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(54) **Title:** HUMANIZED CLDN18.2 ANTIBODIES

(57) **Abstract:** The invention provides humanized antibodies binding to CLDN18.2 with a high affinity. Further, the antibodies do not exhibit cross-reactivity to CLDN18.1. The invention also provides nucleic acids, vectors, host cells and medical uses.

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Humanized CLDN18.2 antibodies

BACKGROUND

Tight junctions are multiprotein complexes connecting adjacent epithelial or endothelial cells to form a barrier, preventing molecules from passing in between the cells, and helping to maintain the cell and tissue polarity. Tight junctions consist of three main groups of transmembrane proteins: claudins and occludin, cytoplasmic plaque proteins, and cingulin. They also contain cytoskeletal and signaling proteins, e.g. actin, myosin II, and PKCζ. These proteins interact to maintain tight junction structure (Yu and Turner 2008).

Claudins form a family of 23 proteins (Hewitt, Agarwal, and Morin 2006). Claudin 18 is human protein encoded by the CLDN18 gene, which forms tight junction strands in epithelial cells. The human CLDN18 can be alternatively spliced with two alternative first exons, resulting in two protein isoforms, CLDN18.1 (or Claudin 18.1) and CLDN18.2 (or Claudin 18.2). CLDN18.2 was first disclosed as Zsig28 protein in WO2000/015659. The two isoforms differ in the N-terminal 69 amino acids, encompassing the first extracellular loop. The first extracellular domain spans from amino acid 28 to amino acid 80. Within this stretch there are 8 amino acid differences between CLDN18.1 and CLDN18.2. The two different isoforms are expressed in different tissues, with CLDN18.1 being predominantly expressed in lung tissue whereas CLDN18.2 displays stomach specificity (Niimi et al. 2001). CLDN18.2 expression in normal stomach is restricted to the differentiated short-lived cells of stomach epithelium. CLDN18.2 expression has further been identified in various tumor tissues. For example, CLDN18.2 has been found to be expressed in pancreatic, esophageal, ovarian, and lung tumors, correlating with distinct histologic subtypes (Sahin et al. 2008).

In view of its restricted expression pattern in normal tissues, and its ectopic expression in human cancers, CLDN18.2 is an attractive pan-cancer target for antibody therapy of epithelial tumors. A number of studies have been made towards such an antibody therapy. WO2004/047863 identified the splice variants of CLDN18 and screened antibodies against different peptides derived from CLDN18.2: peptide DQWSTQDLYN (SEQ ID NO: 68), N-terminal extracellular of CLDN18.2, independent of glycosylation; peptide NNPVTAVFNYQ (SEQ ID NO: 69), N-terminal extracellular of CLDN18.2, mainly unglycosylated; and peptide STQDLYNNPVTAVF (SEQ ID NO: 70), N-terminal extracellular domain of CLDN18.2, unglycosylated. It also disclosed polyclonal rabbit antibodies screened with a pan-CLDN18 peptide TNFWMSTANMYTG (SEQ ID NO: 71) in the C-terminal extracellular domain common to both CLDN18.1 and CLDN18.2 isoforms. WO2005/113587 discloses antibodies against specific epitopes on CLDN18.2 defined by the following peptide sequences: ALMIVGIVLGAIGLLV (SEQ ID NO: 72) and RIGSMEDSAKANMTLTSGIMFIVS (SEQ ID NO: 73). WO200/7059997 discloses CLDN18.2 specific monoclonal antibodies obtained by immunization with the peptide METDTLLLWVLLLWVPGSTGDAAQPARRARRTKLGTELGSTPVWWNSADGRMDQWSTQDLYNNPVTAVFNYQGLWRSCVRESSGFTECRGYFTLLGLPAMLQAVRAAIQHSGGRSRRARTKTHLRRGSE (SEQ ID NO: 74), including the first extracellular domain of CLDN18.2 with N- and C-terminal extensions. Antibodies obtained by this immunization mediate cell killing by complement dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC). Antibody IMAB362, also known as Claudiximab or Zolbetuximab, is disclosed in WO2007/059997 and WO2016/165762. IMAB362 is an IgG1 antibody derived from a murine monoclonal antibody and has been chimerized to display the human IgG1 constant region for clinical use. WO2008/145338 also discloses antibodies binding to overlapping peptides within the first extracellular domain (MDQWSTQDLYNNPVT (SEQ ID NO: 75), LYNNPVTAVFNYQGL (SEQ ID NO: 76), VFNYQGLWRSCVRES (SEQ ID NO: 77), QGLWRSCVRESSGFT (SEQ ID NO: 78), and RSCVRESSGFTECRG (SEQ ID NO: 79)). In an effort to produce antibodies targeting the C-terminal portion of CLDN18.2 for diagnostic purposes to detect CLDN18.2 expression in cells of cancer tissue sections, WO2013/167259 discloses antibodies binding to C-terminal epitopes of CLDN18.2. The sequences of the two epitopes are TEDEVQSYPSKHDYV (SEQ ID NO: 80) and EVQSYPSKHDYV (SEQ ID NO: 81). WO2013/174509 presents combinations of anti-CLDN18.2 antibodies with agents stabilizing γδ T cells or with agents stabilizing or increasing the expression of CLDN18.2. Antibodies may be conjugated to a therapeutic moiety such as a cytotoxin, a drug (e.g. an immunosuppressant) or a radioisotope. WO2014075788 discloses a method of treatment a cancer disease using a bispecific antibody binding CLDN18.2 and CD3. WO2014/127906 discloses combination agents stabilizing or increasing the expression of CLDN18.2. WO2016/166122 discloses anti-CLDN18.2 monoclonal antibodies that can be highly efficiently internalized upon CLDN18.2 binding and therefore, are suitable for antibody-drug conjugate (ADC) development. Furthermore, the conjugation of such antibodies to the drugs DM4 and MMAE using cleavable SPDB or Valine-Citrulline linkers, respectively, is disclosed. However, despite all the antibodies disclosed in the patent applications, only the chimeric IMAB362, disclosed in WO2007/059997 and WO2016/165762, is currently tested in clinical trial. In addition to these antibodies and ADCs, WO2018/006882 discloses chimeric antigen receptor (CAR) based on anti-CLDN18.2 monoclonal antibodies. Antibodies of WO2018/006882 have been humanized and their sequence is disclosed in in the Supplementary Materials section associated with Jiang et al. (2018). CAR T-cells based on the humanized antibody are currently tested in a phase I clinical trial (ClinicalTrials.gov Identifier: NCT03159819) in patients with advanced gastric adenocarcinoma and pancreatic adenocarcinoma. CN109762067 discloses other anti-CLDN18.2 monoclonal antibodies mediating cell killing by CDC and ADCC. WO2019/173420 discloses anti-CLDN18.2 humanized monoclonal antibodies with ADCC activity. WO2019/175617 discloses anti-CLDN18.2 monoclonal antibodies binding to a different epitope than IMAB362. WO2019/219089 discloses monoclonal antibodies binding to a mutant of CLDN18.2.

Chimeric antibodies, having mouse variable regions grafted on human constant domains, are often still immunogenic and this may result in enhanced clearance of the antibody and other safety implications (Sauerborn 2014). Therefore, further modification of the antibody sequence is required to reduce patient immune response and improve its therapeutic activity. Humanization is a process by which xenogeneic antibody sequences are modified to reduce this immunogenicity (Saldanha 2014). However, humanization of an antibody often also leads to loss of affinity. IMAB362, currently the clinically most advanced anti-CLDN18.2 antibody, is a chimeric antibody. Therefore, there is still a need for better anti-CLDN18.2 antibodies. The instant invention is directed to addressing these and other needs, by disclosing humanized IMAB362 antibodies with, surprisingly, higher affinity to CLDN18.2 than IMAB362.

DESCRIPTION OF THE INVENTION

DEFINITIONS

"Antibodies" or “antibody”, also called "immunoglobulins" (Ig), generally comprise four polypeptide chains, two heavy (H) chains and two light (L) chains, and are therefore multimeric proteins, or comprise an equivalent Ig homologue thereof (e.g., a camelid antibody comprising only a heavy chain, single-domain antibodies (sdAb) or nanobodies which can either be derived from a heavy or a light chain). The term “antibodies” includes antibody-based binding proteins, modified antibody formats retaining its target binding capacity. The term “antibodies” also includes full length functional mutants, variants, or derivatives thereof (including, but not limited to, murine, chimeric, humanized and fully human antibodies) which retain the essential epitope binding features of an Ig molecule, and includes dual specific, bispecific, multispecific, and dual variable domain Igs. Ig molecules can be of any class (e.g., IgG, IgE, IgM, IgD, IgA, and IgY), or subclass (e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2) and allotype. Ig molecules may also be mutated e.g. to enhance or reduce affinity for Fcγ receptors or the neonatal Fc receptor (FcRn).

An "antibody fragment", as used herein, relates to a molecule comprising at least one polypeptide chain derived from an antibody that is not full length and exhibits target binding, including, but not limited to (i) a Fab fragment, which is a monovalent fragment consisting of the variable light (VL), variable heavy (VH), constant light (CL) and constant heavy 1 (CH1) domains; (ii) a $F(ab')_2$ fragment, which is a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region (reduction of a $F(ab')_2$ fragment result in two Fab' fragment with a free sulfhydryl group); (iii) a heavy chain portion of a Fab (Fa) fragment, which consists of the VH and CH1 domains; (iv) a variable fragment (Fv) fragment, which consists of the VL and VH domains of a single arm of an antibody; (v) a domain antibody (dAb) fragment, which comprises a single variable domain; (vi) an isolated complementarity determining region (CDR); (vii) a single chain Fv fragment (scFv); (viii) a diabody, which is a bivalent, bispecific antibody in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with the complementarity domains of another chain and creating two antigen binding sites; (ix) a linear antibody, which comprises a pair of tandem Fv segments (VH-CH1-VH-CH1) which, together with complementarity light chain polypeptides, form a pair of antigen binding regions; (x) Dual-Variable Domain Immunoglobulin (xi) other non-full length portions of immunoglobulin heavy and/or light chains, or mutants, variants, or derivatives thereof, alone or in any combination.

An "antibody-based binding protein", as used herein, may represent any protein that contains at least one antibody-derived VH, VL, or CH immunoglobulin domain in the context of other non-immunoglobulin, or non-antibody derived components. Such antibody-based proteins include, but are not limited to (i) Fc-fusion proteins of binding proteins, including receptors or receptor components with all or parts of the immunoglobulin CH domains, (ii) binding proteins, in which VH and or VL domains are coupled to alternative molecular scaffolds, or (iii) molecules, in which immunoglobulin VH, and/or VL, and/or CH domains are combined and/or assembled in a fashion not normally found in naturally occurring antibodies or antibody fragments.

The term "modified antibody format", as used herein, encompasses polyalkylene oxide-modified scFv, monobodies, diabodies, camelid antibodies, domain antibodies, bi- or trispecific antibodies, IgA, or two IgG structures joined by a J chain and a secretory component, shark antibodies, new world primate framework and non-new world primate CDR, IgG4 antibodies with hinge region removed, IgG with two additional binding sites engineered into the CH3 domains, antibodies with altered Fc region to enhance or reduce affinity for Fc gamma receptors, dimerized constructs comprising CH3, VL, and VH, and the like.

The Kabat numbering scheme (Martin and Allemn 2014) has been applied to the disclosed antibodies.

The term “selectively binds to CLDN18.2” or “selective binding to CLDN18.2” as referred to herein refers to an antibody exhibiting binding to CLDN18.2, while exhibiting no (specific) binding to CLDN18.1. Hence, the antibodies selectively binding to CLDN18.2 do not exhibit cross-reactivity to CLDN18.1.

Where the term “comprising” is used in the present description and claims, it does not exclude other elements. For the purposes of the present invention, the term “consisting of” is considered to be a preferred embodiment of the term “comprising of”. If hereinafter a group is defined to comprise at least a certain number of embodiments, this is also to be understood to disclose a group, which preferably consists only of these embodiments.

Where an indefinite or definite article is used when referring to a singular noun, e.g. “a”, “an” or “the”, this includes a plural of that noun unless something else is specifically stated.

Technical terms are used by their common sense. If a specific meaning is conveyed to certain terms, definitions of terms will be given in the following in the context of which the terms are used.

DESCRIPTION

The inventors have surprisingly identified novel anti-CLDN18.2 antibodies as further described in the following embodiments. These antibodies bind to CLDN18.2 with a higher affinity than the IMAB362 antibody.

Therefore, in one embodiment, the invention provides an antibody or fragment thereof binding to CLDN18.2, which comprises the heavy chain complementarity determining regions (HCDR) HCDR1, HCDR2 and HCR3 consensus sequences of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, respectively and the light chain complementary regions (LCDR) LCDR1, LCDR2 and LCDR3 consensus sequences of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively. The respective consensus sequences can be found in Table 1. It is understood that any antibody or fragment thereof based on any combination of CDRs derived from the consensus sequences and binding to CLDN18.2 is part of the invention.

In a preferred embodiment, the isolated antibody or functional fragment thereof binds to CLDN18.2 but not to CLDN18.1. Hence, the provided antibodies specifically bind CLDN18.2.

Table 1: isolated antibody CDR consensus sequences

CDR	**Sequences**	**SEQ ID**
HCDR1	GYXFTSYWIG X in 3rd position is T or S	SEQ ID NO: 1
HCDR2	GXIYPXXXXTXYX X in 2nd position is N or I; X in 6th position is S or G; X in 7th position is A, E or D; X in 8th position is A or S; X in 9th position is Y or D; X in 11th position is N or R; X in last position is A or S	SEQ ID NO: 2
HCDR3	XRXWRGNSFDX X in 1st position is A or T; X in 3rd position is L, M, I or Q; X in last position is A or Y	SEQ ID NO: 3
LCDR1	KSSQSXLNSGNQKNYLX X in 6th position is L or V; X in last position is T or A	SEQ ID NO: 4
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QXDYSYPXT X in 2nd position is N or Q; X in 8th position is L or F	SEQ ID NO: 6

Antibody binding or binding affinity is generally expressed in terms of equilibrium association or dissociation constants (K_a or K_d, respectively), which are in turn reciprocal ratios of dissociation and association rate constants (k_{off} and k_{on}, respectively). Thus, equivalent affinities may correspond to different rate constants, so long as the ratio of the rate constants remains the same. Binding affinities and/or rate constants can be determined using techniques well known in the art or described herein, such as ELISA, flow cytometry (FC) titration, isothermal titration calorimetry (ITC), Biacore (SPR), biolayer inferometry or fluorescent polarization. In some cases, due to the nature of the antigen, the K_a or K_d of antibodies may be difficult to measure. This is especially true for integral membrane proteins such as Claudins (Hashimoto et al. 2018). In such cases, the integral membrane protein may be expressed as proteoliposomes or lipoparticles. Such lipoparticles may be immobilized on plastic and used in ELISA assay to determine the binding affinity of antibodies to the immobilized antigen. Instead of K_a or K_d values, half maximal effective concentration (EC50) values may thus be calculated for each tested antibody or functional fragment thereof, reflecting its binding affinity to the antigen. Example 3 below and Figure 2 exemplify ELISA assay binding affinity curves of antibodies with CDRs comprised in the consensus sequences of Table 1. Therefore, binding can be determined as in Example 4, where binding is quantified using EC50 values (Table 4 in Example 4) and the upper curve values (Figure 4). The EC50 values and upper curves values (maxMFI) show surprisingly that the humanized antibodies of the present invention have a higher binding affinity, i.e. they exhibit increased binding to CLDN18.2 than the IMAB362 antibody. Maximum mean fluorescent intensity (maxMFI) can also be used to quantify the binding of antibodies. When comparing two antibodies binding to the same target, a higher maxMFI is indicative of a higher affinity and/or of a lower off rate. MaxMFI can be determined as shown in Example 4 and maxMFI values for the antibodies of the invention are shown in Table 4, when binding is measured by FC on HEK293T cells expressing CLDN18.2 or PA-TU-8988S-High cells.

Accordingly, preferably the antibodies of the invention or fragments thereof, bind with a higher affinity to CLDN18.2 than the IMAB362 antibody. In turn, Figure 1D shows that all tested antibodies do not bind to HEK293T cells expressing CLDN18.1, and accordingly, all tested antibodies selectively bind to CLDN18.2. Further, in a preferred embodiment, such antibodies or fragments thereof are humanized.

In another embodiment, the invention provides an antibody or fragment thereof that binds to CLDN18.2, comprising:

a. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 9 and SEQ ID NO: 18, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
b. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 10 and SEQ ID NO: 19, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
c. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 10 and SEQ ID NO: 20, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 30, respectively;
d. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 12 and SEQ ID NO: 21, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 26, SEQ ID NO: 5 and SEQ ID NO: 30, respectively;
e. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 13 and SEQ ID NO: 18, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 31, respectively;
f. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 8, SEQ ID NO: 14 and SEQ ID NO: 22, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
g. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 15 and SEQ ID NO: 23, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 27, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
h. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 16 and SEQ ID NO: 23, respectively and

the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively; or

i. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 8, SEQ ID NO: 17 and SEQ ID NO: 24, respectively and
   the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 28, SEQ ID NO: 5 and SEQ ID NO: 31 respectively.

In a preferred embodiment, the antibody is humanized. As described above, these novel humanized antibodies bind with higher affinity to CLDN18.2 than the IMAB362 antibody, as for example shown by EC50 and maxMFI values. Further, the provided antibodies selectively bind to CLDN18.2.

In yet another embodiment, the invention provides for an antibody or fragment thereof that binds CLDN18.2, comprising:

a. a VH sequence of SEQ ID NO: 32;
b. a VH sequence of SEQ ID NO: 34;
c. a VH sequence of SEQ ID NO: 35;
d. a VH sequence of SEQ ID NO: 37;
e. a VH sequence of SEQ ID NO: 39;
f. a VH sequence of SEQ ID NO: 41;
g. a VH sequence of SEQ ID NO: 42;
h. a VH sequence of SEQ ID NO: 44; or
i. a VH sequence of SEQ ID NO: 45;

and

j. a VL sequence of SEQ ID NO: 33;
k. a VL sequence of SEQ ID NO: 36;
l. a VL sequence of SEQ ID NO: 38;
m. a VL sequence of SEQ ID NO: 40;
n. a VL sequence of SEQ ID NO: 43; or
o. a VL sequence of SEQ ID NO: 46.

In a preferred embodiment, the antibody is humanized. As described above, these novel humanized antibodies bind with higher affinity to CLDN18.2 than the IMAB362 antibody, as for example shown by EC50 and maxMFI values. Further, the provided antibodies selectively bind to CLDN18.2. It is understood that any isolated antibody or fragment thereof based on any combination of VH and VL regions and binding to CLDN18.2 is part of the invention. In a preferred embodiment, the antibody or functional fragment thereof binds to CLDN18.2 but not to CLDN18.1.

In another embodiment, the invention relates to an antibody or fragment thereof that binds CLDN18.2, comprising:

a. a VH sequence of SEQ ID NO: 32 and a VL sequence of SEQ ID NO: 33;
b. a VH sequence of SEQ ID NO: 34 and a VL sequence of SEQ ID NO: 33;
c. a VH sequence of SEQ ID NO: 35 and a VL sequence of SEQ ID NO: 36
d. a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 38;
e. a VH sequence of SEQ ID NO: 39 and a VL sequence of SEQ ID NO: 40;
f. a VH sequence of SEQ ID NO: 41 and a VL sequence of SEQ ID NO: 33;
g. a VH sequence of SEQ ID NO: 42 and a VL sequence of SEQ ID NO: 43;
h. a VH sequence of SEQ ID NO: 44 and a VL sequence of SEQ ID NO: 33; or
i. a VH sequence of SEQ ID NO: 45 and a VL sequence of SEQ ID NO: 46.

In a preferred embodiment, the antibody is humanized. Again, as described above, these novel humanized antibodies bind with higher affinity to CLDN18.2 than the IMAB362 antibody, as for example shown by EC50 and maxMFI values. Further, the provided antibodies selectively bind to CLDN18.2.

In a further embodiment, the invention provides an antibody or fragment thereof binding to CLDN18.2, consisting of:

a. the heavy chain sequence of SEQ ID NO: 49 and light chain sequence of SEQ ID NO: 50;
b. the heavy chain sequence of SEQ ID NO: 51 and light chain sequence of SEQ ID NO: 50;
c. the heavy chain sequence of SEQ ID NO: 52 and light chain sequence of SEQ ID NO: 53;
d. the heavy chain sequence of SEQ ID NO: 54 and light chain sequence of SEQ ID NO: 55;
e. the heavy chain sequence of SEQ ID NO: 56 and light chain sequence of SEQ ID NO: 57;

f. the heavy chain sequence of SEQ ID NO: 58 and light chain sequence of SEQ ID NO: 50;
g. the heavy chain sequence of SEQ ID NO: 59 and light chain sequence of SEQ ID NO: 60;
h. the heavy chain sequence of SEQ ID NO: 61 and light chain sequence of SEQ ID NO: 50; or
i. the heavy chain sequence of SEQ ID NO: 62 and light chain sequence of SEQ ID NO: 63.

In a preferred embodiment, the antibody is humanized. Again, as described above, these novel humanized antibodies bind with higher affinity to CLDN18.2 than the IMAB362 antibody, as for example shown by EC50 and maxMFI values. Further, the provided antibodies selectively bind to CLDN18.2.

In another embodiment, the invention provides an antibody or fragment thereof binding to CLDN18.2, wherein the antibody or fragment thereof is humanized. Humanization of monoclonal antibodies has been well-established. The Handbook of Therapeutic Antibodies, Second Edition, gives ample information on humanization of monoclonal antibodies (Saldanha 2014), bioinformatics tools for analysis of such antibodies (Martin and Allemn 2014) or development and manufacture of therapeutic antibodies (Jacobi et al. 2014). When used as human therapeutics, humanized antibodies have a lower risk, compared to chimeric antibodies, of inducing anti-drug antibodies, which would limit the therapeutic benefit and increase the risk of side effects of the antibody of the invention especially after repeated administration.

In another embodiment, the invention provides an isolated antibody or functional fragment thereof binding to CLDN18.2.

In one embodiment, the antibody of the invention does not bind to CLDN18.1. Hence, it does not exhibit cross-reactivity.

In another embodiment, the invention provides an antibody or functional fragment thereof binding to CLDN18.2, consisting of the heavy chain sequence of SEQ ID NO: 58 and light chain sequence of SEQ ID NO: 50.

In yet another embodiment, the invention relates to an antibody having an amino acid sequence with at least 80% identity, at least 85% identity, at least 90% identity, at least 95% identity or at least 98% identity to the amino acid sequence of an antibody described herein. Preferably, the antibody binds with higher affinity to CLDN18.2 than the IMAB362 antibody, as for example shown by EC50 and maxMFI values and/or selectively binds to CLDN18.2. In one embodiment, the antibody is humanized.

