctgcatctgtaggagacagagtcaccatcacttgc |

Figure 55B

Antibody Light chain DNA features

| Sequence Name | CDR1 | FR2 |
|---|---|---|
| Ab1 | caggccagtcagagcattagcagttggttagcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab2 | caggccagtcagagcattagcagttggttagcc | tggtatcagcagaaaccaggaaaagcccctaagctcc |
| Ab3 | caggccagtgaggacattgaaagctatttagcc | tggtatcagcagaaaccagggcagcctcccaaactcc |
| Ab4 | caggccagtgaggacattgaaagctacttagcc | tggtatcagcagaaaccagggcagcctcctaagctcc |
| Ab5 | caggccagtcagagcattagtacctacttagcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab6 | caggccagtgagaacatttataggttattggcc | tggtatcagcagaaaccagggcagcgtcccaagctcc |
| Ab7 | caggccagtcagagcattagcagttggttagcc | tggtatcagcagaaaccagggcagcctccaaagctcc |
| Ab8 | caggccagtcagagcattagcagttggttagcc | tggtatcagcagaaaccaggaaaagcccctaagctcc |
| Ab9 | cagtccagtcagaggatttatagtaattggttatct | tggtatcagcagaaaccagggcagactcccaagcccc |
| Ab10 | cagtccagtcagaggatctatagtaattggttatct | tggtatcagcagaaaccagggaaagcccctaagctcc |
| Ab11 | cagtccagtcagagtgtttataataacaacctcttatcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab12 | caggtcagtcagagcattagtagttggttatcc | tggtatcagaagaaaccagggcagcgtcccaagctcc |
| Ab13 | caggtcagtcagagcattagtagttggttatcc | tggtatcagcagaaaccaggaaaagcccctaagctcc |
| Ab14 | caggccagtgagagcattgaaagctatttagcc | tggtatcagcagaaatcagggcagcctcccaagctcc |
| Ab15 | caggccagtgagagcattagtagctacttagcc | tggtatcagcagaaatcagggcagcctcccaagctcc |
| Ab16 | cagggcagtcagagtctttataataacaacgccttttcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab17 | caggccagtcagagttttttataataacggcgccttttcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab18 | caggccagtcagagcattagcactgcattagcc | tggtatcagcagaaaccagggcagcgtcccaagctcc |
| Ab19 | caggccagtcagagcattgataactacttagcc | tggtatcagcagaaaccagggcagcgtcccaggctcc |
| Ab20 | caggccagtcagagcattgataactacttagcc | tggtatcagcagaaaccagggaaagttcctaagctcc |
| Ab21 | caggccagtgagagcattagtagctacttaaac | tggtatcagcagaaactagggcagcctcccaagctcc |
| Ab23 | caggccagtgagagcattagtacctacttagcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab24 | caggccagtgagagcattagtacctacttagcc | tggtatcagcagaaaccagggaaagttcctaagctcc |
| Ab25 | cagtccagtcagagtgttactaataacaacgacttagcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab26 | caggccagtcagagcattagtagctacttatcc | tggtatcagcagaaaccagggcagcctcccaagctcc |
| Ab27 | caggccagtcagagcgttaatagttggttatcc | tggtatcagcagaaaccagggcagcctcccaagttcc |
| Ab28 | caggccagtcagagcattagcagttggttagcc | tggtatcagcagaaaccaggaaaagcccctaagctcc |

Figure 55C

Antibody Light chain DNA features

| Sequence Name | FR2 | CDR2 | FR3 |
|---|---|---|---|
| Ab1 | tgatctac | caggcatctaaactggcatct | ggggtcccatcgcggttcaaaggcagtggatctgggacagagttca |
| Ab2 | tgatctat | caggcatctaaactggcatct | ggagtcccatcaaggttcagcggcagtggatctggaacagaattca |
| Ab3 | tgatctac | agggcatccgatctggcatct | ggggtctcatcgcggttcaaaggcagtggatctgggacagactaca |
| Ab4 | tgatctat | agggcatccgatctggcatct | ggggtctcatcaaggttcaaaggcagtggatctgggacagattaca |
| Ab5 | tgatctat | gatgcatccgatctggcatct | ggggtctcatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab6 | tgatctat | tctgcatccactctggcatct | ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab7 | tgatctac | gaagcatccaaactggcatct | ggggtcccatcgcggttcagtggcagtggatctgggacacagttca |
| Ab8 | tgatctat | gaagcatccaaactggcatct | ggagtcccatcaaggttcagcggcagtggatctggaacagaattca |
| Ab9 | tgatctat | gctgcatccagcctggcatct | ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab10 | tgatctat | gctgcatccagcctggcatct | ggggtcccatcaaggttcagcggcagtggatctgggacagatttca |
| Ab11 | tgatctgg | ggtgcatcctatctgccatct | ggggtcccagataggttcagcggcagtggatctgggacacagttca |
| Ab12 | tgatctac | agggcatccactctggcatct | ggggtctcatcgcggttcaaaggcagtggatctgggacagagttca |
| Ab13 | tgatctat | agggcatccactctggcatct | ggagtcccatcaaggttcagcggcagtggatctggaacagaattca |
| Ab14 | tgatctac | agggcttccactctggcatct | ggggtctcatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab15 | tgatctac | agggcttccactctggcatct | ggggtctcatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab16 | tgatctat | gatgcttccactctggcgtct | ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab17 | tgatctac | gatgcatccactctggcatct | ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab18 | tgatctac | gatgcatcgaaactggcatct | ggggtctcatcgcggttcaaaggcagtggatctggggcacagttca |
| Ab19 | tgatctat | tatacatccactctggcatct | ggggtcccatcgcggttcaaaggcagtggatctgggacagagtaca |
| Ab20 | tgatctat | tatacatccactctggcatct | ggggtcccatctcgtttcagtggcagtggatctgggacagatttca |
| Ab21 | tgatctac | agggcatccactctgacatct | ggggtctcatcaaggttcaaaggcagtggatctgggacagagtaca |
| Ab23 | tgatctac | agggcatccactctggcatct | ggggtctcatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab24 | tgatctat | agggcatccactctggcatct | ggggtcccatctcgtttcagtggcagtggatctgggacagatttca |
| Ab25 | tgatctac | caggcatccaaactggcatct | ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca |
| Ab26 | tgatctat | ggtgcatccaaactgacatct | ggggtcccatcgcggttcaaaggcagtggatctgggacagagtaca |
| Ab27 | tgatctac | aaggcatccactctggcatct | ggggtctcatcgcggttcaaaggcagtgggattgggacagagttca |
| Ab28 | tgatctat | gaagcatccaaactggcatct | ggagtcccatcaaggttcagcggcagtggatctggaacagaattca |