In one embodiment, the invention provides an antibody or fragment thereof binding to CLDN18.2 that competes for binding with an antibody or fragment thereof as described herein. In a preferred embodiment, the antibody or fragment thereof competes for binding with an antibody consisting of the heavy chain sequence of SEQ ID NO: 58 and the light chain sequence of SEQ ID NO: 50. In one embodiment, the antibody is humanized. In a further preferred embodiment, the antibody exhibits a binding affinity that is identical or increased as compared to the binding affinity of IMAB362. In another preferred embodiment, the antibody exhibits a binding affinity that is identical or increased as compared to the binding affinity of an antibody consisting of the heavy chain sequence of SEQ ID NO: 58 and the light chain sequence of SEQ ID NO: 50. The binding affinity may be measured by any suitable means. For example, the binding of the antibody may be measured as EC50 value or maxMFI by flow cytometry titration on HEK295T cells or PA-TU-8988-High cell expressing CLDN18.2.

In another embodiment, the Fc domain of the antibody (or antibody fragment when present) may comprise modifications or mutations, such as the modifications or mutations listed in Table 2 below. Such a modification or mutation may be introduced to modulate the effector activity of the Fc domain of the antibody. Modification of antibodies may also include peptide tags added to the C-terminal end of the antibody HC and/or LC chain. Such tags may be used e.g. for protein purification or protein conjugation.

In another embodiment, the invention provides an isolated humanized antibody or fragment thereof that binds CLDN18.2, the antibody being in the format selected from an IgA1, IgA2, IgD, IgE, IgG1, IgG2, IgG3, IgG4, synthetic IgG, IgM, F(ab)$_2$, Fv, scFv, IgGΔCH2, F(ab')$_2$, scFvCH3, Fab, VL, VH, scFv4, scFv3, scFv2, dsFv, Fv, scFv-Fc, (scFv)$_2$, a non-depleting IgG, a diabody, a bivalent antibody or Fc-engineered versions thereof.

In a preferred embodiment, the antibody is an IgG1 type of antibody. The Fc region of immunoglobulins interacts with multiple Fcγ receptors (FcγR) and complement proteins (e.g. C1q), and mediates immune effector functions, such as elimination of targeted cells via antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP) or complement-dependent cytotoxicity (CDC). For therapeutic approaches, it may be beneficial to enhance or silence Fc related effector functions. The type of immunoglobulin (IgA, IgD, IgE, IgG, IgM) may be selected according to the desired effector function of the antibody related to the Fc domain given their known activities. One may also employ a synthetic immunoglobulin, such as an immunoglobulin with the IgG2 amino acids 118 to 260 and the IgG4 amino acids 261 to 447 or an IgG2 variant with point mutations from IgG4 (e.g. H268Q/V309L/A30S/P331S). Such synthetic immunoglobulins reduce effector functions of the antibody. Fc-engineered immunoglobulins may also be employed to modulate antibody effector function. Table 2 shows examples of such Fc engineering. Expression in production cell lines with altered fucosylation may also impact FcγR binding in order to modulate pharmacokinetics of the antibody.

Table 2: Examples of modifications to modulate antibody effector function. Unless otherwise noted, the mutations are on the IgG1 subclass (Wang, Mathieu, and Brezski 2018).

Engineering and intended function	**Mutation**	**Reference**
Enhance ADCC		
Increased FcγRIIIa binding	• F243L/R292P/Y300L/V305I/P396L • S239D/I332E • S298A/E333A/K334A • in one heavy chain: L234Y/L235Q/G236W/S239M/H268D/D270E/S298A, in the opposing heavy chain: D270E/K326D/A330M/K334E	• (Stavenhagen et al. 2007) • (Lazar et al. 2006) • (Shields et al. 2001) • (Mimoto et al. 2013)
Increased FcγRIIIa binding, decreased FcγRIIb binding	S239D/I332E/A330L	(Lazar et al. 2006)
Enhance ADCP		
Increased FcγRIIa binding, Increased FcγRIIIa binding	G236A/S239D/I332E	(Richards et al. 2008)
Enhance CDC		
Increased C1q binding	• K326W/E333S • S267E/H268F/S324T • IgG1/IgG3 cross subclass	• (Idusogie et al. 2001) • (Moore et al. 2010) • (Natsume et al. 2008)
Hexamerization	E345R/E430G/S440Y	(Diebolder et al. 2014)
Reduce effector function		
Aglycosylated	N297A or N297Q or N297G	(Bolt et al. 1993; Leabman et al. 2013; Tao and Morrison

Engineering and intended function	Mutation	Reference
		1989; Walker et al. 1989)
Reduced FcγR and C1q binding	• L235E • IgG1: L234A/L235A or L234A/L235A/P329G • IgG4:F234A/L235A • IgG2/IgG4 cross isotype • IgG2: H268Q/V309L/A330S/P331S • IgG2: V234A/G237A/P238S/H268A/V309L/A330S/P331S	• (Alegre et al. 1992) • (Xu et al. 2000; Lo et al. 2017) • (Xu et al. 2000) • (Rother et al. 2007) • (An et al. 2009) • (Vafa et al. 2014)
Increase half-life		
Increased FcRn Binding at pH 6.0	• M252Y/S254T/T256E • M428L/N434S	• (Dall'Acqua et al. 2002) • (Zalevsky et al. 2010)
Increased coengagement		
Increased FcγRIIb binding	S267E/L328F	(Chu et al. 2008)
Increased FcγRIIa binding, decreased FcγRIIIa binding	N325S/L328F	(Shang et al. 2014)

In vivo half-life of antibodies may also be modulated. The Fc domain plays a central role in the stability and serum half-life on antibodies. For therapeutic approaches, antibody half-life may be reduced by using an antibody fragment missing the Fc domain or with truncated Fc domains, such as F(ab)$_2$, Fv, scFv, IgGACH2, F(ab')$_2$, scFvCH3, Fab, VL, VH, scFv4, scFv3, scFv2, dsFv, Fv, scFv-Fc or (scFv)$_2$. The antibodies may also be in the form of diabodies or bivalent antibodies. Diabodies or bivalent antibodies may be used to increase the affinity to the target allowing lower dosage. Functional fragments missing the Fc domain or with truncated Fc domains may also be used in the development of other therapeutic approaches such as chimeric antigen receptor T cell (CAR T cells) or bispecific T cell engagers (BiTEs). In CAR constructs, one VH and one VL domain are typically connected by a short peptide linker to form a single-chain variable fragment (scFv), and the scFv fragment is further linked to a transmembrane domain and an intracytoplasmic T cell immunoreceptor tyrosine-based activation motif (from e.g. CD3ζ) and further domains of co-stimulatory molecules (from e.g. CD28, 4-1BB (CD127), or OX40) (Chang and Chen 2017). The VH and VL domains used in the scFv fragment may be the ones of the antibodies listed in Table 3. BiTEs typically consist of the fusion of two scFv of two different antibodies. One scFv domain may be of the isolated antibodies binding CLDN18.2 listed in Table 3, while the other scFv domain is from an antibody that binds e.g. to CD3, CD16, NKG2D, NKp46, CD2, CD28 or CD25. Ample guidance on BiTEs antibody formats and other bispecific antibody formats used for T-cell redirecting may be found in the review by Diego Ellerman (2019).

In another embodiment, the invention provides a humanized antibody or fragment thereof that binds to CLDN18.2, the antibody having the constant light chain region (CL) of SEQ ID NO: 65 and preferably the constant heavy chain region CH1 and Fc region of SEQ ID NO: 66 with reduced FcγR binding having the L234A/L235A mutations in the constant heavy chain region CH2. More preferably, the invention provides for an antibody with the constant heavy chain region CH1 and Fc region of SEQ ID NO: 67 having the L234A/L235A/P329G mutations in the constant heavy chain region CH1 and Fc region with even further reduced FcγR binding.

In another embodiment, the invention provides an isolated humanized antibody or fragment thereof that binds to CLDN18.2 with a VH sequence of SEQ ID NO: 41 associated to the constant heavy chain region CH1 and Fc region of SEQ ID NO: 66 and the VL sequence of SEQ ID NO: 33 associated to having the constant light chain region (CL) of SEQ ID NO: 65.

In yet another embodiment, the invention provides an antibody or fragment thereof binding to CLDN18.2, wherein the antibody or fragment thereof does not bind to CLDN18.1. Hence, the antibody does not exhibit cross-reactivity or cross-binding to CLDN18.1. Binding of an antibody to a target protein can be tested by flow cytometry on cells expressing the target protein. Specific binding of a tested antibody to its target protein can be visualized on a histogram plot. Such plot results in a peak with high fluorescent signal when the antibody specifically binds to the expressed target protein, and in a peak with low fluorescent signal when the antibody does not, or only very weakly bind to the expressed target protein. Such histogram can be seen in Figure 1, showing binding of antibodies of the invention to CLDN18.2 but not to CLDN18.1 expressed in HEK293T cells. The degree of binding can also be expressed in a bar graph showing the maximal mean fluorescent intensity (maxMFI) measured by flow cytometry, with high maxMFI reflecting strong binding and low/no maxMFI reflecting non-binding. Examples of such binding assays can be found in Example 4.

In another embodiment, the invention provides an antibody or fragment thereof binding to CLDN18.2, the antibody being bound to another moiety. This moiety may include radioisotopes, fluorescent tags, histological markers, cytotoxins or cytokines. Binding of the moiety may be facilitated by linkers known in the art.

In yet another embodiment, the invention provides an antibody or fragment binding to CLDN18.2, wherein the antibody or fragment thereof exhibits stronger binding to CLDN18.2 than antibody IMAB362. Preferably, the invention provides an antibody or fragment binding to CLDN18.2, wherein the antibody or fragment thereof binds with a higher affinity to CLDN18.2 than antibody IMAB362. Binding affinities and/or rate constants can be determined using techniques well known in the art or described herein, such as ELISA, flow cytometry titration, isothermal titration calorimetry (ITC), Biacore (SPR), biolayer inferometry or fluorescent polarization. The inventors have determined the affinity of the antibodies to CLDN18.2 by ELISA as shown for example in Example 3 or by FC titration experiments as shown in Example 4. In ELISA on lipoparticles containing CLDN18.2, all the humanized antibodies hGBA-1 to hGBA-9 have a higher maximum binding values (expressed in MFI) than IMAB362. In FC titration experiments on HEK293T cells overexpressing CLDN18.2 or PA-TU-8988S cells endogenously expressing CLDN18.2, all the humanized antibodies hGBA-1 to hGBA-9 have higher maximum binding values (expressed in MFI units) and lower EC50 values (expressed in µg/ml) than the antibody IMAB362, indicative of higher affinity of the humanized antibodies of the present invention to CLDN18.2 than antibody IMAB362. In one embodiment, the antibodies provided in the invention have a measured EC50 value at least 10% lower, at least 20% lower, at least 40% lower, at least 50% lower or at least 75% lower than the EC50 value measured for antibody IMAB362. In one embodiment, the antibodies provided have a measured maxMFI value at least 10% higher, at least 20% higher, at least 40% higher, at least 50% higher or at least 75% higher than the maxMFI value measured for antibody IMAB362.

The heavy and light chain sequences of the IMAB362 antibody are e.g. provided herein as SEQ ID NO: 47 and SEQ ID NO: 48.

According to one embodiment, the invention provides nucleic acid sequences encoding the antibodies or fragments thereof binding to CLDN18.2. The nucleic acid sequences may encode for the CDRs alone, for the VH and VL regions, or for the entire heavy and light chains of the antibodies. These nucleic acid sequences may be found in Table 3. The nucleic acid sequence may also encode for $F(ab)_2$, Fv, scFv, IgGACH2, $F(ab')_2$, scFvCH3, Fab, VL, VH, scFv4, scFv3, scFv2, dsFv, Fv, scFv-Fc, $(scFv)_2$, a non-depleting IgG, a diabody, a bivalent antibody or Fc-engineered versions thereof. The encoded immunoglobin may be an IgA1, IgA2, IgD, IgE, IgG1, IdG2, IgG3, IgG4, synthetic IgG, IgM or mutated and Fc-engineered versions thereof.

In yet another embodiment, the invention provides an antibody-based binding protein that binds to CLDN18.2, e.g. a protein comprising at least a CLDN18.2 binding domain of the disclosed antibodies and another protein domain not related to antibodies. The invention also provides for a modified humanized antibody format that binds to CLDN18.2. In a preferred embodiment, the antibody-based binding protein does not bind to CLDN18.1.

In another embodiment, the invention provides for a nucleic acid encoding the antibody or fragment thereof. Such nucleic acid sequence may further encode for other elements and may be part of a chimeric antigen receptor (CAR) that binds to CLDN18.2. Ample guidance on construction of CAR T cells may be found in Chang and Chen (2017) or June and Sadelain (2018). In one embodiment, the invention provides a T cell that has been genetically engineered to produce an artificial T-cell receptor, wherein the artificial T-cell receptor comprises the antibody or functional fragment thereof of the present invention that binds to CLDN18.2. In a preferred embodiment, the CAR construct does not bind to CLDN18.1.

The invention also provides expression vectors comprising such nucleic acids. The expression vectors may be expression vectors aimed for mammalian cells, bacteria, fungal or insect cell expression, and chosen for the type of host cell bearing the expression vector comprising the nucleic acid encoding the antibodies or functional fragments thereof. Ample guidance for the construction of such vectors may be found in Green and Sambrook (Green and Sambrook 2012). Preferred are expression vectors for mammalian cells, especially CHO cells.

In another embodiment, the invention provides for host cells comprising the expression vectors of encoding the antibodies or fragments thereof binding to CLDN18.2 or having the nucleic acids encoding the antibodies or fragments thereof binding to CLDN18.2 integrated into its genome. The host cell may be a mammalian cell or cell line, bacteria, fungal or insect cell. Preferred are mammalian cells, especially CHO cells.

In another embodiment, the invention relates to an antibody or fragment thereof binding to CLDN18.2, the nucleic acid encoding the antibody or fragment thereof, the vector comprising the nucleic acid or the host cells comprising the nucleic acid or the vector comprising the nucleic acid, as described herein, for use in the treatment of a subject that is suffering from a neoplastic disease, or is at risk of developing a neoplastic disease, and/or for the treatment of a subject being diagnosed for a neoplastic disease. The disclosed antibodies or fragments thereof may be used as monotherapy or preferably as combinations therapy with the established standard of care of the neoplastic disease.

In yet another embodiment, the invention provides for the use of an antibody or fragment thereof binding to CLDN18.2 as provided herein for the manufacture of a medicament for the treatment of the neoplastic disease.

The neoplastic disease may be at least one disease selected from the group consisting of pancreatic, gastric, esophageal, ovarian and lung cancer. It is understood that the neoplastic disease to be treated is characterized by overexpression of CLDN18.2.

Another embodiment of the invention provides a method to treat a neoplastic disease, including pancreatic, gastric, esophageal, ovarian or lung cancer, with an isolated humanized antibody or fragment thereof that binds to CLDN18.2 as provided herein, wherein the method comprises administering a therapeutically effective amount of the antibody or fragment thereof. The method of treatment may be a monotherapy or preferably a combination therapy with the established standard of care of the neoplastic disease.

Also provided is a pharmaceutical composition comprising the antibody or fragment thereof binding to CLDN18.2, the nucleic acid encoding the antibody or fragment thereof, the vector comprising the nucleic acid or the host cell comprising the nucleic acid or the vector comprising the nucleic acid and a pharmaceutically acceptable carrier.

Preferably, patients suffering from pancreatic, gastric, esophageal, ovarian or lung cancer may be treated with an isolated humanized antibody or fragment thereof that binds to CLDN18.2 as provided herein.

DESCRIPTION OF DRAWINGS

Figure 1: FACS binding assay of humanized antibodies and IMAB362. Binding of selected antibodies to huCLDN1.2 and huCLDN18.1 was tested in HEK293T cells stably expressing huCLDN18.2 or huCLDN18.1. Parental HEK293T cells not expressing the target protein were used as negative control. 1A: A: IMAB362, B: hGBA-1, C: hGBA-2, D: hGBA-3, E: hGBA-4, F: hGBA-5, G: hGBA-6, H: hGBA-7, I: hGBA-8, J: GBA-9, K: secondary antibody alone, L: pan-CLDN18 antibody; 1B: Bar graph showing the Mean Fluorescent Intensity (MFI) of the FACS binding data for each humanized antibody, compared to IMAB362, on parental HEK293T cells and HEK293T cells expressing huCLDN18.2 or huCLDN18.1.

Figure 2: 2A-D: ELISA binding assay on humanized antibodies, compared to IMAB362. The ELISA binding assay was performed on lipoparticles bearing CLDN18.2 or null-lipoparticles without CLDN18.2.

Figure 3: Sorting of PA-TU-8988S cells for expression levels of CLDN18.2. 3A: FACS profile of PA-TU-9888S stained with IMAB362. 3B: FACS profile of PA-TU-8988S cells sorted by FACS for medium and high expression of CLDN18.2.

Figure 4: FC titration assay on PA-TU-8988S-High cells (4A-D) and HEK-293T expressing huCLDN18.2 (4E-H).

EXAMPLES

Example 1: Humanization of Fab fragments

Techniques to humanize monoclonal antibodies have been well-established. The Handbook of Therapeutic Antibodies, Second Edition, gives ample information on humanization of monoclonal antibodies (Saldanha 2014), bioinformatic tools for analysis such antibodies (Martin and Allemn 2014) or development and manufacture of therapeutic antibodies (Jacobi et al. 2014). In brief, the variable domain sequences of the parental IMAB362 antibody were analyzed to reveal the closest human germlines. Next, a structural analysis of the variable regions of IMAB362 was performed to reveal the best fitting Fv model, followed by structural analysis of CDR grafting by *in-silico* modeling. Based on these *in-silico* modeling, humanized VH and VL domains were designed. Combinations of the humanized VH and VL domains were cloned and produced as Fab and IgG1 antibodies and screened for their binding by ELISA and AlphaLISA^{TM} to CLDN18.2-expressing lipoparticles and by flow cytometry with CLDN18.1- and CLDN18.2-expressing pre-B cell L11 (Waldmeier et al. 2016) and HEK293T (ATCC CRL-3216) cell lines. After testing and comparison to IMAB362, one VH and VL combination was selected and a library was designed in scFv format, performing further humanization including the CDRs. The scFv library was further screened by ELISA and AlphaLISA^{TM} to CLDN18.2-expressing lipoparticles and by flow cytometry with CLDN18.1- and CLDN18.2-expressing pre-B cell L11 cell lines. Humanization of IMAB362 thus resulted in the humanized antibodies hGBA-1, hGBA-2, hGBA-3, hGBA-4, hGBA-5, hGBA-6, hGBA-7, hGBA-8 and hGBA-9 antibodies (see Table 3), collectively named hGBA antibodies herein.

Table 3: nucleic acid and amino-acid sequences of selected antibodies

NAME	SEQUENCE	SEQ ID NO
hGBA-1		
HCDR1	GYSFTSYWIG	SEQ ID NO: 7
HCDR2	GNIYPGASDTRYA	SEQ ID NO: 9
HCDR3	ARLWRGNSFDY	SEQ ID NO: 18
VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGASDTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 32
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGASDTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 49
HCDR1	ggctatagctttacatcatattggattgga	SEQ ID NO: 85
HCDR2	gggaacatttaccctggggcatcggatacgcgatacgca	SEQ ID NO: 86
HCDR3	gcgagactttggcgggggaatagcttcgactac	SEQ ID NO: 87
VH	gaagtccaactggtccaatccggcgcggaggttaagaagcccggagaatcgctgaagatctcatgcaaagggagcggctatagctttacatcatattggattggatgggtcaggcaaatgccggggaaggggctggaatggatggggaacatttaccctggggcatcggatacgcgatacgcacctagctttcaagggcaagtcacaatttcggcggacaagagcatctcaacggcatacctgcaatggtcgagcttgaaggcatctgatactgcaatgtactactgcgcgagactttggcgggggaatagcttcgactactgggggcagggtaccctggttacggtctcgagc	SEQ ID NO: 128
LCDR1	KSSQSLLNSGNQKNYLA	SEQ ID NO: 25
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QNDYSYPFT	SEQ ID NO: 29
VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIK	SEQ ID NO: 33
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 50
LCDR1	aaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggca	SEQ ID NO: 88
LCDR2	tgggcaagcacccgagagagc	SEQ ID NO: 89
LCDR3	caaaacgactattcatacccattcaca	SEQ ID NO: 90
VL	gacattgtgatgacgcaaagccccgattcgctggctgtatcgctaggggagcgcgctacgatcaattgcaaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggcatggtatcaa	SEQ ID NO: 129

	caaaaaccggggcaaccgccgaagctgctgatctattgggcaagcacccgagagagcggtgtcccggaccgatttagcgggagcggatcgggcaccgacttcacgctgacaataagctcattgcaagccgaggatgtggcggtctattattgccaaaacgactattcatacccattcacattcgggcaaggtaccaaggtcgagatcaag	
hGBA-2		
HCDR1	GYSFTSYWIG	SEQ ID NO: 7
HCDR2	GNIYPGDADTRYA	SEQ ID NO: 10
HCDR3	ARMWRGNSFDY	SEQ ID NO: 19
VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGDADTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARMWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 34
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGDADTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARMWRGNSFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 51
HCDR1	ggatattcatttacaagctactggatcgga	SEQ ID NO: 91
HCDR2	ggaaatatataccccggagacgcggacacgagatacgca	SEQ ID NO: 92
HCDR3	gcgcggatgtggcgcggcaatagctttgactac	SEQ ID NO: 93
VH	gaagtccaactggtccaatctggagcggaagtcaagaagcctgggagagcctgaaaatttcatgcaaggggagcggatattcatttacaagctactggatcggatgggtccggcaaatgccggggaagggcttggaatggatgggaaatatataccccggagacgcggacacgagatacgcaccgagctttcaagggcaggtcaccattagcgctgataaatcgatttcaaccgcatatctgcaatggtcatcgctgaaggcctccgacaccgcgatgtactattgcgcgcggatgtggcgcggcaatagctttgactactgggggcagggtaccctcgtcacggtctcgagc	SEQ ID NO: 130
LCDR1	KSSQSLLNSGNQKNYLA	SEQ ID NO: 25
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QNDYSYPFT	SEQ ID NO: 29
VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIK	SEQ ID NO: 33
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 50
LCDR1	aaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggca	SEQ ID NO: 88
LCDR2	tgggcaagcacccgagagagc	SEQ ID NO: 89
LCDR3	caaaacgactattcatacccattcaca	SEQ ID NO: 90
VL	gacattgtgatgacgcaaagccccgattcgctggctgtatcgctaggggagcgcgctacgatcaattgcaaaagctcccaaagcct	SEQ ID NO: 129

	attgaactcgggaaaccaaaagaattacttggcatggtatcaa caaaaaccggggcaaccgccgaagctgctgatctattgggcaa gcacccgagagagcggtgtcccggaccgatttagcgggagcgg atcgggcaccgacttcacgctgacaataagctcattgcaagcc gaggatgtggcggtctattattgccaaaacgactattcatacc cattcacattcgggcaaggtaccaaggtcgagatcaag	
hGBA-3		
HCDR1	GYSFTSYWIG	SEQ ID NO: 7
HCDR2	GIIYPGASDTNYA	SEQ ID NO: 11
HCDR3	ARIWRGNSFDY	SEQ ID NO: 20
VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGK GLEWMGIIYPGASDTNYAPSFQGQVTISADKSISTAYLQWSSL KASDTAMYYCARIWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 35
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGK GLEWMGIIYPGASDTNYAPSFQGQVTISADKSISTAYLQWSSL KASDTAMYYCARIWRGNSFDYWGQGTLVTVSSASTKGPSVFPL APSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQ PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	SEQ ID NO: 52
HCDR1	ggctatagctttacatcatattggattgga	SEQ ID NO: 85
HCDR2	gggatcatctatccgggggcatccgataccaactatgcg	SEQ ID NO: 94
HCDR3	gctaggatttggcgaggaaatagctttgattat	SEQ ID NO: 95
VH	gaggtccaactggtccaaagcggcgcggaggtcaagaagccgg gagaatccctgaagattagctgcaaaggctccggctatagctt tacatcatattggatcggatgggtcagacaaatgccgggaaag ggacttgaatggatggggatcatctatccgggggcatccgata ccaactatgcgccgagcttccaagggcaggtcacgatatccgc ggataaatcgattagcaccgcatatctgcaatggagctcgctg aaggcatccgacaccgcgatgtactactgcgctaggatttggc gaggaaatagctttgattattgggggcagggtacccttgtcac ggtctcgagc	SEQ ID NO: 131
LCDR1	KSSQSLLNSGNQKNYLA	SEQ ID NO: 25
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QNDYSYPLT	SEQ ID NO: 29
VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQA EDVAVYYCQNDYSYPLTFGQGTKVEIK	SEQ ID NO: 36
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQA EDVAVYYCQNDYSYPLTFGQGTKVEIKRTVAAPSVFIFPPSDE QLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSF NRGEC	SEQ ID NO: 53
LCDR1	aagagctcgcaaagtttgctgaactccgggaaccaaaagaatt acctggca	SEQ ID NO: 96
LCDR2	tgggcatcaacgcgggaaagc	SEQ ID NO: 97
LCDR3	caaaacgactactcctatccgctgacc	SEQ ID NO: 98