Figure 55D

Antibody Light chain DNA features

| Sequence Name | FR3 | CDR3 |
|---|---|---|
| Ab1 | ctctcaccatcagcggcgtggagtgtgccgatgctgccacttactattgt | caacaggcttatagtgttagtaatg |
| Ab2 | ctctcaccatcagcagcctgcagcctgatgattttgcaacttattactgc | caacaggcttatagtgttagtaatg |
| Ab3 | ctctcaccatcagcggcgtggagtgtgacgatgctgccacttactactgt | caacagggttatactatcgataatg |
| Ab4 | ctctcaccatcagcggcctggagcctgaagatgctgcaacttactattgt | caacagggttatactatcgataatg |
| Ab5 | ctctcaccatcagcggcgtggagtgtgacgatgctgccacttactactgt | caacaggattggagtgatagtaatg |
| Ab6 | ctctcaccatcagcgacctggagtgtgccgatgctgccacttactactgt | caaaactattattatagtagtagga |
| Ab7 | ctctcaccatcagcggcgtggagtgtgccgatgctgccacttactactgt | caacaggcttatagtgttgccaatg |
| Ab8 | ctctcaccatcagcagcctgcagcctgatgattttgcaacttattactgc | caacaggcttatagtgttgccaatg |
| Ab9 | ctctcaccatcagcgacctggagtgtgacgatgctgccagttactactgt | gcaggctattatagtggtcatattt |
| Ab10 | ctctcaccatcagcagcctgcagcctgaagattttgcaacttactattgt | gcaggctactatagtggtcatatct |
| Ab11 | ctctcaccatcagcggcgtgcagtgtgacgatgctgccacttactactgt | ctaggcggttatgatggtgatgctg |
| Ab12 | ctctcaccatcagcggcgtggagtgtgccgatgctgccacttactactgt | caacaggcttatagtgttagtaatg |
| Ab13 | ctctcaccatcagcagcctgcagcctgatgattttgcaacttattactgc | caacaggcttatagtgttagtaatg |
| Ab14 | ctctcaccatcagcggcgtggaatgtgccgatgctgccacttactactgt | caacagggtgatgcttggagtaatg |
| Ab15 | ctctcaccatcagcggcgtggagtgtgccgatgctgccacttactactgt | caacagggtgatgcttggagtaatg |
| Ab16 | ctctcaccatcagtggcgtgcagtgtgcagatgctgccacttactactgt | caaggcgaatttagttgtggtgatg |
| Ab17 | ctctcaccatcagcggcgtacagtgtggagatgctgccacttactactgt | caaggcgaatttagttgtggtagtg |
| Ab18 | ctctcaccatcagcggcgtggagtgtgccgatgctgccacttactactgt | caccagggttatagtagtagtaatg |
| Ab19 | ctctcaccatcagcgacctggagtgtgccgatgctgccacttactactgt | caatttactgcttattatagtactt |
| Ab20 | ctctcaccatcagcagcctgcagcctgaagatgttgcaacttattactgt | caattcactgcttattatagtactt |
| Ab21 | ctctcaccatcagcgacctggagtgtgccgatgctgccacttactactgt | cagcagacttatggttatagtgata |
| Ab23 | ctctcaccatcagcggcgtggagtgtgccgatgctgccacttactactgt | caacagggttatagttatagtaatg |
| Ab24 | ctctcaccatcagcagcctgcagcctgaagatgttgcaacttattactgt | caacagggttatagttatagtaatg |
| Ab25 | ctctcaccatcagcgacctggagtgtgacgatgctgccacttactactgt | caaggcagttatagtggtggtattt |
| Ab26 | ctctcaccatcagcgacctggagtgtgccgatgctgccacttactactgt | caaagcaattatgatatttatagtt |
| Ab27 | ctctcaccatcagcgacctggagtgtgccgatgctgccacgtactattgc | caatttagtaatagtggtactattt |
| Ab28 | ctctcaccatcagcagcctgcagcctgatgattttgcaacttattactgc | caacaggcttatagtgttgccaatg |

Figure 55E

Antibody Light chain DNA features

| Sequence Name | CDR3 | FR4 | Constant region |
|---|---|---|---|
| Ab1 | ttgataatgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtggctgcaccatctg |
| Ab2 | ttgataatgct | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtagcggccccatctg |
| Ab3 | ttgataatact | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab4 | ttgacaatact | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtagcggccccatctg |
| Ab5 | ttgataatgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab6 | gtagttatgatacatataatgtt | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab7 | ttgataatgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab8 | ttgataatgct | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtagcggccccatctg |
| Ab9 | attct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab10 | attct | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtagcggccccatctg |
| Ab11 | atacatataatact | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab12 | ttgataatgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab13 | ttgataatgct | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtggctgcaccatctg |
| Ab14 | ttgataatgtt | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab15 | ttgataatgtt | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab16 | ttgattgtattgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab17 | ctgattgtgttgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab18 | ttgataatact | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab19 | atattggagct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab20 | acattggagct | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtggctgcaccatctg |
| Ab21 | ctgataattct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab23 | ttgataatgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab24 | ttgataatgct | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtggctgcaccatctg |
| Ab25 | gtgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab26 | atgct | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab27 | atgggagtggt | ttcggcggagggaccgaggtggtggtcaaacgt | acggtagcggccccatctg |
| Ab28 | ttgataatgct | ttcggcggaggaaccaaggtggaaatcaaacgt | acggtggctgcaccatctg |

Figure 55F

Antibody Light chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab2 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab3 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab4 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab5 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab6 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab7 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab8 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab9 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab10 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab11 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab12 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab13 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab14 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab15 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab16 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab17 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab18 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab19 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab20 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab21 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab23 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab24 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab25 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab26 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab27 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |
| Ab28 | tcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttct |

Figure 55G

Antibody Light chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab2 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab3 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab4 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab5 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab6 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab7 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab8 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab9 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab10 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab11 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab12 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab13 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab14 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab15 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab16 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab17 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab18 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab19 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab20 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab21 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab23 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab24 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab25 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab26 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab27 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |
| Ab28 | atcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacag |

Figure 55H

Antibody Light chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab2 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab3 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab4 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab5 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab6 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab7 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab8 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab9 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab10 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab11 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab12 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab13 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab14 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab15 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab16 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab17 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab18 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab19 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab20 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab21 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab23 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab24 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab25 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab26 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab27 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |
| Ab28 | agcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacaca |

Figure 55I

Antibody Light chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab2 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab3 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab4 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab5 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab6 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab7 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab8 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab9 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab10 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab11 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab12 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab13 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab14 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab15 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab16 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab17 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab18 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab19 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab20 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab21 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab23 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab24 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab25 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab26 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab27 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |
| Ab28 | aagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggggagagtgt |

Figure 55J

Antibody Light chain DNA features

| Sequence Name | Constant region |
|---|---|
| Ab1 | (SEQ_ID_NO:31) |
| Ab2 | (SEQ_ID_NO:71) |
| Ab3 | (SEQ_ID_NO:111) |
| Ab4 | (SEQ_ID_NO:151) |
| Ab5 | (SEQ_ID_NO:191) |
| Ab6 | (SEQ_ID_NO:231) |
| Ab7 | (SEQ_ID_NO:271) |
| Ab8 | (SEQ_ID_NO:311) |
| Ab9 | (SEQ_ID_NO:351) |
| Ab10 | (SEQ_ID_NO:391) |
| Ab11 | (SEQ_ID_NO:431) |
| Ab12 | (SEQ_ID_NO:471) |
| Ab13 | (SEQ_ID_NO:511) |
| Ab14 | (SEQ_ID_NO:551) |
| Ab15 | (SEQ_ID_NO:591) |
| Ab16 | (SEQ_ID_NO:631) |
| Ab17 | (SEQ_ID_NO:671) |
| Ab18 | (SEQ_ID_NO:711) |
| Ab19 | (SEQ_ID_NO:751) |
| Ab20 | (SEQ_ID_NO:791) |
| Ab21 | (SEQ_ID_NO:831) |
| Ab23 | (SEQ_ID_NO:871) |
| Ab24 | (SEQ_ID_NO:911) |
| Ab25 | (SEQ_ID_NO:951) |
| Ab26 | (SEQ_ID_NO:991) |
| Ab27 | (SEQ_ID_NO:1031) |
| Ab28 | (SEQ_ID_NO:1071) |

Figure 56

Antibody Heavy chain Protein features

| Sequence Name | Variable region coordinates | SEQ ID NO: | CDR1 coordinates | SEQ ID NO: | CDR2 coordinates | SEQ ID NO: | CDR3 coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-116 | 2 | 30-34 | 4 | 49-64 | 6 | 95-105 | 8 |
| Ab2 | 1-119 | 42 | 31-35 | 44 | 50-65 | 46 | 98-108 | 48 |
| Ab3 | 1-117 | 82 | 30-34 | 84 | 49-64 | 86 | 95-106 | 88 |
| Ab4 | 1-117 | 122 | 30-34 | 124 | 49-64 | 126 | 95-106 | 128 |
| Ab5 | 1-113 | 162 | 30-34 | 164 | 49-64 | 166 | 95-102 | 168 |
| Ab6 | 1-116 | 202 | 30-34 | 204 | 49-64 | 206 | 95-105 | 208 |
| Ab7 | 1-116 | 242 | 30-34 | 244 | 49-64 | 246 | 95-105 | 248 |
| Ab8 | 1-119 | 282 | 31-35 | 284 | 50-65 | 286 | 98-108 | 288 |
| Ab9 | 1-120 | 322 | 30-34 | 324 | 49-64 | 326 | 96-109 | 328 |
| Ab10 | 1-122 | 362 | 31-35 | 364 | 50-65 | 366 | 98-111 | 368 |
| Ab11 | 1-128 | 402 | 30-34 | 404 | 49-64 | 406 | 95-117 | 408 |
| Ab12 | 1-116 | 442 | 30-34 | 444 | 49-64 | 446 | 95-105 | 448 |
| Ab13 | 1-119 | 482 | 31-35 | 484 | 50-65 | 486 | 98-108 | 488 |
| Ab14 | 1-116 | 522 | 30-34 | 524 | 49-64 | 526 | 95-105 | 528 |
| Ab15 | 1-116 | 562 | 30-34 | 564 | 49-64 | 566 | 95-105 | 568 |
| Ab16 | 1-119 | 602 | 30-34 | 604 | 49-64 | 606 | 95-108 | 608 |
| Ab17 | 1-119 | 642 | 30-34 | 644 | 49-64 | 646 | 95-108 | 648 |
| Ab18 | 1-120 | 682 | 30-34 | 684 | 49-65 | 686 | 96-109 | 688 |
| Ab19 | 1-118 | 722 | 30-34 | 724 | 49-64 | 726 | 95-107 | 728 |
| Ab20 | 1-121 | 762 | 31-35 | 764 | 50-65 | 766 | 98-110 | 768 |
| Ab21 | 1-117 | 802 | 30-34 | 804 | 49-64 | 806 | 95-106 | 808 |
| Ab23 | 1-116 | 842 | 30-34 | 844 | 49-65 | 846 | 96-105 | 848 |
| Ab24 | 1-119 | 882 | 31-35 | 884 | 50-66 | 886 | 99-108 | 888 |
| Ab25 | 1-118 | 922 | 30-34 | 924 | 49-64 | 926 | 95-107 | 928 |
| Ab26 | 1-119 | 962 | 30-34 | 964 | 49-64 | 966 | 95-108 | 968 |
| Ab27 | 1-123 | 1002 | 30-35 | 1004 | 50-67 | 1006 | 99-112 | 1008 |
| Ab28 | 1-119 | 1042 | 31-35 | 1044 | 50-65 | 1046 | 98-108 | 1048 |