VL	gacattgtcatgacgcaaagccccgactcgctggccgtctcactggggggagcgggcgacaatcaactgcaagagctcgcaaagtttgctgaactccgggaaccaaaagaattacctggcatggtatcaacaaaagccggggcaaccccccgaagctgctgatatattgggcatcaacgcgggaaagcggagtcccggatagatttagcggatctggatcggggaccgacttcacgctgacgatatctagccttcaagccgaggatgtggctgtatattattgccaaaacgactactcctatccgctgaccttcgggcaaggtaccaaggtcgagatcaag	SEQ ID NO: 132
hGBA-4		
HCDR1	GYSFTSYWIG	SEQ ID NO: 7
HCDR2	GIIYPGDAYTRYS	SEQ ID NO: 12
HCDR3	TRLWRGNSFDA	SEQ ID NO: 21
VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDAYTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDAWGQGTLVTVSS	SEQ ID NO: 37
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDAYTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDAWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 54
HCDR1	ggatactcatttacatcatactggatagga	SEQ ID NO: 99
HCDR2	gggattatataccccggcgacgcttacactcgatattcg	SEQ ID NO: 100
HCDR3	acgaggctatggagggggaatagctttgatgcc	SEQ ID NO: 101
VH	gaagtccaactagtccaaagcggagccgaagtcaagaaaccgggggagagccttaagatctcatgcaaggggagcggatactcatttacatcatactggataggatgggtcagacaaatgcccggcaaggggctggaatggatggggattatataccccggcgacgcttacactcgatattcgccatcattccaagggcaggtcacgatatcggccgataaatcgatatccacggcatacctgcaatggagctcactgaaagcatctgatacggcaatgtattattgcacgaggctatggagggggaatagctttgatgcctggggccagggtaccctggtcacggtctcgagc	SEQ ID NO: 133
LCDR1	KSSQSLLNSGNQKNYLT	SEQ ID NO: 26
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QNDYSYPLT	SEQ ID NO: 30
VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPLTFGQGTKVEIK	SEQ ID NO: 38
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 55
LCDR1	aagagctcccaaagcctattgaactcgggaaatcaaaagaattatctgaca	SEQ ID NO: 102
LCDR2	tgggcctcgacaagggagagc	SEQ ID NO: 103

LCDR3	caaaatgactactcatacccgctgaca	SEQ ID NO: 104
VL	gacatagttatgacacaatcgccggatagcctcgcggtcagccttggagagcgggcgacgatcaactgcaagagctcccaaagcctattgaactcgggaaatcaaaagaattatctgacatggtatcaacaaaagccggggcaaccaccgaaactgctgatctattgggcctcgacaagggagagcggagtcccggaccgcttctctggatcggg aagcgggactgacttcacgctgaccataagctcgctgcaagccgaggacgtcgccgtctattattgccaaaatgactactcatacccgctgacatttggccaaggtaccaaggtcgagatcaag	SEQ ID NO: 134
hGBA-5		
HCDR1	GYSFTSYWIG	SEQ ID NO: 7
HCDR2	GIIYPGAAYTRYA	SEQ ID NO: 13
HCDR3	ARLWRGNSFDY	SEQ ID NO: 18
VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGAAYTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 39
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGAAYTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 56
HCDR1	ggatatagctttacgagctactggatcgga	SEQ ID NO: 105
HCDR2	gggataatataccccggagcggcatacacgagatatgcg	SEQ ID NO: 106
HCDR3	gcgagactatggcgcgggaactcatttgattac	SEQ ID NO: 107
VH	gaggtgcaactggtacaatccggggcggaagtgaagaagccgggggaatcgctgaagataagctgcaaaggctctggatatagctttacgagctactggatcggatgggtcaggcaaatgccggggaagggactggaatggatggggataatataccccggagcggcatacacgagatatgcgccgagcttccaagggcaagtgacaataagcgcggacaaatcgattagcacggcatatctgcaatggtcctcgctgaaggcgagcgataccgcaatgtactattgcgcgagactatggcgcgggaactcatttgattactgggggcagggtaccctagtgacggtctcgagc	SEQ ID NO: 135
LCDR1	KSSQSLLNSGNQKNYLA	SEQ ID NO: 25
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QQDYSYPFT	SEQ ID NO: 31
VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQDYSYPFTFGQGTKVEIK	SEQ ID NO: 40
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQDYSYPFTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 57
LCDR1	aaatcatcgcaatcattgctaaattcggggaaccaaaagaattatttggca	SEQ ID NO: 108

LCDR2	tgggcatccacgagagaatcg	SEQ ID NO: 109
LCDR3	caacaagattattcatacccatttaca	SEQ ID NO: 110
VL	gacattgtcatgacgcaaagcccggatagcctggctgtatcgctgggggagagagcgacgatcaactgcaaatcatcgcaatcattgctaaattcggggaaccaaaagaattatttggcatggtatcaacaaaagccggggcaaccgccgaaactgctgatttactgggcatccacgagagaatcgggagtcccggaccgatttagcggatctgggagcgggaccgatttcacgctgaccattagctcgctgcaagcggaggatgtggcggtctattactgccaacaagattattcatacccatttacatttgggcaaggtaccaaggtcgagatcaag	SEQ ID NO: 136
hGBA-6		
HCDR1	GYTFTSYWIG	SEQ ID NO: 8
HCDR2	GNIYPGASYTRYS	SEQ ID NO: 14
HCDR3	TRQWRGNSFDY	SEQ ID NO: 22
VH	EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGNIYPGASYTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRQWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 41
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGNIYPGASYTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRQWRGNSFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 58
HCDR1	ggatatacatttacatcttactggatcgga	SEQ ID NO: 111
HCDR2	gggaacatttatcctggcgcgagctatacgcgctat	SEQ ID NO: 112
HCDR3	acccggcaatggaggggcaatagctttgactac	SEQ ID NO: 113
VH	gaagtacaattggttcaatcgggggccgaagtcaagaagccgggggaatcgctgaagatatcctgcaaggggagcggatatacatttacatcttactggatcggatgggtcagacaaatgcccggaaagggcttgaatggatggggaacatttatcctggcgcgagctatacgcgctatagcccgagcttccaagggcaggtcacgattagcgccgacaagagcatttcgacggcatacctgcaatggagctcgctgaaagcatcggatacggcaatgtattactgcacccggcaatggaggggcaatagctttgactactgggggcagggtaccctagtcacggtctcgagc	SEQ ID NO: 137
LCDR1	KSSQSLLNSGNQKNYLA	SEQ ID NO: 25
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QNDYSYPFT	SEQ ID NO: 29
VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIK	SEQ ID NO: 33
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 50

LCDR1	aaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggca	SEQ ID NO: 88
LCDR2	tgggcaagcacccgagagagc	SEQ ID NO: 89
LCDR3	caaaacgactattcatacccattcaca	SEQ ID NO: 90
VL	gacattgtgatgacgcaaagccccgattcgctggctgtatcgctaggggagcgcgctacgatcaattgcaaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggcatggtatcaacaaaaaccggggcaaccgccgaagctgctgatctattgggcaagcacccgagagagcggtgtcccggaccgatttagcgggagcggatcgggcaccgacttcacgctgacaataagctcattgcaagccgaggatgtggcggtctattattgccaaaacgactattcatacccattcacattcgggcaaggtaccaaggtcgagatcaag	SEQ ID NO: 129
hGBA-7		
HCDR1	GYSFTSYWIG	SEQ ID NO: 7
HCDR2	GNIYPGEAYTRYS	SEQ ID NO: 15
HCDR3	TRLWRGNSFDY	SEQ ID NO: 23
VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGEAYTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 42
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGEAYTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 59
HCDR1	ggatattcctttacatcatactggatcggc	SEQ ID NO: 114
HCDR2	gggaacatatatcccggagaagcctatacgagatactcg	SEQ ID NO: 115
HCDR3	acgcgactatggaggggaaatagctttgactat	SEQ ID NO: 116
VH	gaagttcaattggtccaatctggagccgaagtcaagaagcccggagaatcgctgaagattagctgcaaggggagcggatattcctttacatcatactggatcggctgggtcagacaaatgcccggaaagggactggaatggatggggaacatatatcccggagaagcctatacgagatactcgccatcatttcaaggacaggtcaccataagcgcggacaagagcataagcaccgcatacctgcaatggagctcgctgaaggcatcggacaccgccatgtattactgcacgcgactatggaggggaaatagctttgactattgggggcagggtaccttagtcacggtctcgagc	SEQ ID NO: 138
LCDR1	KSSQSVLNSGNQKNYLT	SEQ ID NO: 27
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QNDYSYPFT	SEQ ID NO: 29
VL	DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIK	SEQ ID NO: 43
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ	SEQ ID NO: 60

	DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
LCDR1	aagagctcccaatcagtcctgaactctgggaatcaaaagaattacctgaca	SEQ ID NO: 117
LCDR2	tgggcgagcacgagggagagc	SEQ ID NO: 118
LCDR3	caaaatgattattcataccccttcaca	SEQ ID NO: 119
VL	gatatagtaatgactcaatcacccgatagcttggctgtgagcctgggagaaagagctacaatcaactgcaagagctcccaatcagtcctgaactctgggaatcaaaagaattacctgacatggtatcaacaaaagcccggacaaccgccgaagctgctgatctactgggcgagcacgagggagagcggagtcccggatcgattttctggctccgggagcggaaccgacttcacactgactattagctcgctgcaagcggaggacgtcgccgtctactattgccaaaatgattattcataccccttcacatttgggcaaggtaccaaggtcgagatcaag	SEQ ID NO: 139
hGBA-8		
HCDR1	GYSFTSYWIG	SEQ ID NO: 7
HCDR2	GNIYPSESYTNYA	SEQ ID NO: 16
HCDR3	TRLWRGNSFDY	SEQ ID NO: 23
VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPSESYTNYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 44
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPSESYTNYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 61
HCDR1	ggatactcctttacatcatattggatcgga	SEQ ID NO: 120
HCDR2	ggaaacatatatccgagcgaatcatatacgaactacgcg	SEQ ID NO: 121
HCDR3	acgaggctatggagggggaatagcttcgactat	SEQ ID NO: 122
VH	gaggtgcaactagtgcaatcgggggccgaagtgaagaaacctggggaatcgctgaagatatcatgcaaggggagcggatactcctttacatcatattggatcggatgggtcaggcaaatgccggggaaggggctggaatggatgggaaacatatatccgagcgaatcatatacgaactacgcgccgagctttcaaggacaagtcacgatatccgcggataaatcgatatcgaccgcatacctgcaatggagctcgctgaaggcttccgacactgcgatgtattactgcacgaggctatggagggggaatagcttcgactattgggggcagggtaccctggtgacggtctcgagc	SEQ ID NO: 140
LCDR1	KSSQSLLNSGNQKNYLA	SEQ ID NO: 25
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QNDYSYPFT	SEQ ID NO: 29
VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIK	SEQ ID NO: 33
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIKRTVAAPSVFIFPPSDE	SEQ ID NO: 50

	QLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
LCDR1	aaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggca	SEQ ID NO: 88
LCDR2	tgggcaagcacccgagagagc	SEQ ID NO: 89
LCDR3	caaaacgactattcatacccattcaca	SEQ ID NO: 90
VL	gacattgtgatgacgcaaagccccgattcgctggctgtatcgctaggggagcgcgctacgatcaattgcaaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggcatggtatcaacaaaaaccggggcaaccgccgaagctgctgatctattgggcaagcacccgagagagcggtgtcccggaccgatttagcgggagcggatcgggcaccgacttcacgctgacaataagctcattgcaagccgaggatgtggcggtctattattgccaaaacgactattcatacccattcacattcgggcaaggtaccaaggtcgagatcaagt	SEQ ID NO: 129
hGBA-9		
HCDR1	GYTFTSYWIG	SEQ ID NO: 8
HCDR2	GIIYPSAAYTRYA	SEQ ID NO: 17
HCDR3	TRMWRGNSFDY	SEQ ID NO: 24
VH	EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGIIYPSAAYTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRMWRGNSFDYWGQGTLVTVSS	SEQ ID NO: 45
Heavy chain	EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGIIYPSAAYTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRMWRGNSFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 62
HCDR1	ggatatacattcacgagctactggatagga	SEQ ID NO: 123
HCDR2	ggaatcatatatccttccgcggcatatacgcgatatgcg	SEQ ID NO: 124
HCDR3	acgcggatgtggaggggaaatagctttgattac	SEQ ID NO: 125
VH	gaagtccaattagtccaatcgggggccgaggtcaagaagccggggaatcgctcaagataagctgcaagggatcgggatatacattcacgagctactggataggatgggtcaggcaaatgccggggaaggggctggaatggatgggaatcatatatccttccgcggcatatacgcgatatgcgccatcatttcaaggacaggtcacgataagcgccgacaagagcattagcaccgcatacctgcaatggtcgagccttaaggcatcggacaccgcgatgtactactgcacgcggatgtggaggggaaatagctttgattactgggggcagggtaccctagtcacggtctcgagc	SEQ ID NO: 141
LCDR1	KSSQSVLNSGNQKNYLA	SEQ ID NO: 28
LCDR2	WASTRES	SEQ ID NO: 5
LCDR3	QQDYSYPFT	SEQ ID NO: 31
VL	DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQDYSYPFTFGQGTKVEIK	SEQ ID NO: 46
Light chain	DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQA	SEQ ID NO: 63

	EDVAVYYCQQDYSYPFTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
LCDR1	aagagctcgcaatcggtcctgaatagcgggaaccaaaagaattatctggcc	SEQ ID NO: 126
LCDR2	tgggcgagcacgagggagagc	SEQ ID NO: 118
LCDR3	caacaagactactcatacccatttaca	SEQ ID NO: 127
VL	gacatcgtcatgacgcaaagcccggactcgctggcggtctcgctggggagcgggccacaataaattgcaagagctcgcaatcggtcctgaatagcgggaaccaaaagaattatctggcctggtatcaacaaaagccggggcaaccaccgaagctgctaatctattgggcgagcacgagggagagcggagtccccgatcgatttagcggatcgggaagcgggaccgatttcacgctgacgatttcgagcctacaagccgaggatgtggcggtctattactgccaacaagactactcatacccatttacatttggacaaggtaccaaggtcgagatcaag	SEQ ID NO: 142

The antibodies described in further Examples 2 to 4 were modified to contain a RLPXTGG tag (SEQ ID NO: 143) at the C-terminal end of the HC and/or a GGGGSLPXTGG tag (SEQ ID NO: 144) at the C-terminal end of the LC, where X is any of the 20 natural amino acids. The C-terminal lysine (K) on the HC was in this case replaced by the Arginine (R) of the tag. The addition of the tags did not change the affinity and selectivity to CLDN18.2 of the antibodies.

Example 2: FACS binding analysis of humanized mAbs

The HEK293T (ATCC CRL-3216) cell line does not endogenously express CLDN18.1 or CLDN18.2. Therefore, in order to test antibody binding activity, CLDN18.1 and CLDN18.2 were overexpressed in the HEK293T cell line. Cells were co-transected by electroporation with a transposase expression construct (pcDNA3.1-hy-mPB), a construct bearing transposable full-length huCLDN18.1 (pPB-Puro-huCldn18.1) or huCLDN18.2 (pPB-Puro-huCldn18.2) along with puromycin expression cassette and a construct carrying EGFP as transfection control (pEGFP-N3). Upon transfection, cells were allowed to recover for two days in growth media at 37°C in a humidified incubator in a 5% CO_2 atmosphere. Transfection was verified by FC analysis of the EGFP expression. Cells expressing huCLDN18.1 or huCLDN18.2 were then selected by the addition of puromycin into culture at 1 µg/ml, and further expanded to allow the generation of frozen stocks in FCS with 10% DMSO. The expression of huCLDN18.2 in the transfected HEK293T cells was analyzed by FACS. In brief, HEK293T cells were trypsinized and collected by centrifugation, resuspended in PBS/2% FCS and stained for huCLDN18.2 using IMAB362 as primary antibody at 2 µg/ml on ice for 30 min and, upon washing in PBS/2% FCS, stained with PE-labelled anti-human Fcγ-specific IgG goat antibody (eBioscience) as secondary antibody for 30 min on ice. Upon further wash, resuspended stained cells in ice-cold FACS buffer were analyzed using a FACSCalibur^{TM} instrument (see Figure 1A). Un-transfected parental cells, not expressing CLDN18.2, were used as negative control. The expression of CLDN18.1 was analyzed in a similar fashion, using a proprietary pan-CLDN18 antibody recognizing CLDN18.1 and CLDN18.2. Any pan-CLDN18 antibody usable for flow cytometry measurement would also be adequate such as antibody anti Claudin-18/CLDN18 (C-term) provided by OriGene Technologies (catalog number AP50944PU-N), CLDN18 (C-Term) Rabbit pAb from MyBioSource (catalog number MBS8555451) or the CLDN18 Antibody from ProSci (catalog number 63-847).

The HEK293T cells stably expressing huCLDN18.1 and huCLDN18.2 were consequently used to test the binding specificity of the humanized antibodies hGBA-1, hGBA-2, hGBA-3, hGBA-4, hGBA-5, hGBA-6, hGBA-7, hGBA-8 and hGBA-9 to CLDN18.2 and not to huCLDN18.1. The cells were stained on ice for 30 min using the antibodies at 2µg/ml and, upon washing in FACS buffer (PBS/2% FCS), stained with PE-labelled anti-human Fcγ-specific IgG goat antibody (eBioscience) as secondary antibody for 30 min on ice. Expression of CLDN18.1 in the HEK293T cells stably expressing huCLDN18.1 was verified with a pan-CLDN18 antibody (see Figure 1, panel L) and expression of CLDN18.2 in the HEK293T cells stably expressing huCLDN18.2 was verified with the IMAB362 (see Figure 1, panel A). Figure 1 shows that all humanized antibodies bind specifically to huCLDN18.2 expressed by HEK293T cells, and not to huCLDN18.1. Furthermore, all humanized antibodies bind to huCLDN18.2 stronger than the parental antibody IMAB362.

Example 3: ELISA binding analysis of humanized mAbs

The binding affinity to CLDN18.2 of the humanized antibodies (hGBA) was tested in an ELISA assay with lipoparticles bearing CLDN18.2 as source of antigen. CLDN18.2-lipoparticles and Null-lipoparticles (without antigen as a negative control) were used to coat 96-well plates at a final concentration of 10 U/ml. Upon washing with PBS/0.05% Tween-20 (PBS-T) and blocking with PBS-T/3% BSA for at least 1 h at 37°C, 1:3 serial dilutions of hGBA and IMAB362 antibodies with a starting concentration of 2 µg/ml in PBS-T/1% BSA were added to the coated wells and incubated for at least 1 h at 37°C. The presence of bound antibodies was revealed through binding of an HRP-goat anti-human secondary antibody diluted in PBS-T/1% BSA, development with Sigma-Fast OPD as peroxidase substrate and the reaction was stopped by adding 2M H_2SO_4, followed by reading the OD at 490 nm on an ELISA plate reader.

Representative binding curves are shown in Figure 2. Surprisingly, the binding curves in Figure 2 show that all humanized antibodies (hGBA-1 to hGBA-9) bind to CLDN18.2-lipoparticles with a higher affinity than IMAB362, shown by a higher maximal binding value.

Example 4: FC titration on HEK293T and PA-TU-8988 High cells

PA-TU-8988S cells (Creative Bioarray, catalog number CSC-C0326) expressing high levels of CLDN18.2 were selected by FACS. Herein, these cells are designated as PA-TU-8988S-High cells. Based on FACS staining with IMAB362, the PA-TU-8988S cell population expresses different levels of CLDN18.2, with a high and a medium level of expression (see Figure 3A). In order to have a more homogenous cell population, the cells were sorted by FACS to select only cells with a higher CLDN18.2 expression. In brief, PA-TU-8988S cells suspended in FACS buffer (PBS, 2% FCS) were incubated on ice for 30 min with IMAB362 at 2 μg/ml. After wash in FACS buffer, the cells were incubated with the PE-labeled Fcγ specific IgG goat anti-human secondary antibody (eBioscience) on ice for 30 min. After wash, the stained cells were resuspended in FACS buffer, analyzed and sorted by a FACSAria™ instrument, separating medium expressing cells (Figure 3B) from high expressing cells (Figure 3B). After sorting, the collected PA-TU-8988S-High cells were resuspended in growth media, expanded in growth media and frozen aliquots were preserved in liquid N_2.