Figure 57

Antibody Heavy chain Protein features

| Sequence Name | FR1 coordinates | SEQ ID NO: | FR2 coordinates | SEQ ID NO: | FR3 coordinates | SEQ ID NO: | FR4 coordinates | SEQ ID NO: | Constant region coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-29 | 3 | 35-48 | 5 | 65-94 | 7 | 106-116 | 9 | 117-446 | 10 |
| Ab2 | 1-30 | 43 | 36-49 | 45 | 66-97 | 47 | 109-119 | 49 | 120-449 | 50 |
| Ab3 | 1-29 | 83 | 35-48 | 85 | 65-94 | 87 | 107-117 | 89 | 118-447 | 90 |
| Ab4 | 1-29 | 123 | 35-48 | 125 | 65-94 | 127 | 107-117 | 129 | 118-447 | 130 |
| Ab5 | 1-29 | 163 | 35-48 | 165 | 65-94 | 167 | 103-113 | 169 | 114-443 | 170 |
| Ab6 | 1-29 | 203 | 35-48 | 205 | 65-94 | 207 | 106-116 | 209 | 117-446 | 210 |
| Ab7 | 1-29 | 243 | 35-48 | 245 | 65-94 | 247 | 106-116 | 249 | 117-446 | 250 |
| Ab8 | 1-30 | 283 | 36-49 | 285 | 66-97 | 287 | 109-119 | 289 | 120-449 | 290 |
| Ab9 | 1-29 | 323 | 35-48 | 325 | 65-95 | 327 | 110-120 | 329 | 121-450 | 330 |
| Ab10 | 1-30 | 363 | 36-49 | 365 | 66-97 | 367 | 112-122 | 369 | 123-452 | 370 |
| Ab11 | 1-29 | 403 | 35-48 | 405 | 65-94 | 407 | 118-128 | 409 | 129-458 | 410 |
| Ab12 | 1-29 | 443 | 35-48 | 445 | 65-94 | 447 | 106-116 | 449 | 117-446 | 450 |
| Ab13 | 1-30 | 483 | 36-49 | 485 | 66-97 | 487 | 109-119 | 489 | 120-449 | 490 |
| Ab14 | 1-29 | 523 | 35-48 | 525 | 65-94 | 527 | 106-116 | 529 | 117-446 | 530 |
| Ab15 | 1-29 | 563 | 35-48 | 565 | 65-94 | 567 | 106-116 | 569 | 117-446 | 570 |
| Ab16 | 1-29 | 603 | 35-48 | 605 | 65-94 | 607 | 109-119 | 609 | 120-449 | 610 |
| Ab17 | 1-29 | 643 | 35-48 | 645 | 65-94 | 647 | 109-119 | 649 | 120-449 | 650 |
| Ab18 | 1-29 | 683 | 35-48 | 685 | 66-95 | 687 | 110-120 | 689 | 121-450 | 690 |
| Ab19 | 1-29 | 723 | 35-48 | 725 | 65-94 | 727 | 108-118 | 729 | 119-448 | 730 |
| Ab20 | 1-30 | 763 | 36-49 | 765 | 66-97 | 767 | 111-121 | 769 | 122-451 | 770 |
| Ab21 | 1-29 | 803 | 35-48 | 805 | 65-94 | 807 | 107-117 | 809 | 118-447 | 810 |
| Ab23 | 1-29 | 843 | 35-48 | 845 | 66-95 | 847 | 106-116 | 849 | 117-446 | 850 |
| Ab24 | 1-30 | 883 | 36-49 | 885 | 67-98 | 887 | 109-119 | 889 | 120-449 | 890 |
| Ab25 | 1-29 | 923 | 35-48 | 925 | 65-94 | 927 | 108-118 | 929 | 119-448 | 930 |
| Ab26 | 1-29 | 963 | 35-48 | 965 | 65-94 | 967 | 109-119 | 969 | 120-449 | 970 |
| Ab27 | 1-29 | 1003 | 36-49 | 1005 | 68-98 | 1007 | 113-123 | 1009 | 124-453 | 1010 |
| Ab28 | 1-30 | 1043 | 36-49 | 1045 | 66-97 | 1047 | 109-119 | 1049 | 120-449 | 1050 |

Figure 58

Antibody Light chain Protein features

| Sequence Name | Variable region coordinates | SEQ ID NO: | CDR1 coordinates | SEQ ID NO: | CDR2 coordinates | SEQ ID NO: | CDR3 coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-111 | 22 | 24-34 | 24 | 50-56 | 26 | 89-100 | 28 |
| Ab2 | 1-111 | 62 | 24-34 | 64 | 50-56 | 66 | 89-100 | 68 |
| Ab3 | 1-111 | 102 | 24-34 | 104 | 50-56 | 106 | 89-100 | 108 |
| Ab4 | 1-111 | 142 | 24-34 | 144 | 50-56 | 146 | 89-100 | 148 |
| Ab5 | 1-111 | 182 | 24-34 | 184 | 50-56 | 186 | 89-100 | 188 |
| Ab6 | 1-116 | 222 | 25-35 | 224 | 51-57 | 226 | 90-105 | 228 |
| Ab7 | 1-111 | 262 | 24-34 | 264 | 50-56 | 266 | 89-100 | 268 |
| Ab8 | 1-111 | 302 | 24-34 | 304 | 50-56 | 306 | 89-100 | 308 |
| Ab9 | 1-109 | 342 | 23-34 | 344 | 50-56 | 346 | 89-98 | 348 |
| Ab10 | 1-110 | 382 | 24-35 | 384 | 51-57 | 386 | 90-99 | 388 |
| Ab11 | 1-113 | 422 | 23-35 | 424 | 51-57 | 426 | 90-102 | 428 |
| Ab12 | 1-111 | 462 | 24-34 | 464 | 50-56 | 466 | 89-100 | 468 |
| Ab13 | 1-111 | 502 | 24-34 | 504 | 50-56 | 506 | 89-100 | 508 |
| Ab14 | 1-111 | 542 | 24-34 | 544 | 50-56 | 546 | 89-100 | 548 |
| Ab15 | 1-111 | 582 | 24-34 | 584 | 50-56 | 586 | 89-100 | 588 |
| Ab16 | 1-113 | 622 | 23-35 | 624 | 51-57 | 626 | 90-102 | 628 |
| Ab17 | 1-113 | 662 | 23-35 | 664 | 51-57 | 666 | 90-102 | 668 |
| Ab18 | 1-111 | 702 | 24-34 | 704 | 50-56 | 706 | 89-100 | 708 |
| Ab19 | 1-111 | 742 | 24-34 | 744 | 50-56 | 746 | 89-100 | 748 |
| Ab20 | 1-111 | 782 | 24-34 | 784 | 50-56 | 786 | 89-100 | 788 |
| Ab21 | 1-111 | 822 | 24-34 | 824 | 50-56 | 826 | 89-100 | 828 |
| Ab23 | 1-111 | 862 | 24-34 | 864 | 50-56 | 866 | 89-100 | 868 |
| Ab24 | 1-111 | 902 | 24-34 | 904 | 50-56 | 906 | 89-100 | 908 |
| Ab25 | 1-110 | 942 | 23-35 | 944 | 51-57 | 946 | 90-99 | 948 |
| Ab26 | 1-110 | 982 | 25-35 | 984 | 51-57 | 986 | 90-99 | 988 |
| Ab27 | 1-112 | 1022 | 25-35 | 1024 | 51-57 | 1026 | 90-101 | 1028 |
| Ab28 | 1-111 | 1062 | 24-34 | 1064 | 50-56 | 1066 | 89-100 | 1068 |