In order to quantify the affinity of the antibodies to CLDN18.2, 250 x 10^3 cells/well of HEK293T cells overexpressing CLDN18.2 or PA-TU-8988-High cells were seeded in FC buffer (PBS/2% FCS) into 96-well plates and allowed to settle by centrifugation. IMAB362 and hGBA antibodies to be tested were diluted at 4 μg/ml, followed by 1:4 serial dilutions and incubated with the platted cells for 30 min at 4°C. A PE-coupled secondary anti-human IgG antibody was added to the cells for additional 30 min at 4°C after washes with the FACS buffer, followed by further washes with FC buffer. The cells were then resuspended in 100 μl FC buffer and measured with a FACSCalibur™ cell analyzer (BD Biosciences, USA). The FC analysis (see Figure 4 and Table 4) shows that all hGBA antibodies have a stronger binding affinity to CLDN18.2 (reflected by a higher Max MFI for all tested new antibodies, see Table 4) than IMAB362, in both cell lines. The binding affinity of all hGBA antibodies is similar between each other but is significantly higher than the parental antibody IMAB362.

Table 4: Maximum MFI and EC50 (μg/ml) measured on all the hGBA and IMAB362 antibodies on the HEK293T cells lines overexpressing CLDN18.2 and on the PA-TU-8988S-High cell lines.

Antibody	**HEK293T-CLDN18.2**		**PA-TU-8988S-High**	
	Max MFI	**EC50 (μg/ml)**	**Max MFI**	**EC50 (μg/ml)**
	EXP. 2	**EXP. 2**	**EXP. 2**	**EXP. 2**
IMAB362	1968	0.3878	1046	0.5082
hGBA1	3031	0.2586	2527	0.4439
hGBA2	2967	0.2486	2403	0.5836
hGBA3	2750	0.2734	2156	0.3525
hGBA4	2790	0.3575	2011	0.4123
hGBA5	3321	0.3052	2560	0.1593
hGBA6	2888	0.2567	2236	0.1913
hGBA7	3250	0.4196	2318	0.3232
hGBA8	2704	0.187	2366	0.3034
hGBA9	3124	0.2414	2445	0.286

The invention is also described by the following embodiments:

1. An antibody or fragment thereof binding to CLDN18.2, which comprises: HCDR1, HCDR2 and HCR3 sequences of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, respectively and LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively.

2. The antibody or fragment thereof of embodiment 1, comprising:
    a. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 9 and SEQ ID NO: 18, respectively and
    the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
    b. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 10 and SEQ ID NO: 19, respectively and
    the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
    c. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 10 and SEQ ID NO: 20, respectively and
    the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 30, respectively;
    d. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 12 and SEQ ID NO: 21, respectively and
    the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 26, SEQ ID NO: 5 and SEQ ID NO: 30, respectively;
    e. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 13 and SEQ ID NO: 18, respectively and
    the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 31, respectively;
    f. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 8, SEQ ID NO: 14 and SEQ ID NO: 22, respectively and
    the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
    g. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 15 and SEQ ID NO: 23, respectively and

the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 27, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;

h. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 16 and SEQ ID NO: 23, respectively and
the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively; or

i. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 8, SEQ ID NO: 17 and SEQ ID NO: 24, respectively and
the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 28, SEQ ID NO: 5 and SEQ ID NO: 31, respectively.

3. The antibody or fragment thereof of embodiments 1 and 2, comprising:
   a. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 32;
   b. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 34;
   c. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 35;
   d. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 37;
   e. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 39;
   f. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 41;
   g. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 42;
   h. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 44 or
   i. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 45;

   and

j. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 33;
k. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 36;
l. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 38;
m. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 40;
n. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 43; or
o. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 46.

4. The antibody or fragment thereof of any one of embodiments 1 to 3, comprising:
   a. a VH sequence of SEQ ID NO: 32;
   b. a VH sequence of SEQ ID NO: 34;
   c. a VH sequence of SEQ ID NO: 35;
   d. a VH sequence of SEQ ID NO: 37;
   e. a VH sequence of SEQ ID NO: 39;
   f. a VH sequence of SEQ ID NO: 41;
   g. a VH sequence of SEQ ID NO: 42;
   h. a VH sequence of SEQ ID NO: 44; or
   i. a VH sequence of SEQ ID NO: 45;

   and

   j. a VL sequence of SEQ ID NO: 33;
   k. a VL sequence of SEQ ID NO: 36;
   l. a VL sequence of SEQ ID NO: 38;
   m. a VL sequence of SEQ ID NO: 40;
   n. a VL sequence of SEQ ID NO: 43; or
   o. a VL sequence of SEQ ID NO: 46.

5. The antibody or fragment thereof of any one of embodiments 1 to 4, comprising:

a. a VH sequence of SEQ ID NO: 32 and a VL sequence of SEQ ID NO: 33;
b. a VH sequence of SEQ ID NO: 34 and a VL sequence of SEQ ID NO: 33;
c. a VH sequence of SEQ ID NO: 35 and a VL sequence of SEQ ID NO: 36;
d. a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 38;
e. a VH sequence of SEQ ID NO: 39 and a VL sequence of SEQ ID NO: 40;
f. a VH sequence of SEQ ID NO: 41 and a VL sequence of SEQ ID NO: 33;
g. a VH sequence of SEQ ID NO: 42 and a VL sequence of SEQ ID NO: 43;
h. a VH sequence of SEQ ID NO: 44 and a VL sequence of SEQ ID NO: 33; or
i. a VH sequence of SEQ ID NO: 45 and a VL sequence of SEQ ID NO: 46.

6. The antibody or fragment thereof of any one of embodiments 1 to 5, consisting of:
    a. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 49 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50;
    b. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 51 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50;
    c. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 52 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 53;
    d. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 54 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 55;
    e. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID

NO: 56 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 57;

f. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 58 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50;

g. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 59 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 60;

h. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 61 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50; or

i. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 62 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 63.

7. The antibody or fragment thereof of any one of embodiments 1 to 6, consisting of:
    a. the heavy chain sequence of SEQ ID NO: 49 and light chain sequence of SEQ ID NO: 50;
    b. the heavy chain sequence of SEQ ID NO: 51 and light chain sequence of SEQ ID NO: 50;
    c. the heavy chain sequence of SEQ ID NO: 52 and light chain sequence of SEQ ID NO: 53;
    d. the heavy chain sequence of SEQ ID NO: 54 and light chain sequence of SEQ ID NO: 55;

   e. the heavy chain sequence of SEQ ID NO: 56 and light chain sequence of SEQ ID NO: 57;
   f. the heavy chain sequence of SEQ ID NO: 58 and light chain sequence of SEQ ID NO: 50;
   g. the heavy chain sequence of SEQ ID NO: 59 and light chain sequence of SEQ ID NO: 60;
   h. the heavy chain sequence of SEQ ID NO: 61 and light chain sequence of SEQ ID NO: 50; or
   i. the heavy chain sequence of SEQ ID NO: 62 and light chain sequence of SEQ ID NO: 63.

8. An antibody or fragment thereof that competes for binding with an antibody or fragment thereof of any one of embodiments 1 to 7.

9. The antibody or fragment thereof of any one of embodiments 1 to 8, wherein the format of the antibody or fragment thereof is selected from the group consisting of IgA1, IgA2, IgD, IgE, IgG1, IgG2, IgG3, IgG4, synthetic IgG, IgM, $F(ab)_2$, Fv, scFv, IgGACH2, $F(ab')_2$, scFvCH3, Fab, VL, VH, scFv4, scFv3, scFv2, dsFv, Fv, scFv-Fc, $(scFv)_2$, a non-depleting IgG, a diabody, and a bivalent antibody, or Fc-engineered versions thereof.

10. The antibody or fragment thereof of any one of embodiments 1 to 9, wherein the antibody or fragment thereof is humanized.

11. The antibody or fragment thereof of any one of embodiments 1 to 10, wherein the antibody or fragment thereof is isolated.

12. The antibody or fragment thereof of any one of embodiments 1 to 11, wherein the antibody or fragment thereof does not bind to CLDN18.1.

13. The antibody or fragment thereof of any one of embodiments 1 to 12, wherein the antibody or fragment thereof exhibits increased binding to CLDN18.2 as compared to antibody IMAB362.

14. The antibody or fragment of embodiment 13 wherein increased binding is measured as EC50 value and/or maxMFI value by flow cytometry titration on cells expressing CLDN18.2, preferably wherein the cells are HEK293T cells or PA-TU-8988-High cells.

15. The antibody or fragment of embodiment 14, wherein the measured EC50 value of the antibody is at least 10% lower, at least 20% lower, at least 40% lower, at least 50% lower or at least 75% lower than the EC50 value of antibody IMAB362.

16. The antibody or fragment of embodiment 14, wherein the measured maxMFI value of the antibody is at least 10% higher, at least 20% higher, at least 40% higher, at least 50% higher or at least 75% higher than the maxMFI value of antibody IMAB362.

17. A nucleic acid encoding the antibody or fragment thereof of any of embodiments 1 to 16.

18. A vector comprising the nucleic acid of embodiment 17.

19. A host cell comprising the nucleic acid of embodiment 17 or a vector of embodiment 18.

20. The antibody or fragment thereof of any one of embodiments 1 to 16, the nucleic acid of embodiment 17, the vector of embodiment 18 or the host cell of embodiment 19 for use in the treatment of a subject
    a. suffering from,
    b. at risk of developing, and/or
    c. being diagnosed for
    a neoplastic disease.

21. The antibody or fragment thereof for the use of embodiment 20, wherein the neoplastic disease is selected from the group consisting of pancreatic, gastric, esophageal, ovarian and lung cancer.

SEQUENCES

SEQ ID NO: 1	GYXFTSYWIG X in 3rd position is T or S
SEQ ID NO: 2	GXIYPXXXXTXYX X in 2nd position is N or I; X in 6th position is S or G; X in 7th position is A, E or D; X in 8th position is A or S; X in 9th position is Y or D; X in 11th position is N or R; X in last position is A or S
SEQ ID NO: 3	XRXWRGNSFDX X in 1st position is A or T; X in 3rd position is L, M, I or Q; X in last position is A or Y
SEQ ID NO: 4	KSSQSXLNSGNQKNYLX X in 6th position is L or V; X in last position is T or A
SEQ ID NO: 5	WASTRES
SEQ ID NO: 6	QXDYSYPXT X in 2nd position is N or Q; X in L or F
SEQ ID NO: 7	GYSFTSYWIG
SEQ ID NO: 8	GYTFTSYWIG
SEQ ID NO: 9	GNIYPGASDTRYA
SEQ ID NO: 10	GNIYPGDADTRYA
SEQ ID NO: 11	GIIYPGASDTNYA
SEQ ID NO: 12	GIIYPGDAYTRYS
SEQ ID NO: 13	GIIYPGAAYTRYA
SEQ ID NO: 14	GNIYPGASYTRYS
SEQ ID NO: 15	GNIYPGEAYTRYS
SEQ ID NO: 16	GNIYPSESYTNYA
SEQ ID NO: 17	GIIYPSAAYTRYA
SEQ ID NO: 18	ARLWRGNSFDY
SEQ ID NO: 19	ARMWRGNSFDY
SEQ ID NO: 20	ARIWRGNSFDY
SEQ ID NO: 21	TRLWRGNSFDA
SEQ ID NO: 22	TRQWRGNSFDY
SEQ ID NO: 23	TRLWRGNSFDY
SEQ ID NO: 24	TRMWRGNSFDY
SEQ ID NO: 25	KSSQSLLNSGNQKNYLA
SEQ ID NO: 26	KSSQSLLNSGNQKNYLT

SEQ ID NO: 27 KSSQSVLNSGNQKNYLT

SEQ ID NO: 28 KSSQSVLNSGNQKNYLA

SEQ ID NO: 29 QNDYSYPFT

SEQ ID NO: 30 QNDYSYPLT

SEQ ID NO: 31 QQDYSYPFT

SEQ ID NO: 32 hGBA-1 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGASDTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGTLVTVSS

SEQ ID NO: 33 hGBA-1, hGBA-2, hGBA-6 , hGBA-8 LC variable region
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIK

SEQ ID NO: 34 hGBA-2 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGDADTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARMWRGNSFDYWGQGTLVTVSS

SEQ ID NO: 35 hGBA-3 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGASDTNYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARIWRGNSFDYWGQGTLVTVSS

SEQ ID NO: 36 hGBA-3 LC variable region
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPLTFGQGTKVEIK

SEQ ID NO: 37 hGBA-4 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDAYTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDAWGQGTLVTVSS

SEQ ID NO: 38 hGBA-4 LC variable region
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPLTFGQGTKVEIK

SEQ ID NO: 39 hGBA-5 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGAAYTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGTLVTVSS

SEQ ID NO: 40 hGBA-5 LC variable region
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQDYSYPFTFGQGTKVEIK

SEQ ID NO: 41 hGBA-6 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGNIYPGAS
YTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRQWRGNSFDYWGQGT
LVTVSS

SEQ ID NO: 42 hGBA-7 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGEA
YTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGT
LVTVSS

SEQ ID NO: 43 hGBA-7 LC variable region
DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLTWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIK

SEQ ID NO: 44 hGBA-8 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPSES
YTNYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGT
LVTVSS

SEQ ID NO: 45 hGBA-9 HC variable region
EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGIIYPSAA
YTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRMWRGNSFDYWGQGT
LVTVSS

SEQ ID NO: 46 hGBA-9LC variable region
DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQDYSYPFTFGQGTKVEIK

SEQ ID NO: 47 IMAB362 HC full
QVQLQQPGAELVRPGASVKLSCKASGYTFTSYWINWVKQRPGQGLEWIGNIYPSDSY
TNYNQKFKDKATLTVDKSSSTAYMQLSSPTSEDSAVYYCTRSWRGNSFDYWGQGTT
LTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF
PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPP
CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 48 IMAB362 LC full
DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWA
STRESGVPDRFTGSGSGTDFTLTISSVQAEDLAVYYCQNDYSYPFTFGSGTKLEIKRTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 49 hGBA-1 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGAS
DTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV

HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 50 hGBA-1, hGBA-2, hGBA-6, hGBA-8 LC full
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIKRT
VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 51 hGBA-2 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGDA
DTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARMWRGNSFDYWGQG
TLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 52 hGBA-3 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGASD
TNYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARIWRGNSFDYWGQGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF
PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPP
CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 53 hGBA-3 LC full
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPLTFGQGTKVEIKRT
VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 54 hGBA-4 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDA
YTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDAWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 55 hGBA-4 LC full
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPLTFGQGTKVEIKRT

VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 56 hGBA-5 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGAA
YTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARLWRGNSFDYWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 57 hGBA-5 LC full
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQDYSYPFTFGQGTKVEIKRT
VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 58 hGBA-6 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGNIYPGAS
YTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRQWRGNSFDYWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 59 hGBA-7 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPGEA
YTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 60 hGBA-7 LC full
DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLTWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPFTFGQGTKVEIKRT
VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 61 hGBA-8 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGNIYPSES
YTNYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRLWRGNSFDYWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT

FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 62 hGBA-9 HC full
EVQLVQSGAEVKKPGESLKISCKGSGYTFTSYWIGWVRQMPGKGLEWMGIIYPSAA
YTRYAPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRMWRGNSFDYWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 63 hGBA-9, LC full
DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQDYSYPFTFGQGTKVEIKRT
VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 64 constant heavy chain - CH1 + Fc domain
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ
SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE
LLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK
PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF
LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 65
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT
EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 66
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ
SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE
AAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT
KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 67
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ
SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE
AAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT
KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREP
QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 68 DQWSTQDLYN

SEQ ID NO: 69 NNPVTAVFNYQ

SEQ ID NO: 70 STQDLYNNPVTAVF

SEQ ID NO: 71 TNFWMSTANMYTG

SEQ ID NO: 72 ALMIVGIVLGAIGLLV

SEQ ID NO: 73 RIGSMEDSAKANMTLTSGIMFIVS

SEQ ID NO: 74
METDTLLLWVLLLWVPGSTGDAAQPARRARRTKLGTELGSTPVWWNSADGRMDQWSTQDLYNNPVTAVFNYQGLWRSCVRESSGFTECRGYFTLLGLPAMLQAVRAAIQHSGGRSRRARTKTHLRRGSE

SEQ ID NO: 75 MDQWSTQDLYNNPVT

SEQ ID NO: 76 LYNNPVTAVFNYQGL

SEQ ID NO: 77 VFNYQGLWRSCVRES

SEQ ID NO: 78 QGLWRSCVRESSGFT

SEQ ID NO: 79 RSCVRESSGFTECRG

SEQ ID NO: 80 TEDEVQSYPSKHDYV

SEQ ID NO: 81 EVQSYPSKHDYV

SEQ ID NO: 82 consensus including IMAB362 HC CDR1

GYXFTSYWIX X in 3rd position is T or S, X in the last position is G or N

SEQ ID NO: 83 consensus including IMAB362 HC CDR2

GXIYPXXXXTXYX X in 2nd position is N or I; X in 6th position is S or G; X in 7th position is A, E or D; X in 8th position is A or S; X in 9th position is Y or D; X in 11th position is N or R; X in last position is A, N or S

SEQ ID NO: 84 consensus including IMAB362 HC CDR3

XRXWRGNSFDX X in 1st position is A or T; X in 3rd position is L, M, I, S or Q; X in last position is A or Y

SEQ ID NO: 85 ggctatagctttacatcatattggattgga

SEQ ID NO: 86 gggaacatttaccctggggcatcggatacgcgatacgca

SEQ ID NO: 87 gcgagactttggcgggggaatagcttcgactac

SEQ ID NO: 88 aaaagctcccaaagcctattgaactcgggaaaccaaaagaattacttggca

SEQ ID NO: 89 tgggcaagcacccgagagagc

SEQ ID NO: 90 caaaacgactattcatacccattcaca

SEQ ID NO: 91	ggatattcatttacaagctactggatcgga
SEQ ID NO: 92	ggaaatatataccccggagacgcggacacgagatacgca
SEQ ID NO: 93	gcgcggatgtggcgcggcaatagctttgactac
SEQ ID NO: 94	gggatcatctatccgggggcatccgataccaactatgcg
SEQ ID NO: 95	gctaggatttggcgaggaaatagctttgattat
SEQ ID NO: 96	aagagctcgcaaagtttgctgaactccgggaaccaaaagaattacctggca
SEQ ID NO: 97	tgggcatcaacgcgggaaagc
SEQ ID NO: 98	caaaacgactactcctatccgctgacc
SEQ ID NO: 99	ggatactcatttacatcatactggatagga
SEQ ID NO: 100	gggattatataccccggcgacgcttacactcgatattcg
SEQ ID NO: 101	acgaggctatggagggggaatagctttgatgcc
SEQ ID NO: 102	aagagctcccaaagcctattgaactcgggaaatcaaaagaattatctgaca
SEQ ID NO: 103	tgggcctcgacaagggagagc
SEQ ID NO: 104	caaaatgactactcatacccgctgaca
SEQ ID NO: 105	ggatatagctttacgagctactggatcgga
SEQ ID NO: 106	gggataatataccccggagcggcatacacgagatatgcg
SEQ ID NO: 107	gcgagactatggcgcgggaactcatttgattac
SEQ ID NO: 108	aaatcatcgcaatcattgctaaattcggggaaccaaaagaattatttggca
SEQ ID NO: 109	tgggcatccacgagagaatcg
SEQ ID NO: 110	caacaagattattcatacccatttaca
SEQ ID NO: 111	ggatatacatttacatcttactggatcgga
SEQ ID NO: 112	gggaacatttatcctggcgcgagctatacgcgctat
SEQ ID NO: 113	acccggcaatggaggggcaatagctttgactac
SEQ ID NO: 114	ggatattcctttacatcatactggatcggc
SEQ ID NO: 115	gggaacatatatcccggagaagcctatacgagatactcg
SEQ ID NO: 116	acgcgactatggaggggaaatagctttgactat
SEQ ID NO: 117	aagagctcccaatcagtcctgaactctgggaatcaaaagaattacctgaca
SEQ ID NO: 118	tgggcgagcacgagggagagc
SEQ ID NO: 119	caaaatgattattcataccccttcaca
SEQ ID NO: 120	ggatactcctttacatcatattggatcgga

SEQ ID NO: 121 ggaaacatatatccgagcgaatcatatacgaactacgcg

SEQ ID NO: 122 acgaggctatggagggggaatagcttcgactat

SEQ ID NO: 123 ggatatacattcacgagctactggatagga

SEQ ID NO: 124 ggaatcatatatccttccgcggcatatacgcgatatgcg

SEQ ID NO: 125 acgcggatgtggaggggaaatagctttgattac

SEQ ID NO: 126 aagagctcgcaatcggtcctgaatagcgggaaccaaaagaattatctggcc

SEQ ID NO: 127 caacaagactactcatacccatttaca

SEQ ID NO: 128

gaagtccaactggtccaatccggcgcggaggttaagaagcccggagaatcgctgaagatctcatgcaaagggagcggctatagctttacatcatattggattggatgggtcaggcaaatgccggggaaggggctggaatggatggggaacatttaccctggggcatcggatacgcgatacgcacctagctttcaagggcaagtcacaatttcggcggacaagagcatctcaacggcatacctgcaatggtcgagcttgaaggcatctgatactgcaatgtactactgcgcgagactttggcgggggaatagcttcgactactgggggcagggtaccctggttacggtctcgagc

SEQ ID NO: 129

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SEQ ID NO: 130

gaagtccaactggtccaatctggagcggaagtcaagaagcctggggagagcctgaaaatttcatgcaaggggagcggatattcatttacaagctactggatcggatgggtccggcaaatgccggggaagggcttggaatggatgggaaatatataccccggagacgcggacacgagatacgcaccgagctttcaagggcaggtcaccattagcgctgataaatcgatttcaaccgcatatctgcaatggtcatcgctgaaggcctccgacaccgcgatgtactattgcgcgcggatgtggcgcggcaatagctttgactactgggggcagggtaccctcgtcacggtctcgagc

SEQ ID NO: 131

gaggtccaactggtccaaagcggcgcggaggtcaagaagccgggagaatccctgaagattagctgcaaaggctccggctatagctttacatcatattggatcggatgggtcagacaaatgccgggaaagggacttgaatggatggggatcatctatccgggggcatccgataccaactatgcgccgagcttccaagggcaggtcacgatatccgcggataaatcgattagcaccgcatatctgcaatggagctcgctgaaggcatccgacaccgcgatgtactactgcgctaggatttggcgaggaaatagctttgattattgggggcagggtacccttgtcacggtctcgagc