Figure 59

Antibody Light chain Protein features

| Sequence Name | FR1 coordinates | SEQ ID NO: | FR2 coordinates | SEQ ID NO: | FR3 coordinates | SEQ ID NO: | FR4 coordinates | SEQ ID NO: | Constant region coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-23 | 23 | 35-49 | 25 | 57-88 | 27 | 101-111 | 29 | 112-217 | 30 |
| Ab2 | 1-23 | 63 | 35-49 | 65 | 57-88 | 67 | 101-111 | 69 | 112-217 | 70 |
| Ab3 | 1-23 | 103 | 35-49 | 105 | 57-88 | 107 | 101-111 | 109 | 112-217 | 110 |
| Ab4 | 1-23 | 143 | 35-49 | 145 | 57-88 | 147 | 101-111 | 149 | 112-217 | 150 |
| Ab5 | 1-23 | 183 | 35-49 | 185 | 57-88 | 187 | 101-111 | 189 | 112-217 | 190 |
| Ab6 | 1-24 | 223 | 36-50 | 225 | 58-89 | 227 | 106-116 | 229 | 117-222 | 230 |
| Ab7 | 1-23 | 263 | 35-49 | 265 | 57-88 | 267 | 101-111 | 269 | 112-217 | 270 |
| Ab8 | 1-23 | 303 | 35-49 | 305 | 57-88 | 307 | 101-111 | 309 | 112-217 | 310 |
| Ab9 | 1-22 | 343 | 35-49 | 345 | 57-88 | 347 | 99-109 | 349 | 110-215 | 350 |
| Ab10 | 1-23 | 383 | 36-50 | 385 | 58-89 | 387 | 100-110 | 389 | 111-216 | 390 |
| Ab11 | 1-22 | 423 | 36-50 | 425 | 58-89 | 427 | 103-113 | 429 | 114-219 | 430 |
| Ab12 | 1-23 | 463 | 35-49 | 465 | 57-88 | 467 | 101-111 | 469 | 112-217 | 470 |
| Ab13 | 1-23 | 503 | 35-49 | 505 | 57-88 | 507 | 101-111 | 509 | 112-217 | 510 |
| Ab14 | 1-23 | 543 | 35-49 | 545 | 57-88 | 547 | 101-111 | 549 | 112-217 | 550 |
| Ab15 | 1-23 | 583 | 35-49 | 585 | 57-88 | 587 | 101-111 | 589 | 112-217 | 590 |
| Ab16 | 1-22 | 623 | 36-50 | 625 | 58-89 | 627 | 103-113 | 629 | 114-219 | 630 |
| Ab17 | 1-22 | 663 | 36-50 | 665 | 58-89 | 667 | 103-113 | 669 | 114-219 | 670 |
| Ab18 | 1-23 | 703 | 35-49 | 705 | 57-88 | 707 | 101-111 | 709 | 112-217 | 710 |
| Ab19 | 1-23 | 743 | 35-49 | 745 | 57-88 | 747 | 101-111 | 749 | 112-217 | 750 |
| Ab20 | 1-23 | 783 | 35-49 | 785 | 57-88 | 787 | 101-111 | 789 | 112-217 | 790 |
| Ab21 | 1-23 | 823 | 35-49 | 825 | 57-88 | 827 | 101-111 | 829 | 112-217 | 830 |
| Ab23 | 1-23 | 863 | 35-49 | 865 | 57-88 | 867 | 101-111 | 869 | 112-217 | 870 |
| Ab24 | 1-23 | 903 | 35-49 | 905 | 57-88 | 907 | 101-111 | 909 | 112-217 | 910 |
| Ab25 | 1-22 | 943 | 36-50 | 945 | 58-89 | 947 | 100-110 | 949 | 111-216 | 950 |
| Ab26 | 1-24 | 983 | 36-50 | 985 | 58-89 | 987 | 100-110 | 989 | 111-216 | 990 |
| Ab27 | 1-24 | 1023 | 36-50 | 1025 | 58-89 | 1027 | 102-112 | 1029 | 113-218 | 1030 |
| Ab28 | 1-23 | 1063 | 35-49 | 1065 | 57-88 | 1067 | 101-111 | 1069 | 112-217 | 1070 |

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Figure 60

Antibody Heavy chain DNA features

| Sequence Name | Variable region coordinates | SEQ ID NO: | CDR1 coordinates | SEQ ID NO: | CDR2 coordinates | SEQ ID NO: | CDR3 coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-348 | 12 | 88-102 | 14 | 145-192 | 16 | 283-315 | 18 |
| Ab2 | 1-357 | 52 | 91-105 | 54 | 148-195 | 56 | 292-324 | 58 |
| Ab3 | 1-351 | 92 | 88-102 | 94 | 145-192 | 96 | 283-318 | 98 |
| Ab4 | 1-351 | 132 | 88-102 | 134 | 145-192 | 136 | 283-318 | 138 |
| Ab5 | 1-339 | 172 | 88-102 | 174 | 145-192 | 176 | 283-306 | 178 |
| Ab6 | 1-348 | 212 | 88-102 | 214 | 145-192 | 216 | 283-315 | 218 |
| Ab7 | 1-348 | 252 | 88-102 | 254 | 145-192 | 256 | 283-315 | 258 |
| Ab8 | 1-357 | 292 | 91-105 | 294 | 148-195 | 296 | 292-324 | 298 |
| Ab9 | 1-360 | 332 | 88-102 | 334 | 145-192 | 336 | 286-327 | 338 |
| Ab10 | 1-366 | 372 | 91-105 | 374 | 148-195 | 376 | 292-333 | 378 |
| Ab11 | 1-384 | 412 | 88-102 | 414 | 145-192 | 416 | 283-351 | 418 |
| Ab12 | 1-348 | 452 | 88-102 | 454 | 145-192 | 456 | 283-315 | 458 |
| Ab13 | 1-357 | 492 | 91-105 | 494 | 148-195 | 496 | 292-324 | 498 |
| Ab14 | 1-348 | 532 | 88-102 | 534 | 145-192 | 536 | 283-315 | 538 |
| Ab15 | 1-348 | 572 | 88-102 | 574 | 145-192 | 576 | 283-315 | 578 |
| Ab16 | 1-357 | 612 | 88-102 | 614 | 145-192 | 616 | 283-324 | 618 |
| Ab17 | 1-357 | 652 | 88-102 | 654 | 145-192 | 656 | 283-324 | 658 |
| Ab18 | 1-360 | 692 | 88-102 | 694 | 145-195 | 696 | 286-327 | 698 |
| Ab19 | 1-354 | 732 | 88-102 | 734 | 145-192 | 736 | 283-321 | 738 |
| Ab20 | 1-363 | 772 | 91-105 | 774 | 148-195 | 776 | 292-330 | 778 |
| Ab21 | 1-351 | 812 | 88-102 | 814 | 145-192 | 816 | 283-318 | 818 |
| Ab23 | 1-348 | 852 | 88-102 | 854 | 145-195 | 856 | 286-315 | 858 |
| Ab24 | 1-357 | 892 | 91-105 | 894 | 148-198 | 896 | 295-324 | 898 |
| Ab25 | 1-354 | 932 | 88-102 | 934 | 145-192 | 936 | 283-321 | 938 |
| Ab26 | 1-357 | 972 | 88-102 | 974 | 145-192 | 976 | 283-324 | 978 |
| Ab27 | 1-369 | 1012 | 88-105 | 1014 | 148-201 | 1016 | 295-336 | 1018 |
| Ab28 | 1-357 | 1052 | 91-105 | 1054 | 148-195 | 1056 | 292-324 | 1058 |

Figure 61

Antibody Heavy chain DNA features

| Sequence Name | FR1 coordinates | SEQ ID NO: | FR2 coordinates | SEQ ID NO: | FR3 coordinates | SEQ ID NO: | FR4 coordinates | SEQ ID NO: | Constant region coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-87 | 13 | 103-144 | 15 | 193-282 | 17 | 316-348 | 19 | 349-1338 | 20 |
| Ab2 | 1-90 | 53 | 106-147 | 55 | 196-291 | 57 | 325-357 | 59 | 358-1347 | 60 |
| Ab3 | 1-87 | 93 | 103-144 | 95 | 193-282 | 97 | 319-351 | 99 | 352-1341 | 100 |
| Ab4 | 1-87 | 133 | 103-144 | 135 | 193-282 | 137 | 319-351 | 139 | 352-1341 | 140 |
| Ab5 | 1-87 | 173 | 103-144 | 175 | 193-282 | 177 | 307-339 | 179 | 340-1329 | 180 |
| Ab6 | 1-87 | 213 | 103-144 | 215 | 193-282 | 217 | 316-348 | 219 | 349-1338 | 220 |
| Ab7 | 1-87 | 253 | 103-144 | 255 | 193-282 | 257 | 316-348 | 259 | 349-1338 | 260 |
| Ab8 | 1-90 | 293 | 106-147 | 295 | 196-291 | 297 | 325-357 | 299 | 358-1347 | 300 |
| Ab9 | 1-87 | 333 | 103-144 | 335 | 193-285 | 337 | 328-360 | 339 | 361-1350 | 340 |
| Ab10 | 1-90 | 373 | 106-147 | 375 | 196-291 | 377 | 334-366 | 379 | 367-1356 | 380 |
| Ab11 | 1-87 | 413 | 103-144 | 415 | 193-282 | 417 | 352-384 | 419 | 385-1374 | 420 |
| Ab12 | 1-87 | 453 | 103-144 | 455 | 193-282 | 457 | 316-348 | 459 | 349-1338 | 460 |
| Ab13 | 1-90 | 493 | 106-147 | 495 | 196-291 | 497 | 325-357 | 499 | 358-1347 | 500 |
| Ab14 | 1-87 | 533 | 103-144 | 535 | 193-282 | 537 | 316-348 | 539 | 349-1338 | 540 |
| Ab15 | 1-87 | 573 | 103-144 | 575 | 193-282 | 577 | 316-348 | 579 | 349-1338 | 580 |
| Ab16 | 1-87 | 613 | 103-144 | 615 | 193-282 | 617 | 325-357 | 619 | 358-1347 | 620 |
| Ab17 | 1-87 | 653 | 103-144 | 655 | 193-282 | 657 | 325-357 | 659 | 358-1347 | 660 |
| Ab18 | 1-87 | 693 | 103-144 | 695 | 196-285 | 697 | 328-360 | 699 | 361-1350 | 700 |
| Ab19 | 1-87 | 733 | 103-144 | 735 | 193-282 | 737 | 322-354 | 739 | 355-1344 | 740 |
| Ab20 | 1-90 | 773 | 106-147 | 775 | 196-291 | 777 | 331-363 | 779 | 364-1353 | 780 |
| Ab21 | 1-87 | 813 | 103-144 | 815 | 193-282 | 817 | 319-351 | 819 | 352-1341 | 820 |
| Ab23 | 1-87 | 853 | 103-144 | 855 | 196-285 | 857 | 316-348 | 859 | 349-1338 | 860 |
| Ab24 | 1-90 | 893 | 106-147 | 895 | 199-294 | 897 | 325-357 | 899 | 358-1347 | 900 |
| Ab25 | 1-87 | 933 | 103-144 | 935 | 193-282 | 937 | 322-354 | 939 | 355-1344 | 940 |
| Ab26 | 1-87 | 973 | 103-144 | 975 | 193-282 | 977 | 325-357 | 979 | 358-1347 | 980 |
| Ab27 | 1-87 | 1013 | 106-147 | 1015 | 202-294 | 1017 | 337-369 | 1019 | 370-1359 | 1020 |
| Ab28 | 1-90 | 1053 | 106-147 | 1055 | 196-291 | 1057 | 325-357 | 1059 | 358-1347 | 1060 |