SEQ ID NO: 132

gacattgtcatgacgcaaagccccgactcgctggccgtctcactgggggagcgggcgacaatcaactgcaagagctcgcaaagtttgctgaactccgggaaccaaaagaattacctggcatggtatcaacaaaagccggggcaacccccgaagctgctgatatattgggcatcaacgcgggaaagcggagtcccggatagatttagcggatctggatcggggaccgacttcacgctgacgatatctagccttcaagccgaggatgtggctgtatattattgccaaaacgactactcctatccgctgaccttcgggcaaggtaccaaggtcgagatcaag

SEQ ID NO: 133

gaagtccaactagtccaaagcggagccgaagtcaagaaaccgggggagagccttaagatctcatgcaaggggagcggatactcatttacatcatactggataggatgggtcagacaaatgcccggcaaggggctggaatggatggggattatataccccggcgacgcttacactcgatattcgccatcattccaagggcaggtcacgatatcggccgataaatcgatatccacggcatacctgcaatggagctcac tgaaagcatctgatacggcaatgtattattgcacgaggctatggagggggaatagctttgatgcctgggggcagggtaccctggtcacggtctcgagc

SEQ ID NO: 134

gacatagttatgacacaatcgccggatagcctcgcggtcagccttggagagcgggcgacgatcaactgcaagagctcccaaagcctattgaactcgggaaatcaaaagaattatctgacatggtatcaacaaaagccggggcaaccaccgaaactgctgatctattgggcctcgacaagggagagcggagtcccggaccgcttctctggatcgggaagcgggactgacttcacgctgaccataagctcgctgcaagccgaggacgtcgccgtctattattgccaaaatgactactcatacccgctgacatttggccaaggtaccaaggtcgagatcaag

SEQ ID NO: 135

gaggtgcaactggtacaatccggggcggaagtgaagaagccgggggaatcgctgaagataagctgcaaaggctctggatatagctttacgagctactggatcggatgggtcaggcaaatgccggggaagggactggaatggatggggataatataccccggagcggcatacacgagatatgcgccgagcttccaagggcaagtgacaataagcgcggacaaatcgattagcacggcatatctgcaatggtcctcgctgaaggcgagcgataccgcaatgtactattgcgcgagactatggcgcgggaactcatttgattactgggggcagggtaccctagtgacggtctcgagc

SEQ ID NO: 136

gacattgtcatgacgcaaagcccggatagcctggctgtatcgctgggggagagagcgacgatcaactgcaaatcatcgcaatcattgctaaattcggggaaccaaaagaattatttggcatggtatcaacaaaagccggggcaaccgccgaaactgctgatttactgggcatccacgagagaatcgggagtcccggaccgatttagcggatctgggagcgggaccgatttcacgctgaccattagctcgctgcaagcggaggatgtggcggtctattactgccaacaagattattcatacccatttacatttgggcaaggtaccaaggtcgagatcaag

SEQ ID NO: 137

gaagtacaattggttcaatcgggggccgaagtcaagaagccgggggaatcgctgaagatatcctgcaaggggagcggatatacatttacatcttactggatcggatgggtcagacaaatgcccggaaaggggcttgaatggatggggaacatttatcctggcgcgagctatacgcgctatagcccgagcttccaagggcaggtcacgattagcgccgacaagagcatttcgacggcatacctgcaatggagctcgctgaaagcatcggatacggcaatgtattactgcacccggcaatggaggggcaatagctttgactactgggggcagggtaccctagtcacggtctcgagc

SEQ ID NO: 138

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SEQ ID NO: 139

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SEQ ID NO: 140

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SEQ ID NO: 141

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SEQ ID NO: 142

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SEQ ID NO: 143 sortase tag

RLPXTGG

X is any of the 20 natural amino acids

SEQ ID NO: 144 sortase tag

GGGGSLPXTGG

X is any of the 20 natural amino acids

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CLAIMS

1. An antibody or fragment thereof binding to CLDN18.2, which comprises: HCDR1, HCDR2 and HCR3 sequences of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, respectively and LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively.

2. The antibody or fragment thereof of claim 1, comprising:
   a. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 9 and SEQ ID NO: 18, respectively and
      the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
   b. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 10 and SEQ ID NO: 19, respectively and
      the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;
   c. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 10 and SEQ ID NO: 20, respectively and
      the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 30, respectively;
   d. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 12 and SEQ ID NO: 21, respectively and
      the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 26, SEQ ID NO: 5 and SEQ ID NO: 30, respectively;
   e. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 13 and SEQ ID NO: 18, respectively and
      the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 31, respectively;
   f. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 8, SEQ ID NO: 14 and SEQ ID NO: 22, respectively and
      the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;

g. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 15 and SEQ ID NO: 23, respectively and
the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 27, SEQ ID NO: 5 and SEQ ID NO: 29, respectively;

h. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 7, SEQ ID NO: 16 and SEQ ID NO: 23, respectively and
the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 25, SEQ ID NO: 5 and SEQ ID NO: 29, respectively; or

i. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 8, SEQ ID NO: 17 and SEQ ID NO: 24, respectively and
the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 28, SEQ ID NO: 5 and SEQ ID NO: 31, respectively.

3. The antibody or fragment thereof of claims 1 and 2, comprising:
    a. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 32;
    b. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 34;
    c. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 35;
    d. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 37;
    e. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 39;
    f. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 41;
    g. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 42;
    h. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 44 or
    i. a VH sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 45;

and

j. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 33;
k. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 36;
l. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 38;
m. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 40;
n. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 43; or
o. a VL sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 46;

preferably comprising:

p. a VH sequence of SEQ ID NO: 32;
q. a VH sequence of SEQ ID NO: 34;
r. a VH sequence of SEQ ID NO: 35;
s. a VH sequence of SEQ ID NO: 37;
t. a VH sequence of SEQ ID NO: 39;
u. a VH sequence of SEQ ID NO: 41;
v. a VH sequence of SEQ ID NO: 42;
w. a VH sequence of SEQ ID NO: 44 or
x. a VH sequence of SEQ ID NO: 45;

and

y. a VL sequence of SEQ ID NO: 33;
z. a VL sequence of SEQ ID NO: 36;
aa. a VL sequence of SEQ ID NO: 38;
bb. a VL sequence of SEQ ID NO: 40;
cc. a VL sequence of SEQ ID NO: 43; or
dd. a VL sequence of SEQ ID NO: 46.

4. The antibody or fragment thereof of any one of claims 1 to 3, comprising:

    a. a VH sequence of SEQ ID NO: 32 and a VL sequence of SEQ ID NO: 33;
    b. a VH sequence of SEQ ID NO: 34 and a VL sequence of SEQ ID NO: 33;
    c. a VH sequence of SEQ ID NO: 35 and a VL sequence of SEQ ID NO: 36;
    d. a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 38;
    e. a VH sequence of SEQ ID NO: 39 and a VL sequence of SEQ ID NO: 40;
    f. a VH sequence of SEQ ID NO: 41 and a VL sequence of SEQ ID NO: 33;
    g. a VH sequence of SEQ ID NO: 42 and a VL sequence of SEQ ID NO: 43;
    h. a VH sequence of SEQ ID NO: 44 and a VL sequence of SEQ ID NO: 33; or
    i. a VH sequence of SEQ ID NO: 45 and a VL sequence of SEQ ID NO: 46.

5. The antibody or fragment thereof of any one of claims 1 to 4, consisting of:
    a. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 49 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50;
    b. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 51 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50;
    c. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 52 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 53;
    d. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 54 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 55;

e. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 56 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 57;
f. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 58 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50;
g. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 59 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 60;
h. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 61 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 50; or
i. a heavy chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 62 and a light chain sequence having at least 80%, at least 85%, at least 90%, at least 95% or at least 98% sequence identity with the amino acid sequence of SEQ ID NO: 63;

preferably consisting of:

j. the heavy chain sequence of SEQ ID NO: 49 and light chain sequence of SEQ ID NO: 50;
k. the heavy chain sequence of SEQ ID NO: 51 and light chain sequence of SEQ ID NO: 50;
l. the heavy chain sequence of SEQ ID NO: 52 and light chain sequence of SEQ ID NO: 53;

m. the heavy chain sequence of SEQ ID NO: 54 and light chain sequence of SEQ ID NO: 55;
n. the heavy chain sequence of SEQ ID NO: 56 and light chain sequence of SEQ ID NO: 57;
o. the heavy chain sequence of SEQ ID NO: 58 and light chain sequence of SEQ ID NO: 50;
p. the heavy chain sequence of SEQ ID NO: 59 and light chain sequence of SEQ ID NO: 60;
q. the heavy chain sequence of SEQ ID NO: 61 and light chain sequence of SEQ ID NO: 50; or
r. the heavy chain sequence of SEQ ID NO: 62 and light chain sequence of SEQ ID NO: 63.

6. An antibody or fragment thereof that competes for binding with an antibody or fragment thereof of any one of claims 1 to 5.

7. The antibody or fragment thereof of any one of claims 1 to 6, wherein the format of the antibody or fragment thereof is selected from the group consisting of IgA1, IgA2, IgD, IgE, IgG1, IgG2, IgG3, IgG4, synthetic IgG, IgM, $F(ab)_2$, Fv, scFv, IgGACH2, $F(ab')_2$, scFvCH3, Fab, VL, VH, scFv4, scFv3, scFv2, dsFv, Fv, scFv-Fc, $(scFv)_2$, a non-depleting IgG, a diabody, and a bivalent antibody, or Fc-engineered versions thereof.

8. The antibody or fragment thereof of any one of claims 1 to 7, wherein the antibody or fragment thereof

   (i) is humanized;
   (ii) is isolated; and/or
   (iii) does not bind to CLDN18.1.

9. The antibody or fragment thereof of any one of claims 1 to 8, wherein the antibody or fragment thereof exhibits increased binding to CLDN18.2 as compared to a reference antibody, optionally wherein increased binding is measured as EC50 value and/or maxMFI value by flow cytometry titration on cells expressing CLDN18.2, preferably wherein the cells are HEK293T cells or PA-TU-8988-High cells, wherein the reference

antibody comprises a heavy chain sequence of SEQ ID NO: 47 and a light chain sequence of SEQ ID NO: 48.

10. The antibody or fragment of claim 9, wherein

(i) the measured EC50 value of the antibody is at least 10% lower, at least 20% lower, at least 40% lower, at least 50% lower or at least 75% lower than the EC50 value of a reference antibody; and/or

(ii) the measured maxMFI value of the antibody is at least 10% higher, at least 20% higher, at least 40% higher, at least 50% higher or at least 75% higher than the maxMFI value of a reference antibody;

wherein the reference antibody comprises a heavy chain sequence of SEQ ID NO: 47 and a light chain sequence of SEQ ID NO: 48.

11. A nucleic acid encoding the antibody or fragment thereof of any of claims 1 to 10.

12. A vector comprising the nucleic acid of claim 11.

13. A host cell comprising the nucleic acid of claim 11 or a vector of claim 12.

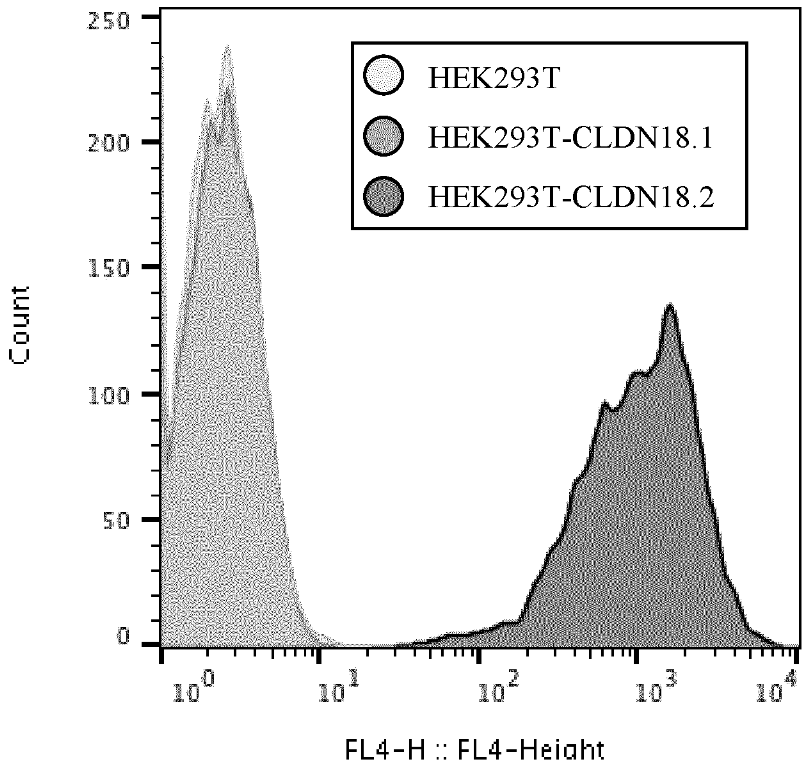
14. The antibody or fragment thereof of any one of claims 1-10, the nucleic acid of claim 11, the vector of claim 12 or the host cell of claim 13 for use in the treatment of a subject

    a. suffering from,
    b. at risk of developing, and/or
    c. being diagnosed for

    a neoplastic disease.

15. The antibody or fragment thereof for the use of claim 14, wherein the neoplastic disease is selected from the group consisting of pancreatic, gastric, esophageal, ovarian and lung cancer.

A IMAB362



B hGBA-1

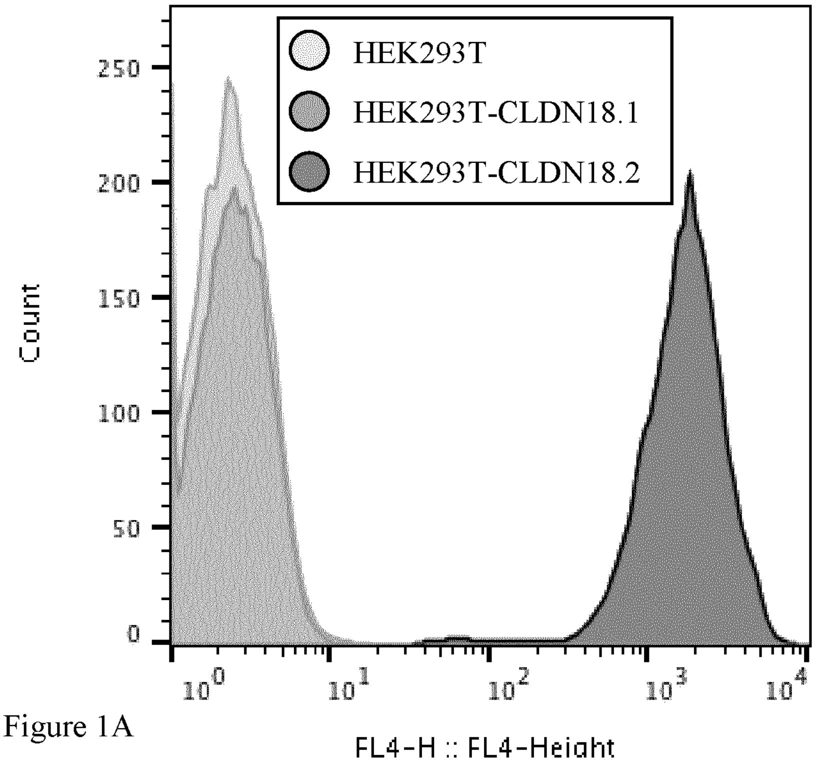
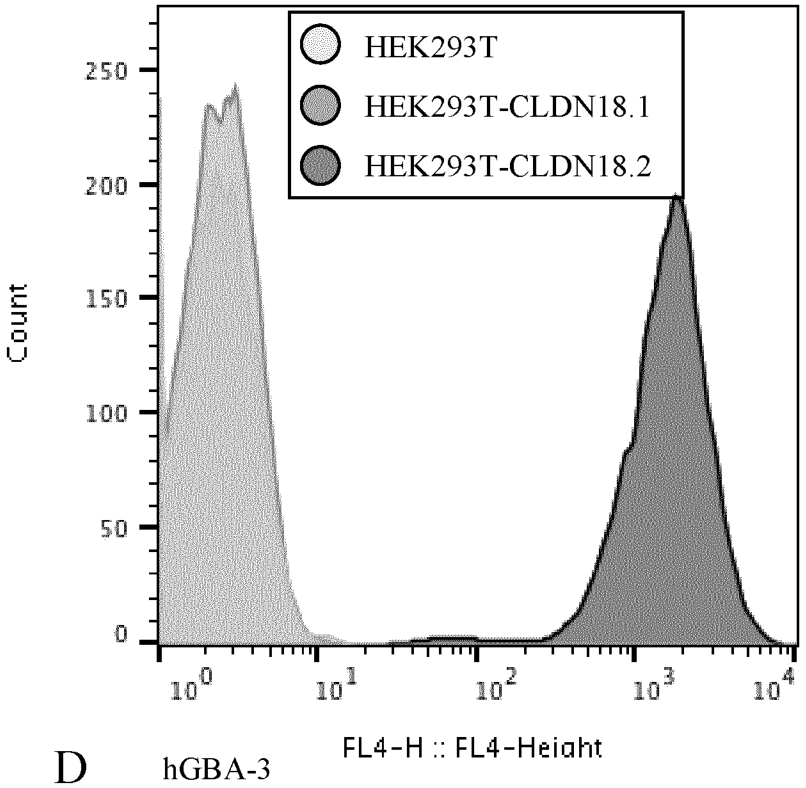


Figure 1A

C hGBA-2



D hGBA-3

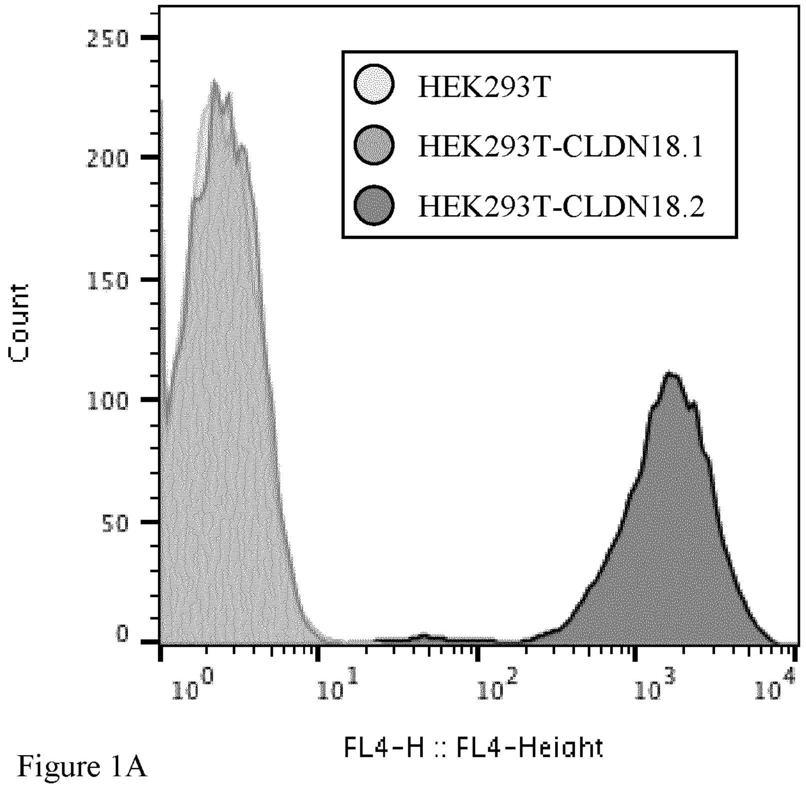


Figure 1A

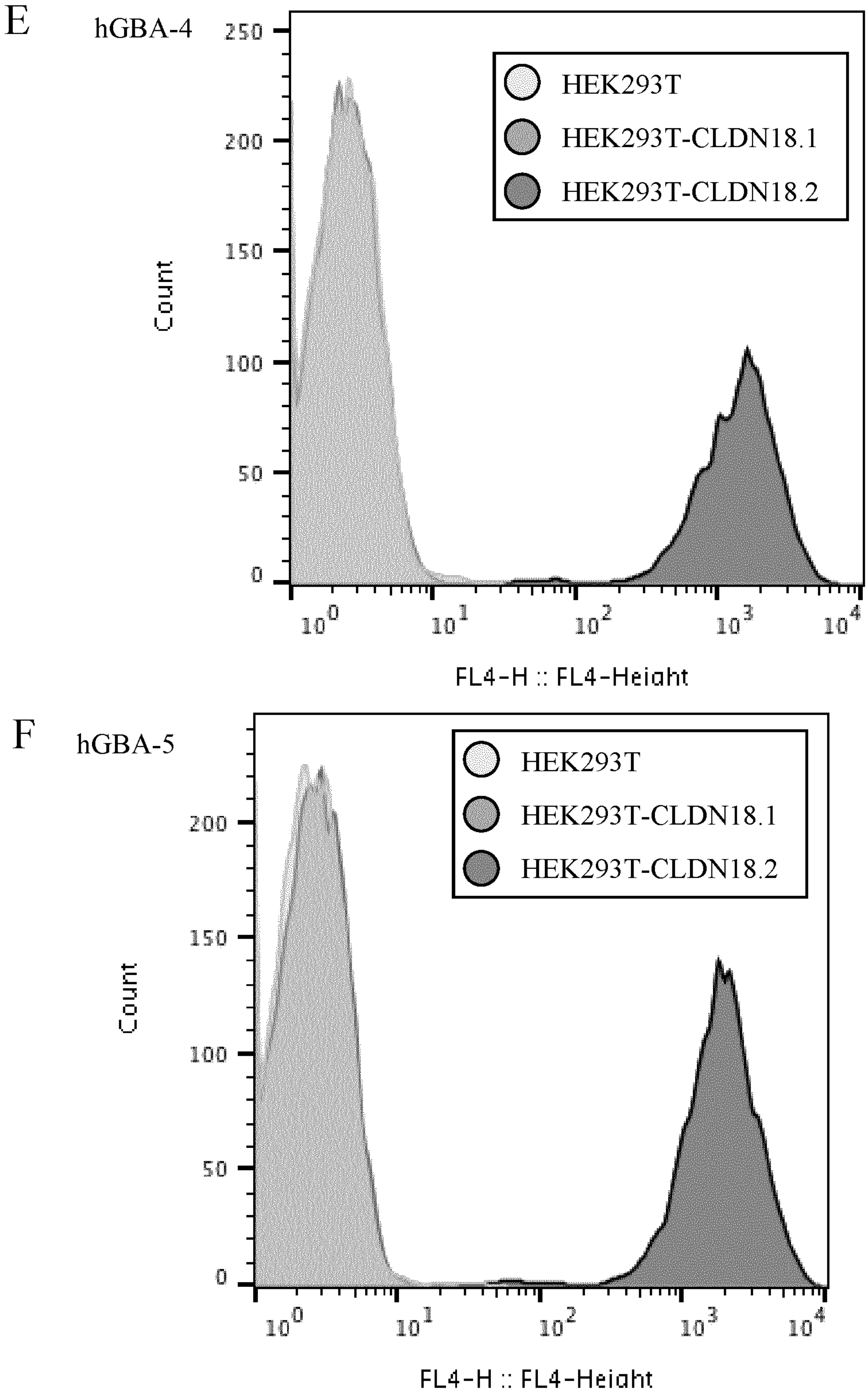
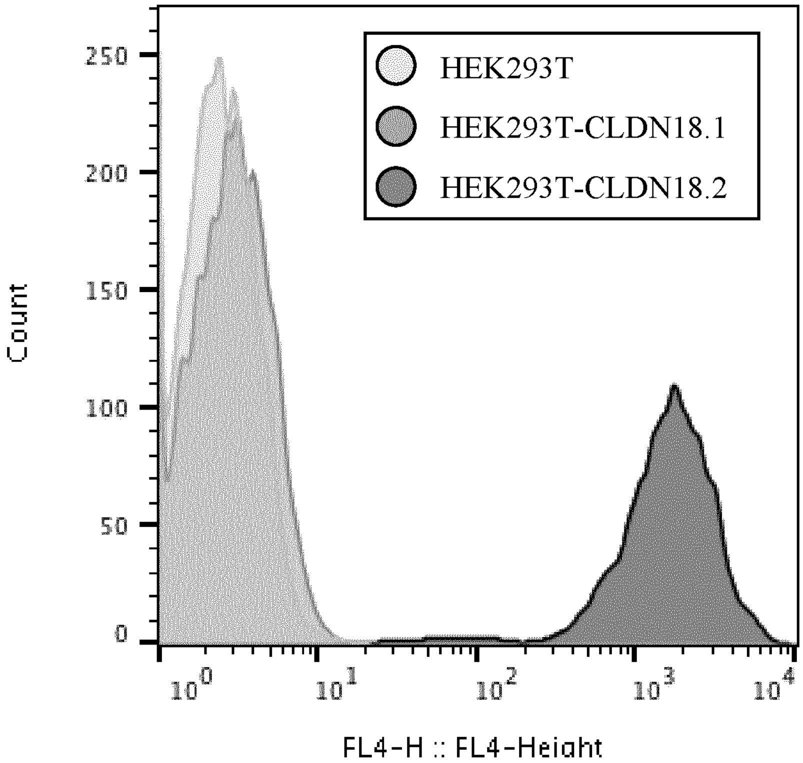