Figure 62

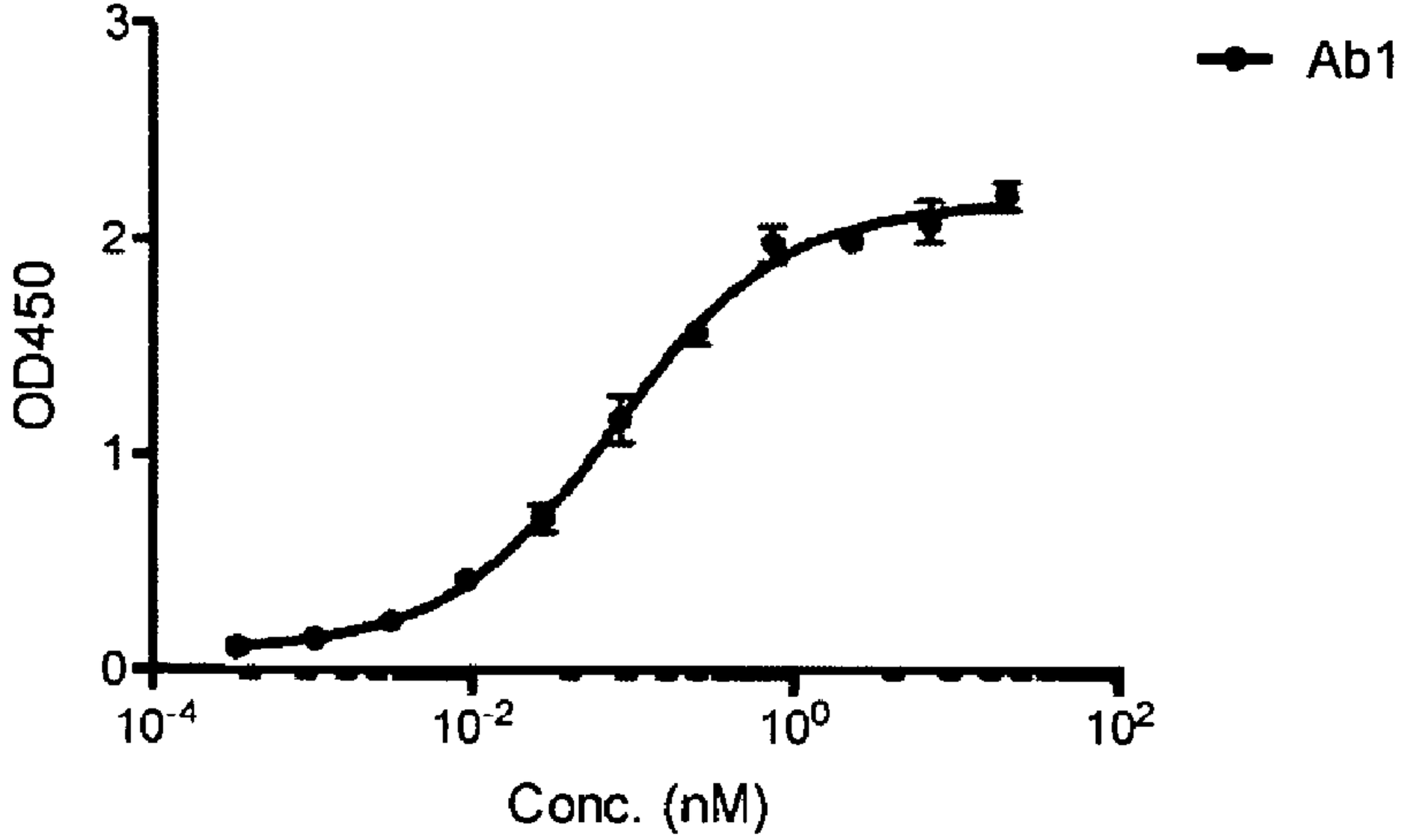
Antibody Light chain DNA features

| Sequence Name | Variable region coordinates | SEQ ID NO: | CDR1 coordinates | SEQ ID NO: | CDR2 coordinates | SEQ ID NO: | CDR3 coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-333 | 32 | 70-102 | 34 | 148-168 | 36 | 265-300 | 38 |
| Ab2 | 1-333 | 72 | 70-102 | 74 | 148-168 | 76 | 265-300 | 78 |
| Ab3 | 1-333 | 112 | 70-102 | 114 | 148-168 | 116 | 265-300 | 118 |
| Ab4 | 1-333 | 152 | 70-102 | 154 | 148-168 | 156 | 265-300 | 158 |
| Ab5 | 1-333 | 192 | 70-102 | 194 | 148-168 | 196 | 265-300 | 198 |
| Ab6 | 1-348 | 232 | 73-105 | 234 | 151-171 | 236 | 268-315 | 238 |
| Ab7 | 1-333 | 272 | 70-102 | 274 | 148-168 | 276 | 265-300 | 278 |
| Ab8 | 1-333 | 312 | 70-102 | 314 | 148-168 | 316 | 265-300 | 318 |
| Ab9 | 1-327 | 352 | 67-102 | 354 | 148-168 | 356 | 265-294 | 358 |
| Ab10 | 1-330 | 392 | 70-105 | 394 | 151-171 | 396 | 268-297 | 398 |
| Ab11 | 1-339 | 432 | 67-105 | 434 | 151-171 | 436 | 268-306 | 438 |
| Ab12 | 1-333 | 472 | 70-102 | 474 | 148-168 | 476 | 265-300 | 478 |
| Ab13 | 1-333 | 512 | 70-102 | 514 | 148-168 | 516 | 265-300 | 518 |
| Ab14 | 1-333 | 552 | 70-102 | 554 | 148-168 | 556 | 265-300 | 558 |
| Ab15 | 1-333 | 592 | 70-102 | 594 | 148-168 | 596 | 265-300 | 598 |
| Ab16 | 1-339 | 632 | 67-105 | 634 | 151-171 | 636 | 268-306 | 638 |
| Ab17 | 1-339 | 672 | 67-105 | 674 | 151-171 | 676 | 268-306 | 678 |
| Ab18 | 1-333 | 712 | 70-102 | 714 | 148-168 | 716 | 265-300 | 718 |
| Ab19 | 1-333 | 752 | 70-102 | 754 | 148-168 | 756 | 265-300 | 758 |
| Ab20 | 1-333 | 792 | 70-102 | 794 | 148-168 | 796 | 265-300 | 798 |
| Ab21 | 1-333 | 832 | 70-102 | 834 | 148-168 | 836 | 265-300 | 838 |
| Ab23 | 1-333 | 872 | 70-102 | 874 | 148-168 | 876 | 265-300 | 878 |
| Ab24 | 1-333 | 912 | 70-102 | 914 | 148-168 | 916 | 265-300 | 918 |
| Ab25 | 1-330 | 952 | 67-105 | 954 | 151-171 | 956 | 268-297 | 958 |
| Ab26 | 1-330 | 992 | 73-105 | 994 | 151-171 | 996 | 268-297 | 998 |
| Ab27 | 1-336 | 1032 | 73-105 | 1034 | 151-171 | 1036 | 268-303 | 1038 |
| Ab28 | 1-333 | 1072 | 70-102 | 1074 | 148-168 | 1076 | 265-300 | 1078 |

Figure 63

Antibody Light chain DNA features

| Sequence Name | FR1 coordinates | SEQ ID NO: | FR2 coordinates | SEQ ID NO: | FR3 coordinates | SEQ ID NO: | FR4 coordinates | SEQ ID NO: | Constant region coordinates | SEQ ID NO: |