E
hGBA-4
HEK293T
HEK293T-CLDN18.1
HEK293T-CLDN18.2
Count
250
200
150
100
50
0
10^0
10^1
10^2
10^3
10^4
FL4-H :: FL4-Height
F
hGBA-5
HEK293T
HEK293T-CLDN18.1
HEK293T-CLDN18.2
Count
200
150
100
50
0
10^0
10^1
10^2
10^3
10^4
FL4-H :: FL4-Height

Figure 1A

G hGBA-6



H hGBA-7

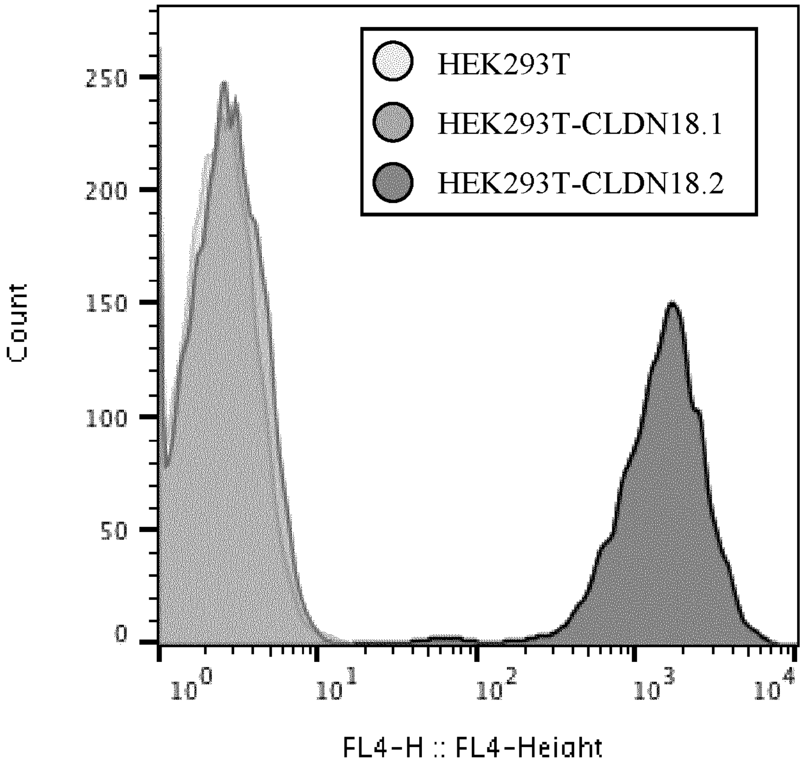
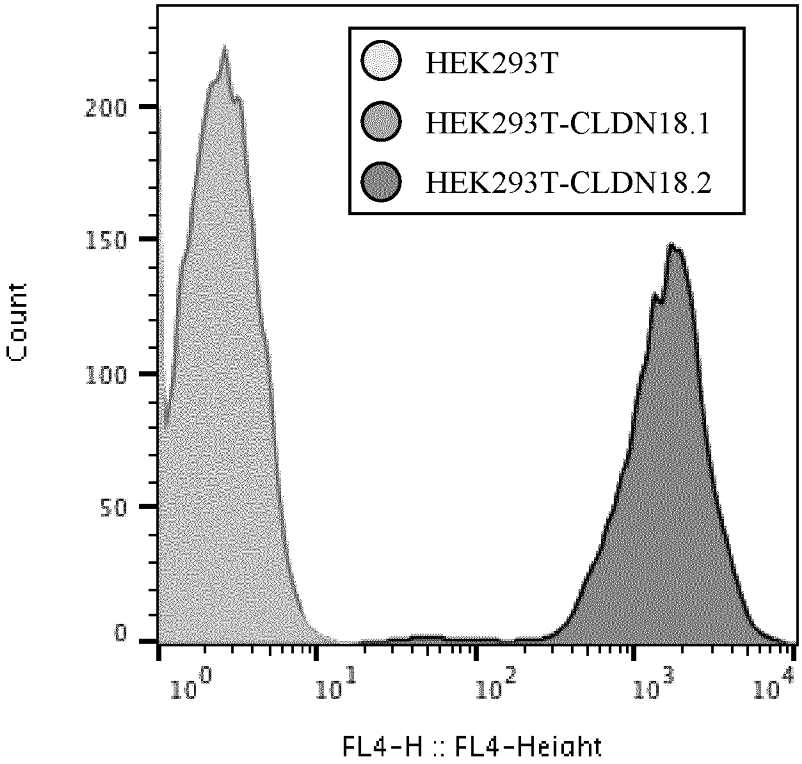


Figure 1A

I hGBA-8



J hGBA-9

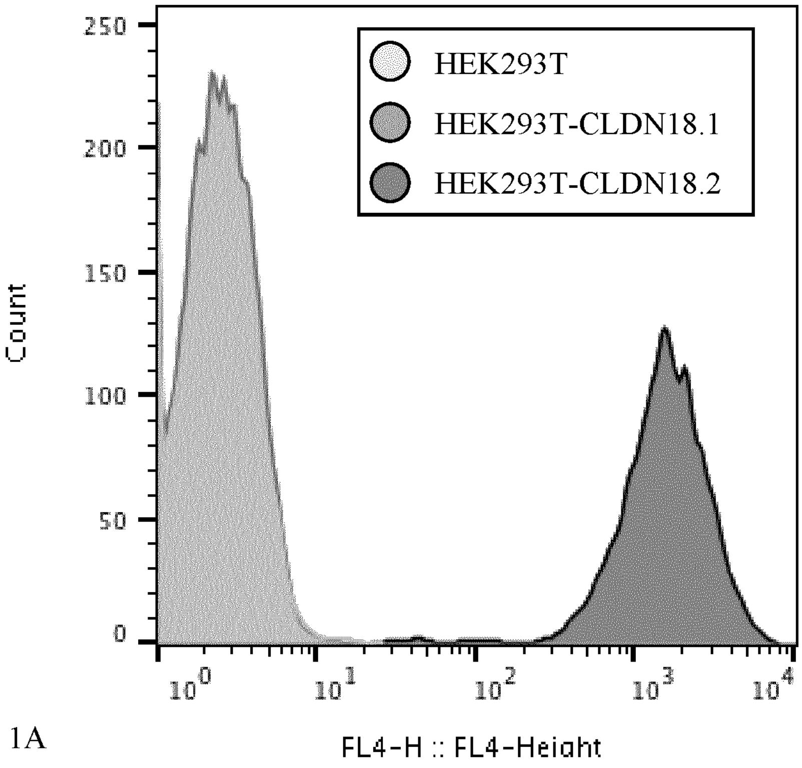
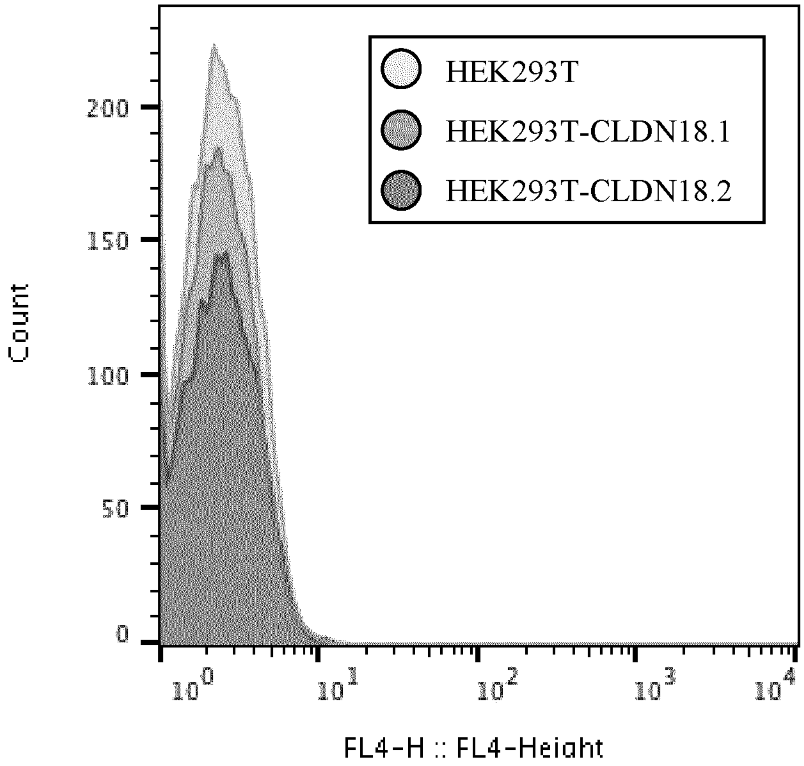


Figure 1A

K secondary only



L pan-CLDN18

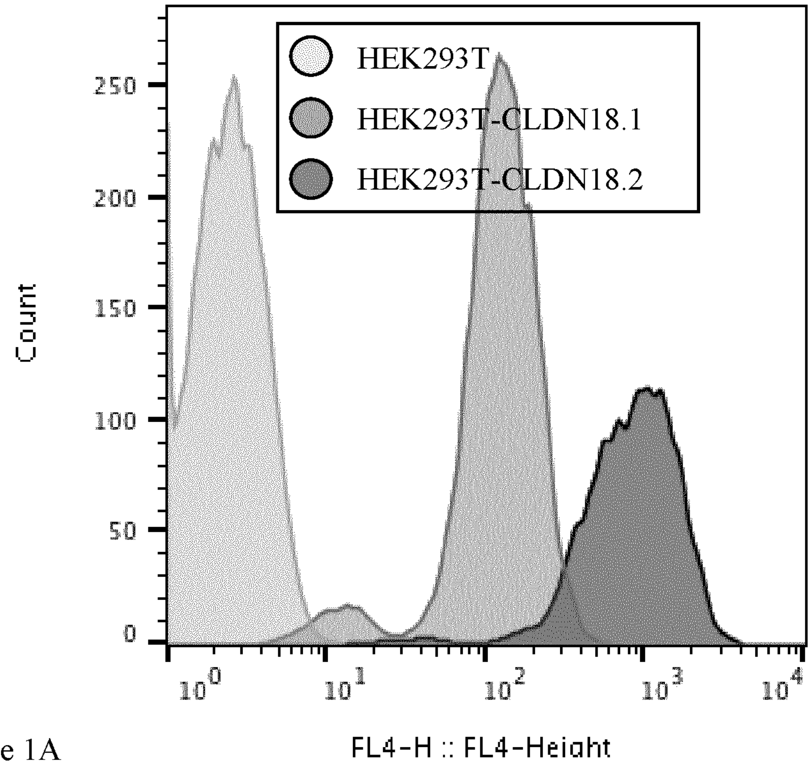


Figure 1A

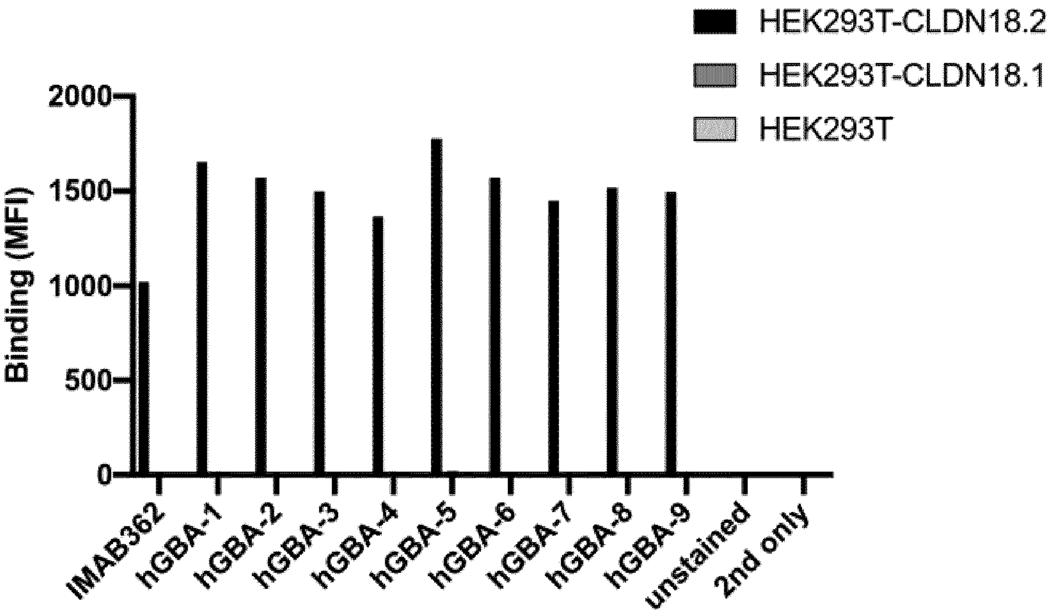

HEK293T-CLDN18.2
HEK293T-CLDN18.1
HEK293T
Binding (MFI)
2000
1500
1000
500
0
IMAB362
hGBA-1
hGBA-2
hGBA-3
hGBA-4
hGBA-5
hGBA-6
hGBA-7
hGBA-8
hGBA-9
unstained
2nd only

Figure 1B

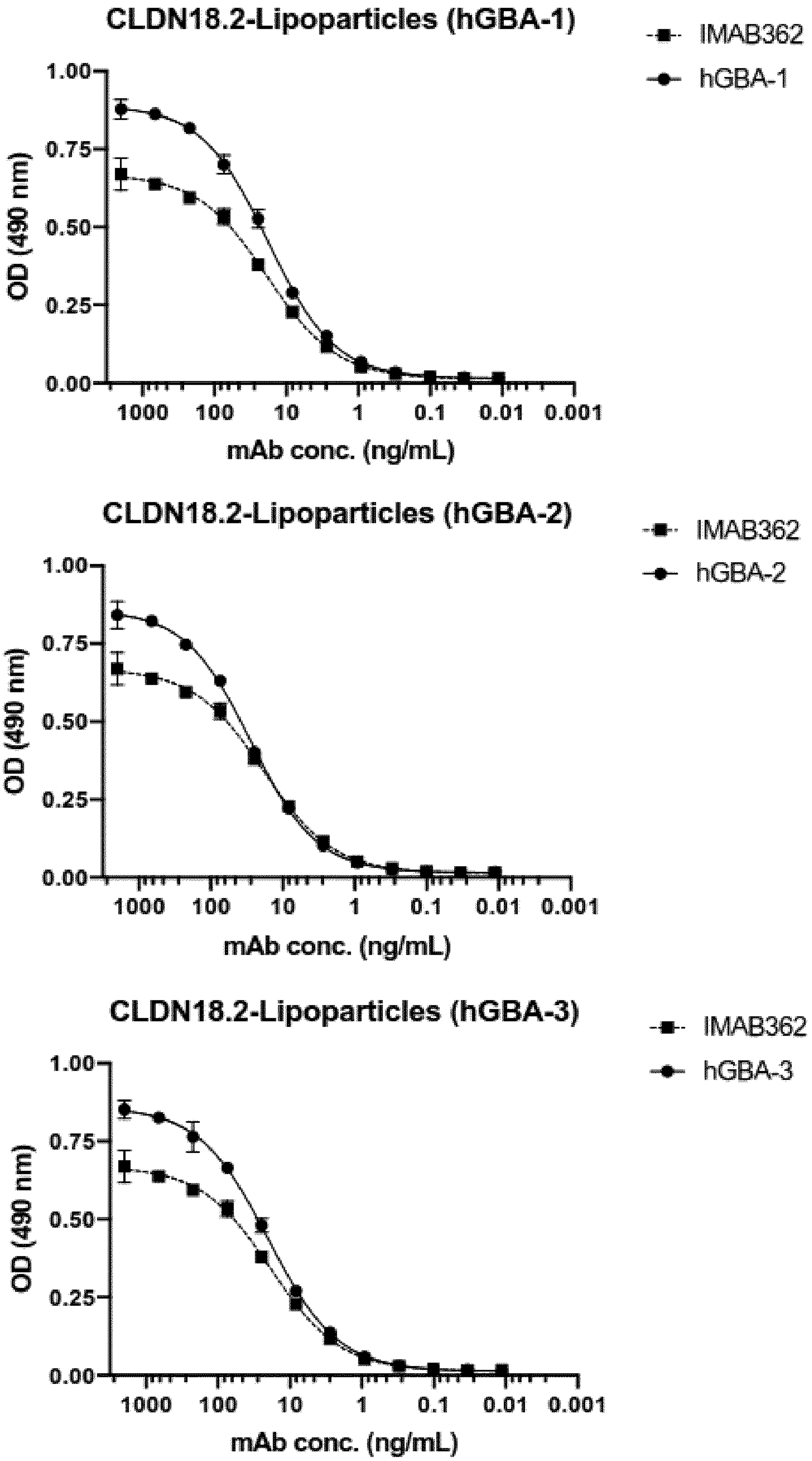

CLDN18.2-Lipoparticles (hGBA-1)
IMAB362
hGBA-1
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)
CLDN18.2-Lipoparticles (hGBA-2)
IMAB362
hGBA-2
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)
CLDN18.2-Lipoparticles (hGBA-3)
IMAB362
hGBA-3
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)

Figure 2A

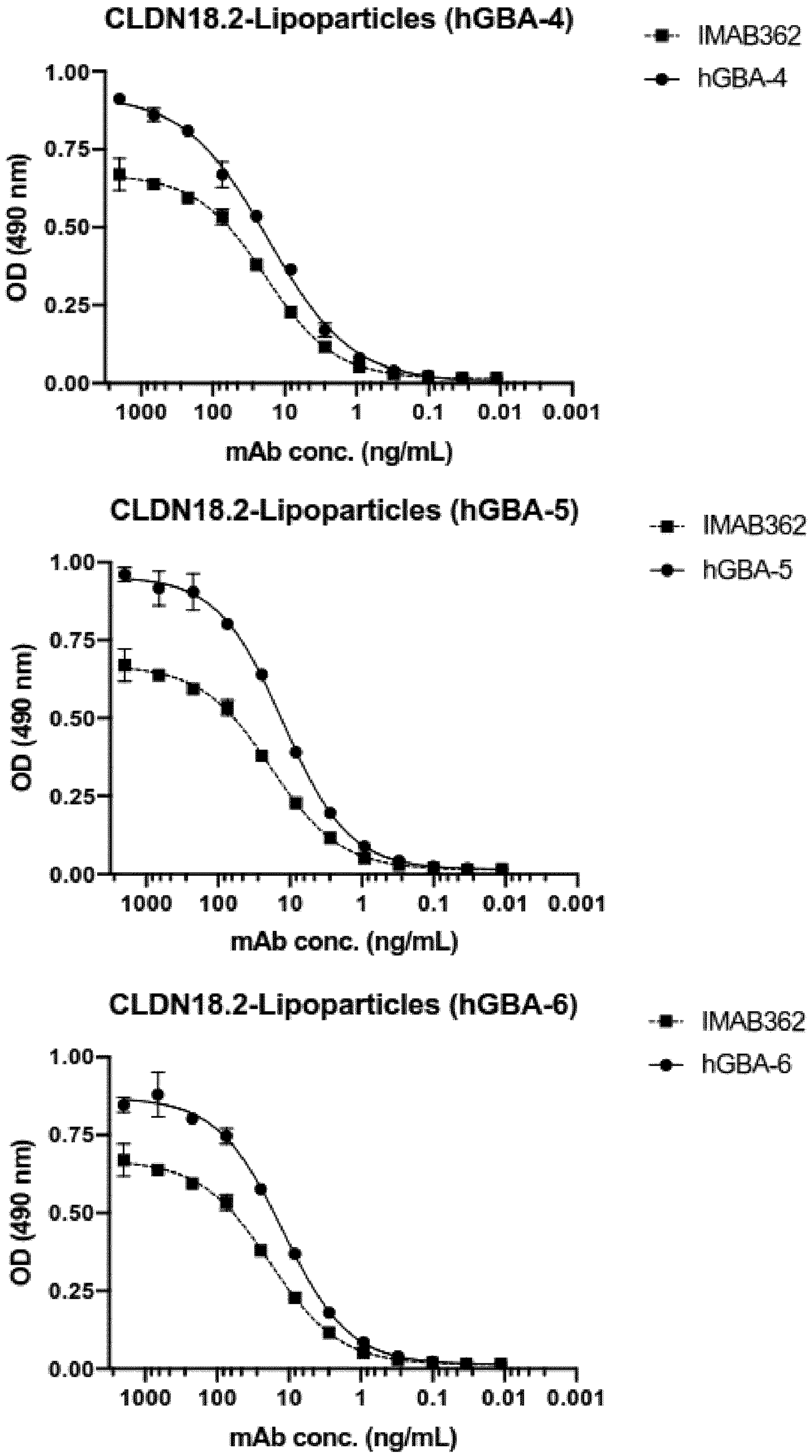

CLDN18.2-Lipoparticles (hGBA-4)
IMAB362
hGBA-4
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)
CLDN18.2-Lipoparticles (hGBA-5)
IMAB362
hGBA-5
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)
CLDN18.2-Lipoparticles (hGBA-6)
IMAB362
hGBA-6
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)

Figure 2B

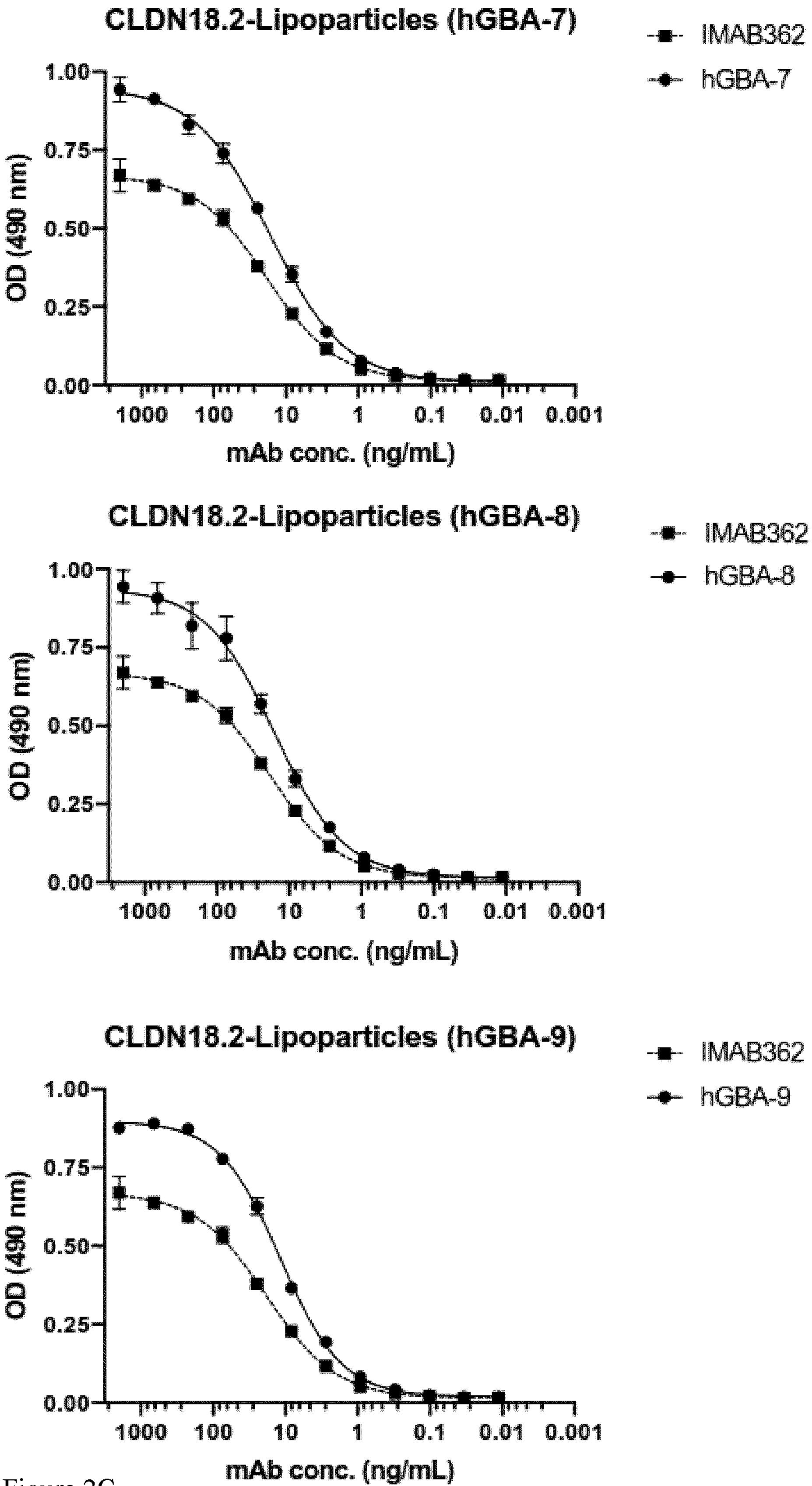

CLDN18.2-Lipoparticles (hGBA-7)
IMAB362
hGBA-7
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)
CLDN18.2-Lipoparticles (hGBA-8)
IMAB362
hGBA-8
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)
CLDN18.2-Lipoparticles (hGBA-9)
IMAB362
hGBA-9
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)

Figure 2C

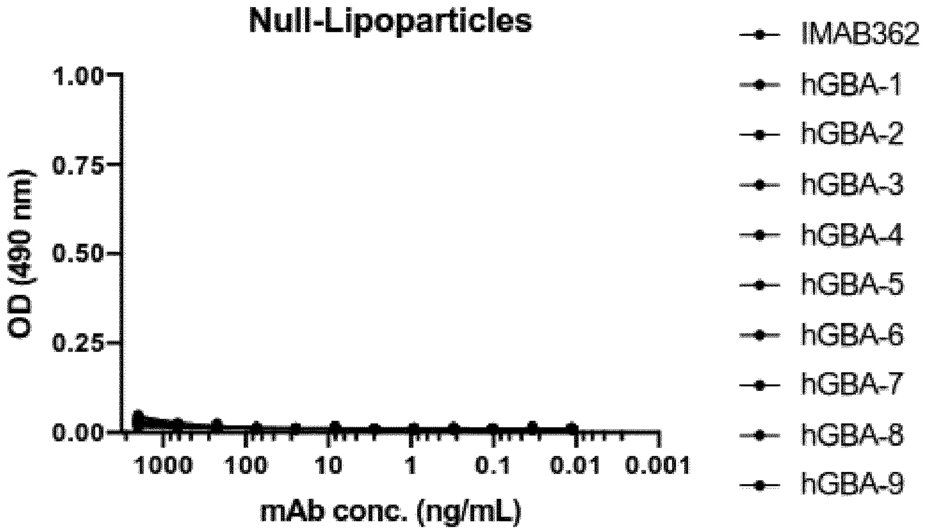

Null-Lipoparticles
OD (490 nm)
1.00
0.75
0.50
0.25
0.00
1000
100
10
1
0.1
0.01
0.001
mAb conc. (ng/mL)
IMAB362
hGBA-1
hGBA-2
hGBA-3
hGBA-4
hGBA-5
hGBA-6
hGBA-7
hGBA-8
hGBA-9

Figure 2D

A

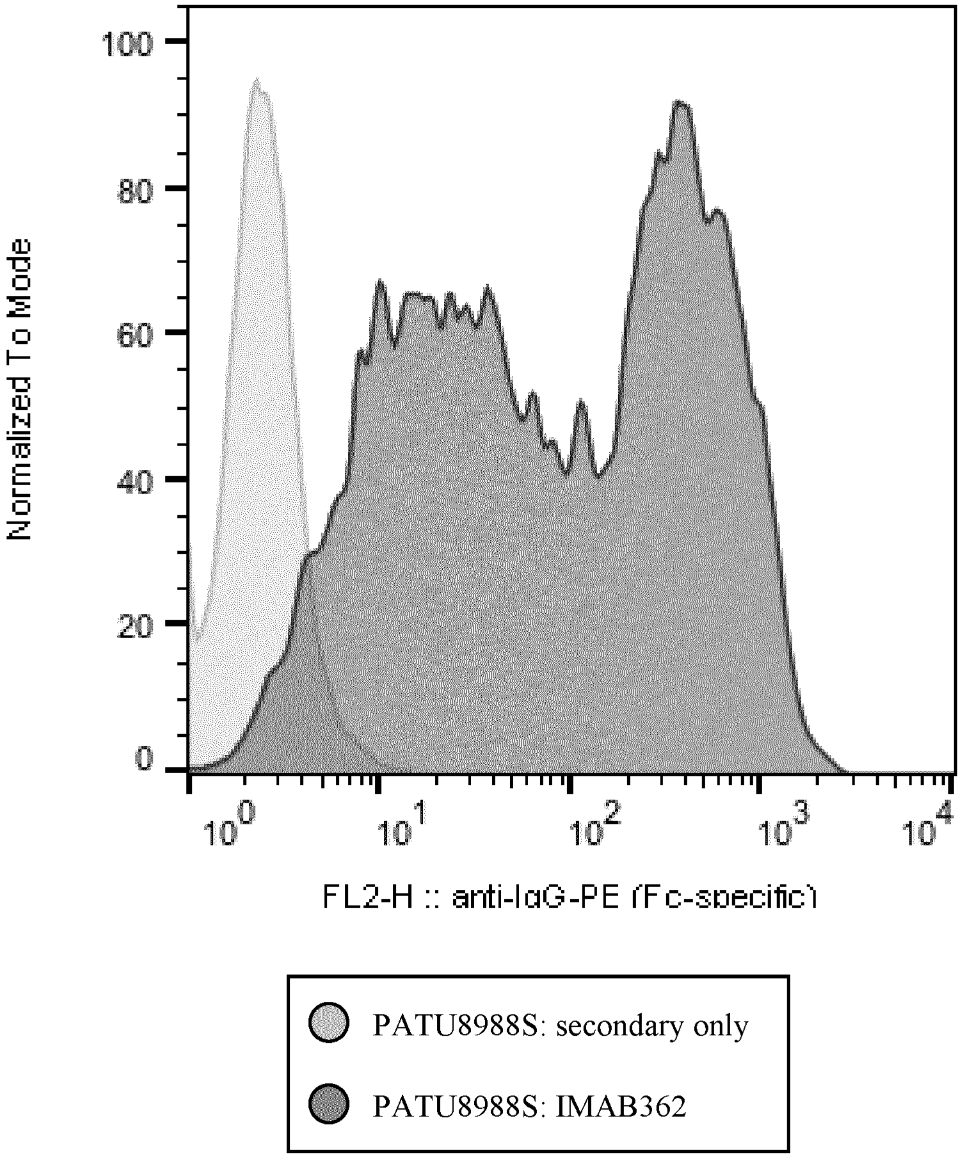
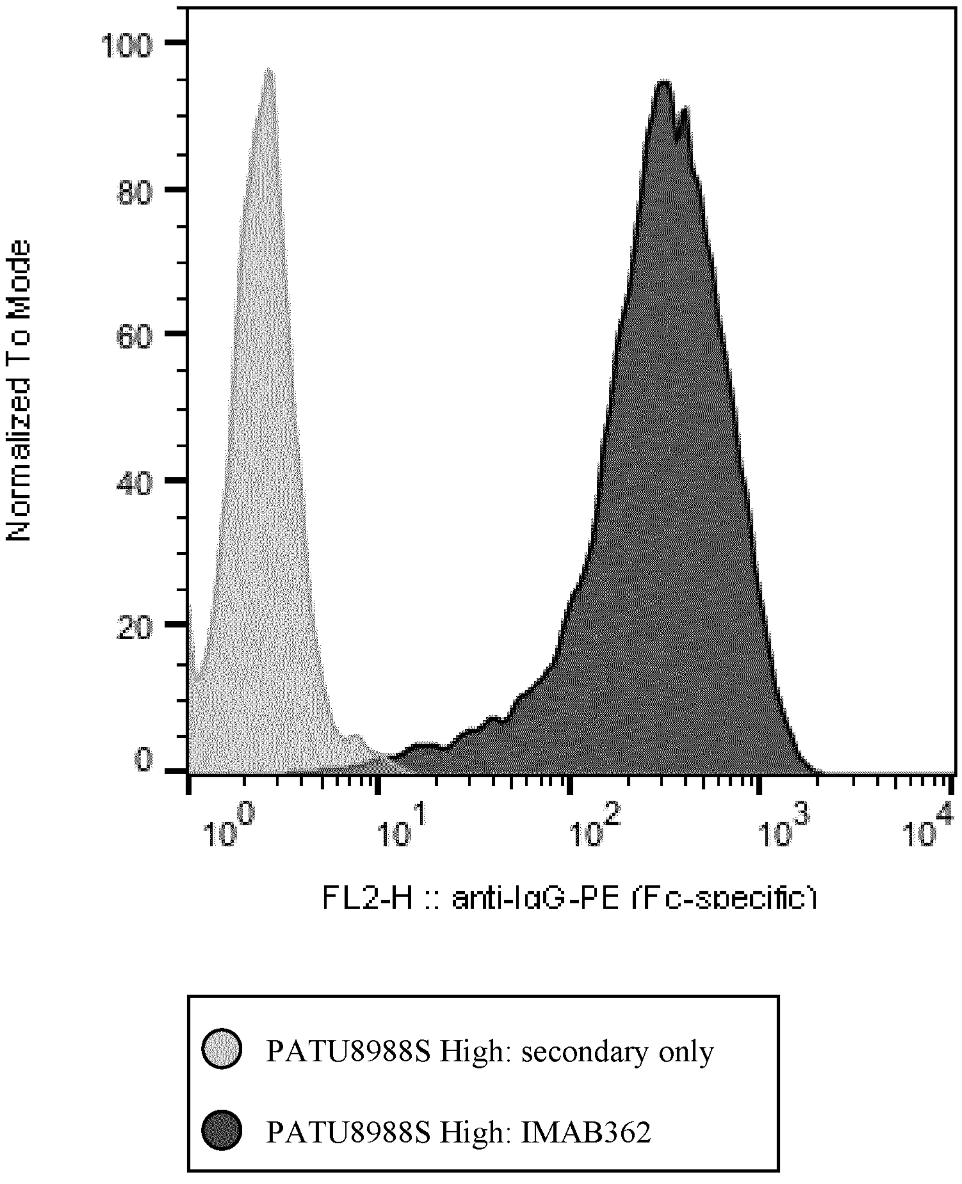

100
80
60
40
20
0
Normalized To Mode
10^0
10^1
10^2
10^3
10^4
FL2-H :: anti-IgG-PE (Fc-specific)
PATU8988S: secondary only
PATU8988S: IMAB362

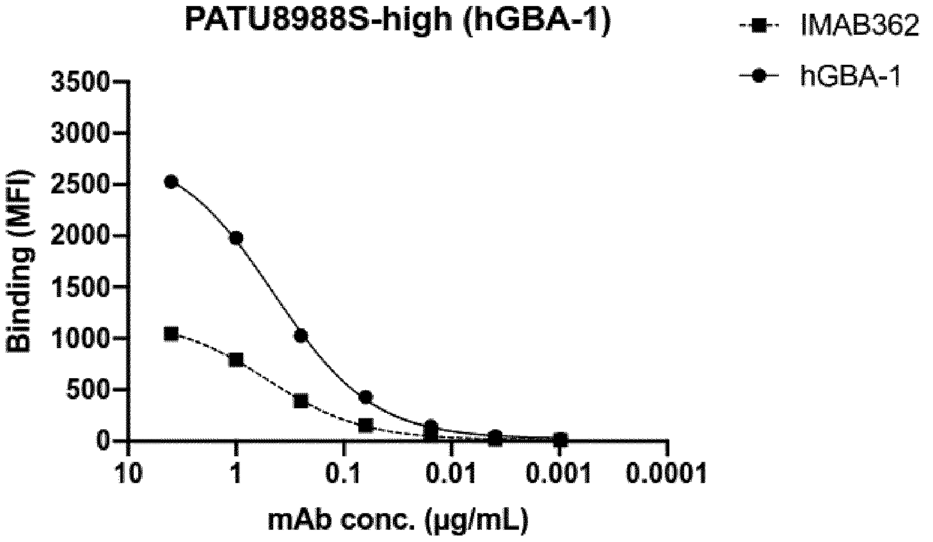
Figure 3A

B



100
80
60
40
20
0
Normalized To Mode
10^0
10^1
10^2
10^3
10^4
FL2-H :: anti-IgG-PE (Fc-specific)
PATU8988S High: secondary only
PATU8988S High: IMAB362

Figure 3B


PATU8988S-high (hGBA-1)
IMAB362
hGBA-1
Binding (MFI)
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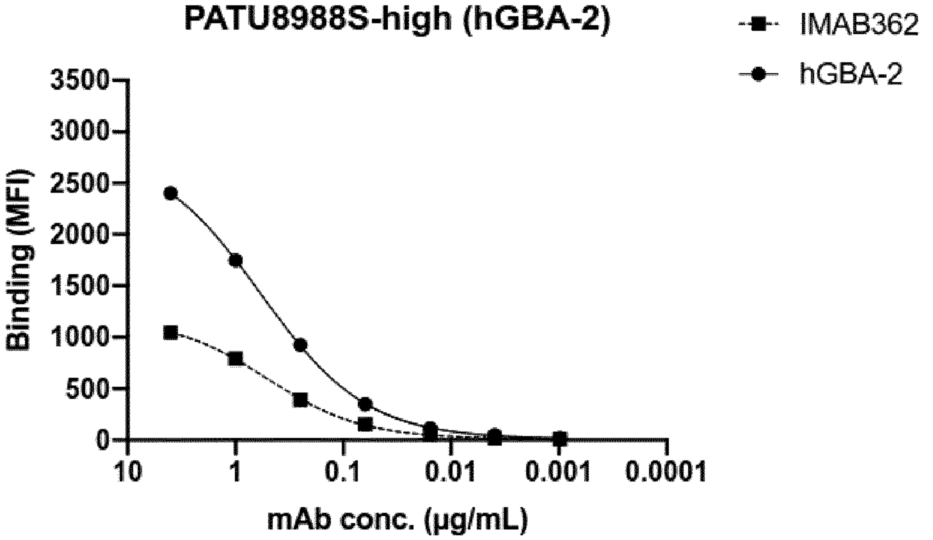
3000
2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)


PATU8988S-high (hGBA-2)
IMAB362
hGBA-2
Binding (MFI)
3500
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2500
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1500
1000
500
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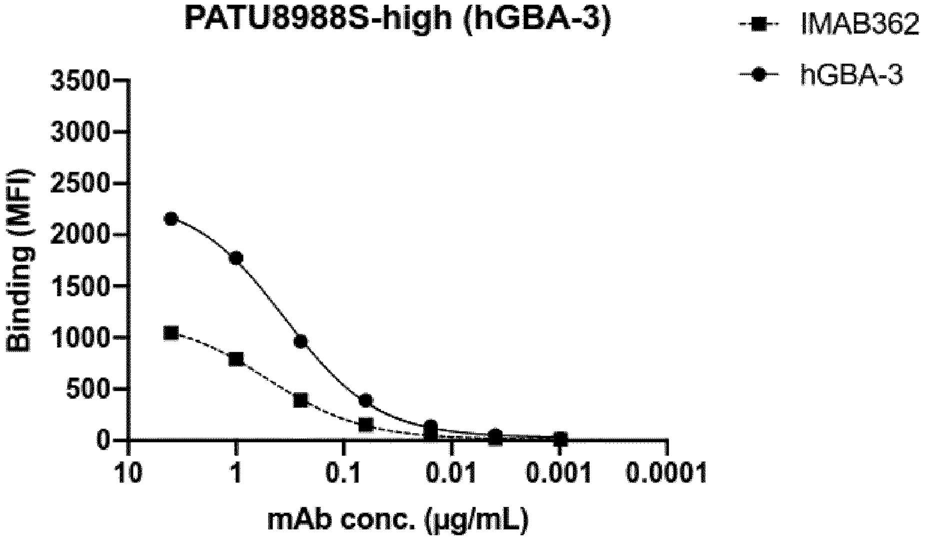
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)


PATU8988S-high (hGBA-3)
IMAB362
hGBA-3
Binding (MFI)
3500
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10
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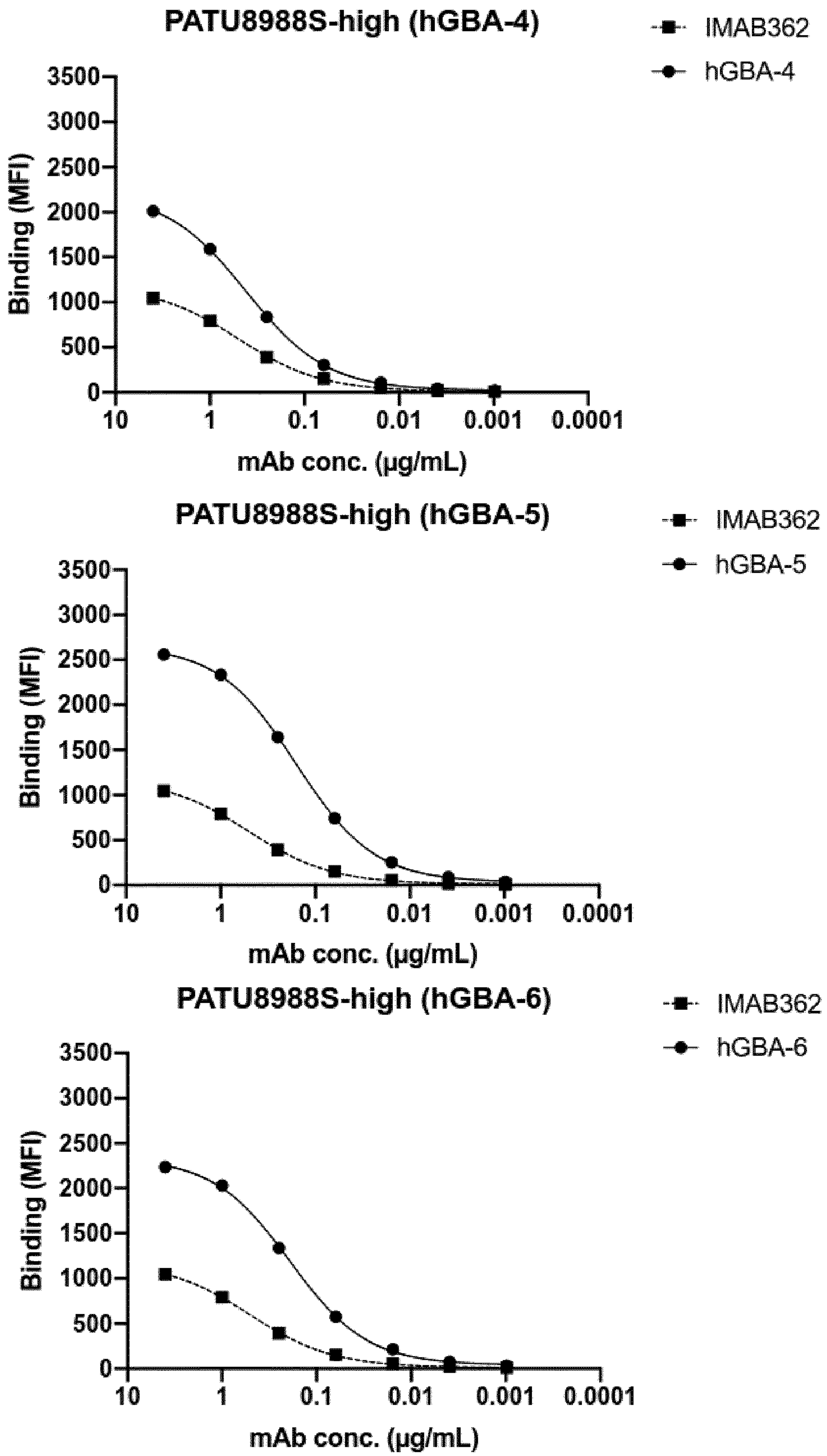
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)