|---|---|---|---|---|---|---|---|---|---|---|
| Ab1 | 1-69 | 33 | 103-147 | 35 | 169-264 | 37 | 301-333 | 39 | 334-651 | 40 |
| Ab2 | 1-69 | 73 | 103-147 | 75 | 169-264 | 77 | 301-333 | 79 | 334-651 | 80 |
| Ab3 | 1-69 | 113 | 103-147 | 115 | 169-264 | 117 | 301-333 | 119 | 334-651 | 120 |
| Ab4 | 1-69 | 153 | 103-147 | 155 | 169-264 | 157 | 301-333 | 159 | 334-651 | 160 |
| Ab5 | 1-69 | 193 | 103-147 | 195 | 169-264 | 197 | 301-333 | 199 | 334-651 | 200 |
| Ab6 | 1-72 | 233 | 106-150 | 235 | 172-267 | 237 | 316-348 | 239 | 349-666 | 240 |
| Ab7 | 1-69 | 273 | 103-147 | 275 | 169-264 | 277 | 301-333 | 279 | 334-651 | 280 |
| Ab8 | 1-69 | 313 | 103-147 | 315 | 169-264 | 317 | 301-333 | 319 | 334-651 | 320 |
| Ab9 | 1-66 | 353 | 103-147 | 355 | 169-264 | 357 | 295-327 | 359 | 328-645 | 360 |
| Ab10 | 1-69 | 393 | 106-150 | 395 | 172-267 | 397 | 298-330 | 399 | 331-648 | 400 |
| Ab11 | 1-66 | 433 | 106-150 | 435 | 172-267 | 437 | 307-339 | 439 | 340-657 | 440 |
| Ab12 | 1-69 | 473 | 103-147 | 475 | 169-264 | 477 | 301-333 | 479 | 334-651 | 480 |
| Ab13 | 1-69 | 513 | 103-147 | 515 | 169-264 | 517 | 301-333 | 519 | 334-651 | 520 |
| Ab14 | 1-69 | 553 | 103-147 | 555 | 169-264 | 557 | 301-333 | 559 | 334-651 | 560 |
| Ab15 | 1-69 | 593 | 103-147 | 595 | 169-264 | 597 | 301-333 | 599 | 334-651 | 600 |
| Ab16 | 1-66 | 633 | 106-150 | 635 | 172-267 | 637 | 307-339 | 639 | 340-657 | 640 |
| Ab17 | 1-66 | 673 | 106-150 | 675 | 172-267 | 677 | 307-339 | 679 | 340-657 | 680 |
| Ab18 | 1-69 | 713 | 103-147 | 715 | 169-264 | 717 | 301-333 | 719 | 334-651 | 720 |
| Ab19 | 1-69 | 753 | 103-147 | 755 | 169-264 | 757 | 301-333 | 759 | 334-651 | 760 |
| Ab20 | 1-69 | 793 | 103-147 | 795 | 169-264 | 797 | 301-333 | 799 | 334-651 | 800 |
| Ab21 | 1-69 | 833 | 103-147 | 835 | 169-264 | 837 | 301-333 | 839 | 334-651 | 840 |
| Ab23 | 1-69 | 873 | 103-147 | 875 | 169-264 | 877 | 301-333 | 879 | 334-651 | 880 |
| Ab24 | 1-69 | 913 | 103-147 | 915 | 169-264 | 917 | 301-333 | 919 | 334-651 | 920 |
| Ab25 | 1-66 | 953 | 106-150 | 955 | 172-267 | 957 | 298-330 | 959 | 331-648 | 960 |
| Ab26 | 1-72 | 993 | 106-150 | 995 | 172-267 | 997 | 298-330 | 999 | 331-648 | 1000 |
| Ab27 | 1-72 | 1033 | 106-150 | 1035 | 172-267 | 1037 | 304-336 | 1039 | 337-654 | 1040 |
| Ab28 | 1-69 | 1073 | 103-147 | 1075 | 169-264 | 1077 | 301-333 | 1079 | 334-651 | 1080 |




| EC50 (pM) | 77 |
|---|---|