Figure 4A


PATU8988S-high (hGBA-4)
IMAB362
hGBA-4
Binding (MFI)
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2000
1500
1000
500
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10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
PATU8988S-high (hGBA-5)
IMAB362
hGBA-5
Binding (MFI)
3500
3000
2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
PATU8988S-high (hGBA-6)
IMAB362
hGBA-6
Binding (MFI)
3500
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2000
1500
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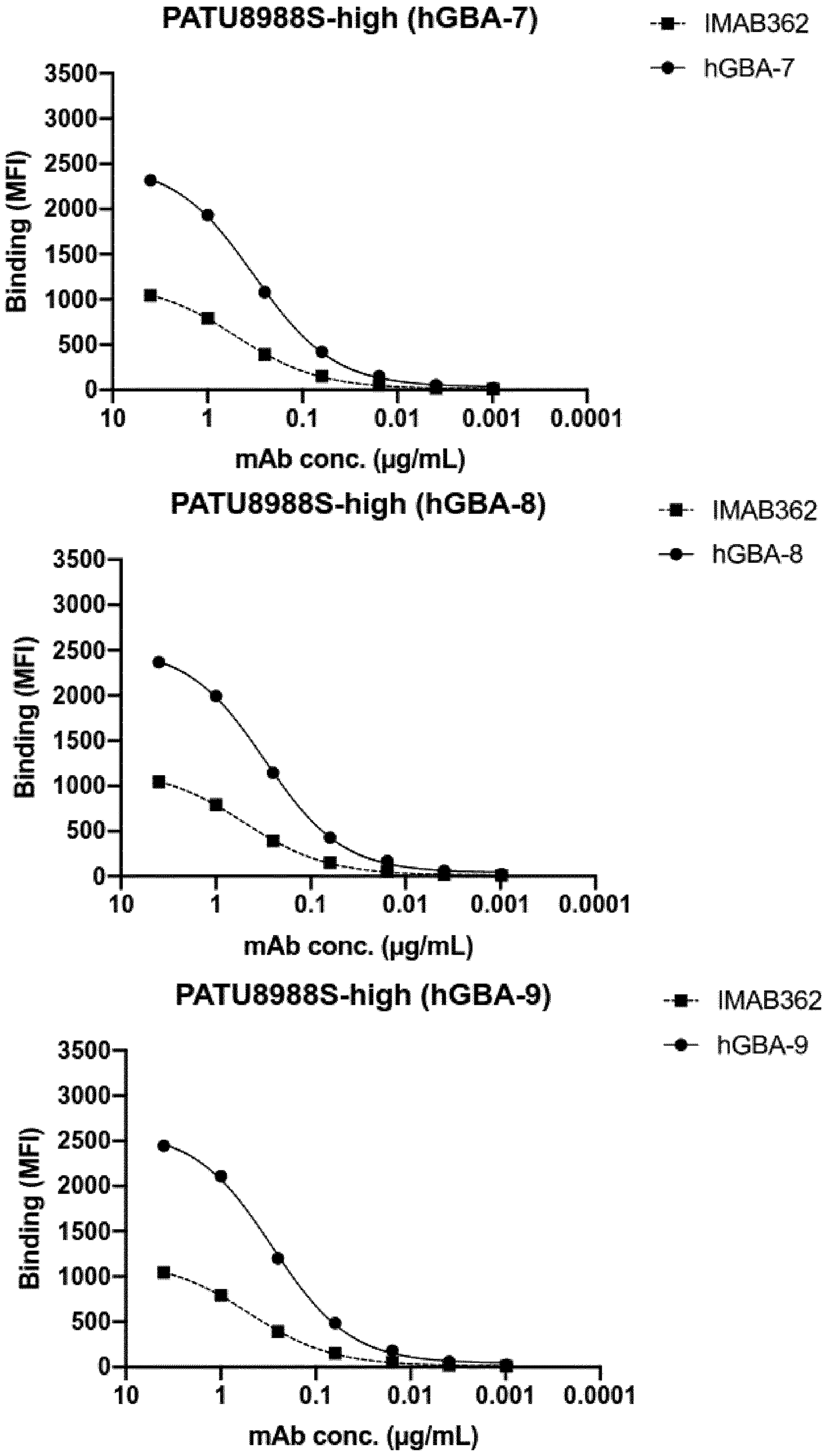
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)

Figure 4B


PATU8988S-high (hGBA-7)
IMAB362
hGBA-7
Binding (MFI)
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1500
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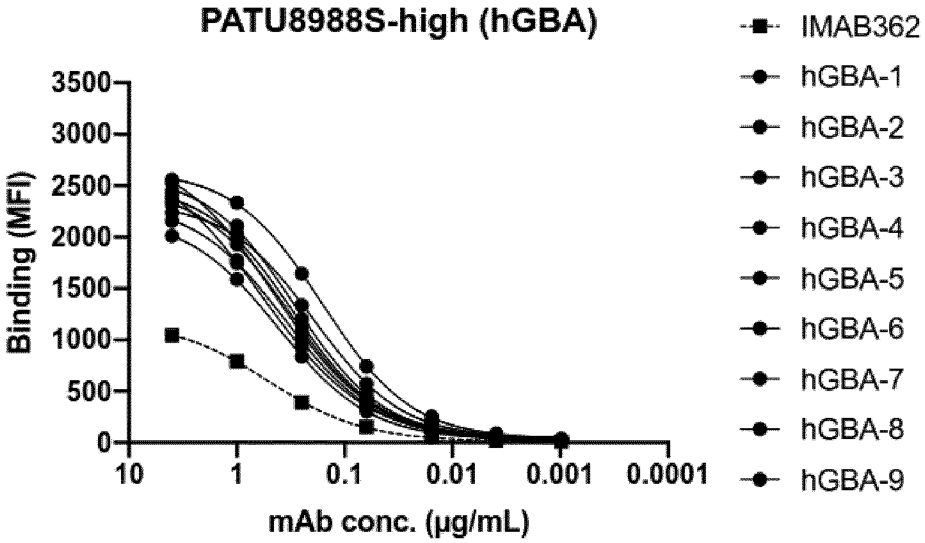
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
PATU8988S-high (hGBA-8)
IMAB362
hGBA-8
Binding (MFI)
mAb conc. (µg/mL)
PATU8988S-high (hGBA-9)
IMAB362
hGBA-9
Binding (MFI)
mAb conc. (µg/mL)

Figure 4C


PATU8988S-high (hGBA)
Binding (MFI)
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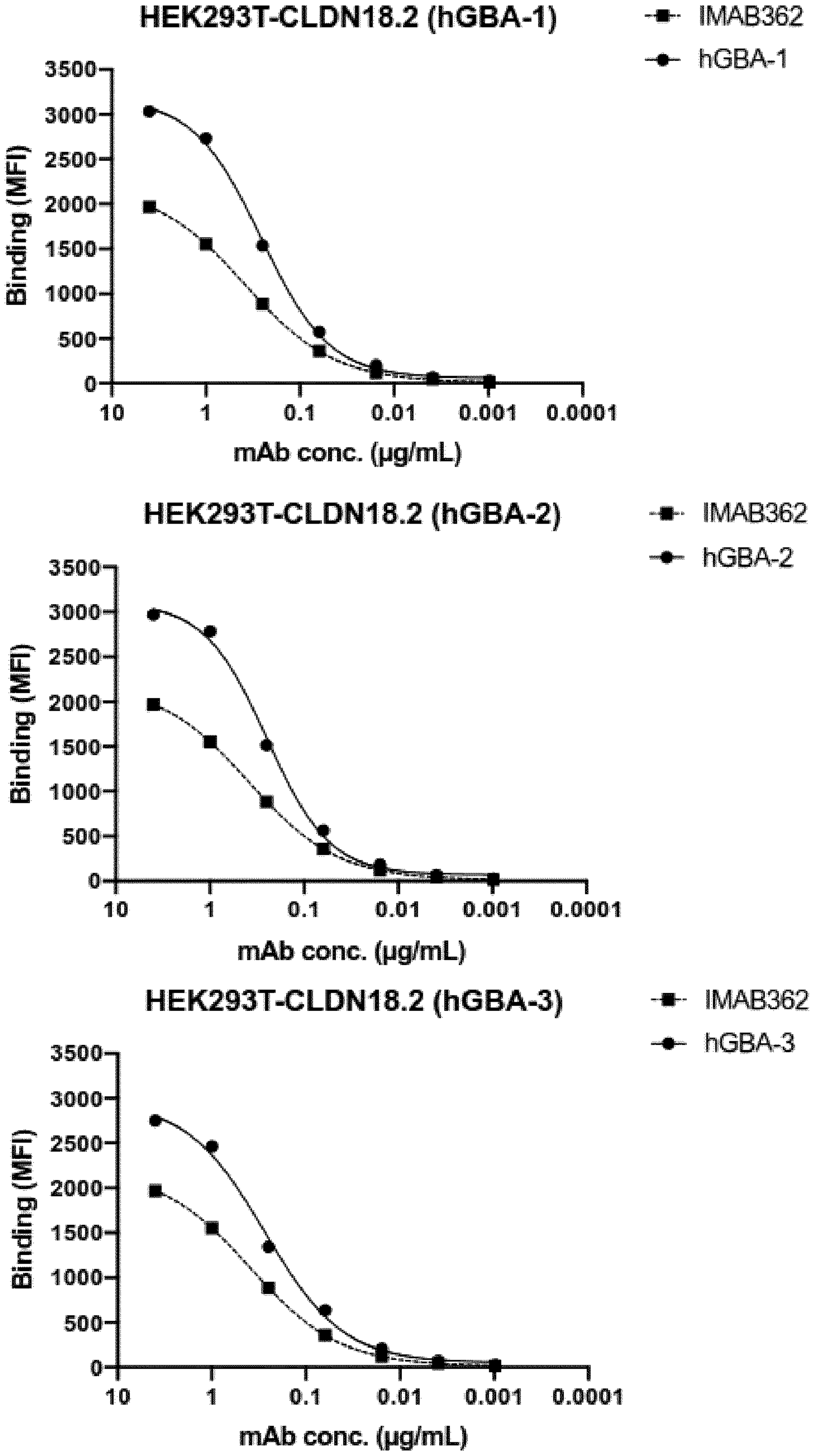
3000
2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
IMAB362
hGBA-1
hGBA-2
hGBA-3
hGBA-4
hGBA-5
hGBA-6
hGBA-7
hGBA-8
hGBA-9

Figure 4D


HEK293T-CLDN18.2 (hGBA-1)
IMAB362
hGBA-1
Binding (MFI)
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2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
HEK293T-CLDN18.2 (hGBA-2)
IMAB362
hGBA-2
Binding (MFI)
3500
3000
2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
HEK293T-CLDN18.2 (hGBA-3)
IMAB362
hGBA-3
Binding (MFI)
3500
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500
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10
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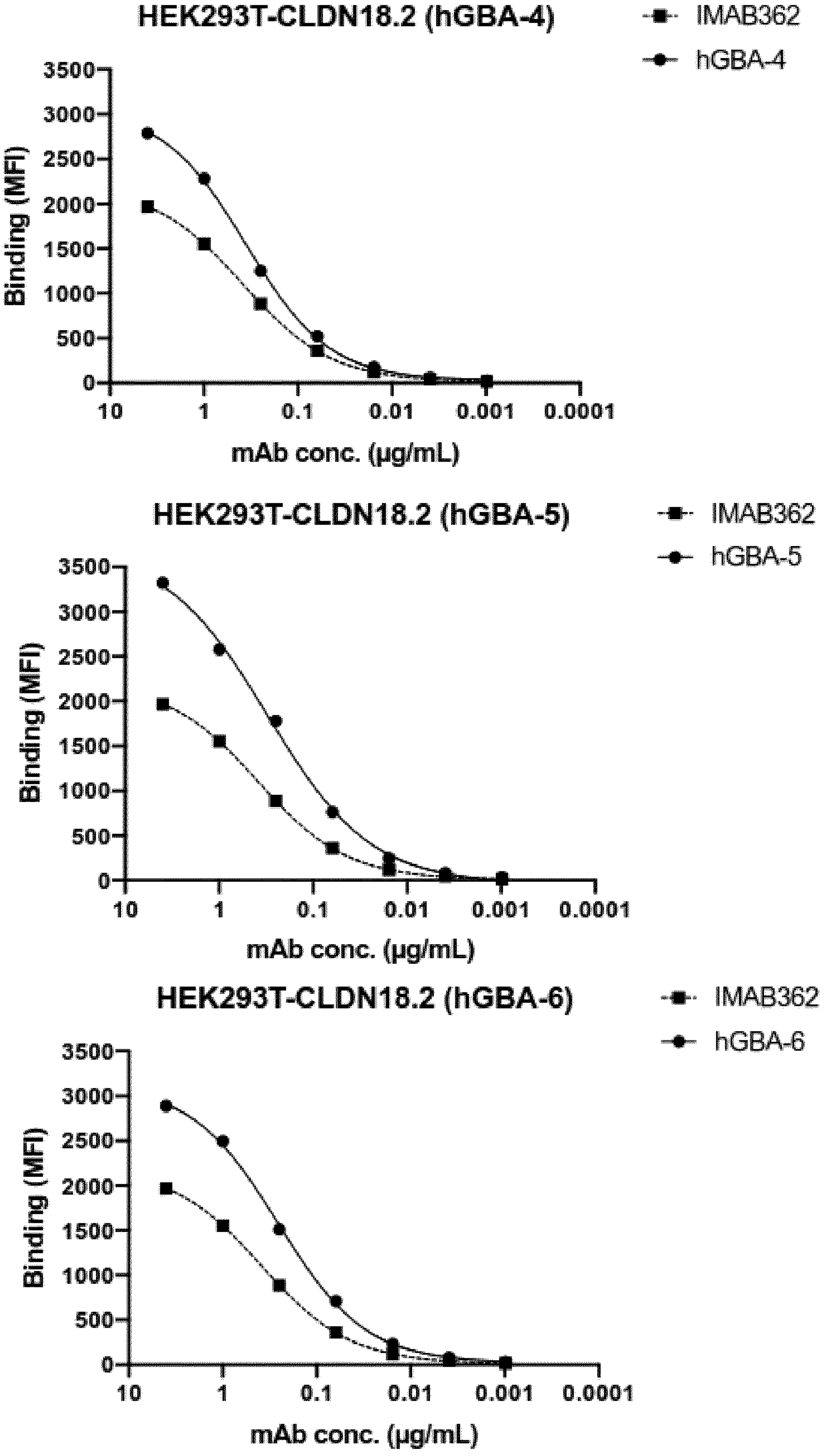
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)

Figure 4E


HEK293T-CLDN18.2 (hGBA-4)
IMAB362
hGBA-4
Binding (MFI)
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2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
HEK293T-CLDN18.2 (hGBA-5)
IMAB362
hGBA-5
Binding (MFI)
3500
3000
2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)
HEK293T-CLDN18.2 (hGBA-6)
IMAB362
hGBA-6
Binding (MFI)
3500
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2500
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500
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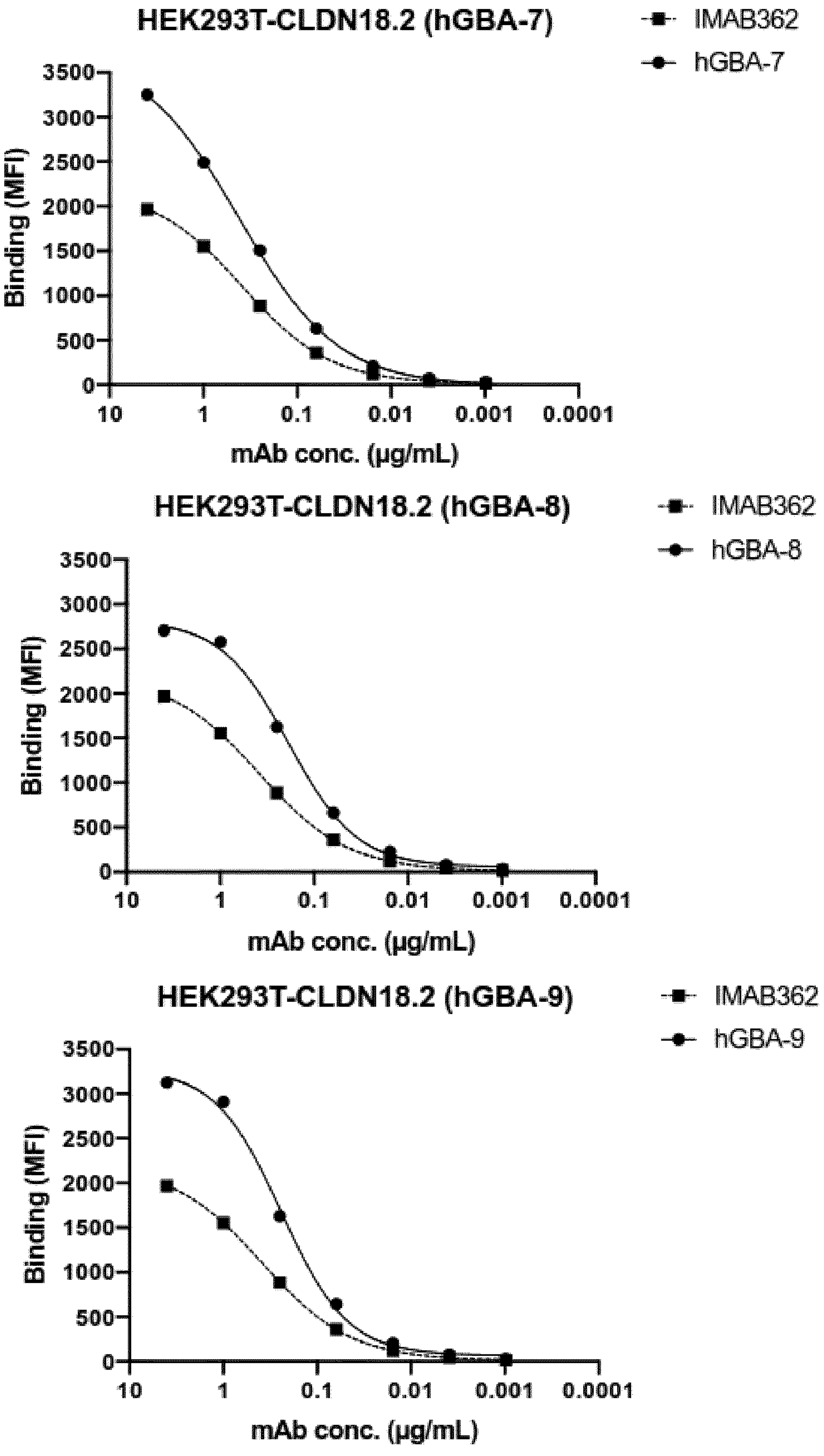
10
1
0.1
0.01
0.001
0.0001
mAb conc. (µg/mL)

Figure 4F


HEK293T-CLDN18.2 (hGBA-7)
IMAB362
hGBA-7
Binding (MFI)
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2000
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1000
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10
1
0.1
0.01
0.001
0.0001
mAb conc. (μg/mL)
HEK293T-CLDN18.2 (hGBA-8)
IMAB362
hGBA-8
Binding (MFI)
3500
3000
2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (μg/mL)
HEK293T-CLDN18.2 (hGBA-9)
IMAB362
hGBA-9
Binding (MFI)
3500
3000
2500
2000
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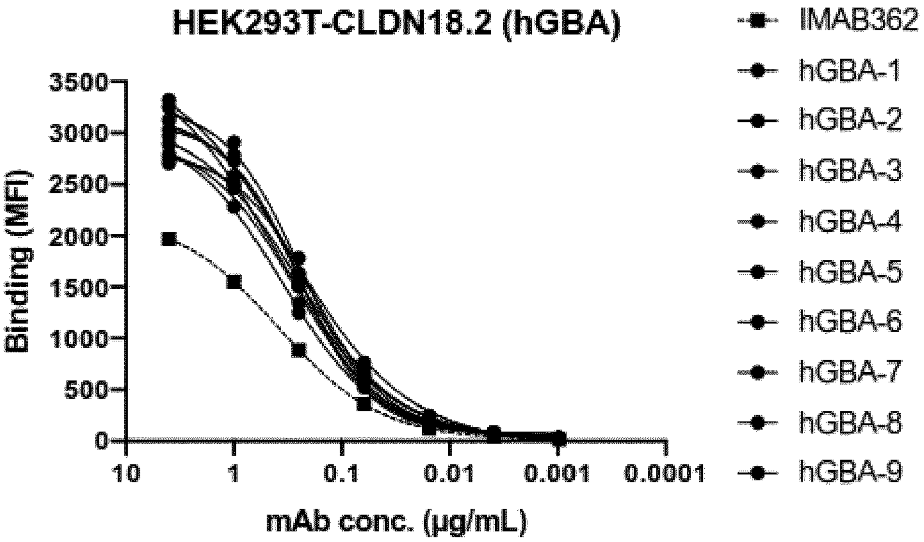
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (μg/mL)

Figure 4G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Binding (MFI)
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2500
2000
1500
1000
500
0
10
1
0.1
0.01
0.001
0.0001
mAb conc. (μg/mL)
IMAB362
hGBA-1
hGBA-2
hGBA-3
hGBA-4
hGBA-5
hGBA-6
hGBA-7
hGBA-8
hGBA-9

Figure 4H

```
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<110>  SOTIO a.s.

<120>  Humanized CLDN18.2 antibodies

<130>  S12415WO / SOTCLD-1903WO

<150>  EP 19 214 104.2
<151>  2019-12-06

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<170>  PatentIn version 3.5

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<223>  T or S

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<223>  S or G

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<223>  A, E or D

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<223>  A or S

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<223>  Y or D
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<223>  N or R

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<400>  2

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<210>  3
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<223>  HCDR3 Consensus Sequence


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<220>
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<223>  L, M, I or Q

<220>
<221>  MISC_FEATURE
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<400>  3

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1               5                   10


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<220>
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<223>  L or V

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<400>  4

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Xaa

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<223> LCDR3 Consensus Sequence

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> N or Q

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> L or F

<400> 6

Gln Xaa Asp Tyr Ser Tyr Pro Xaa Thr
1   5

<210> 7
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-1, hGBA-2, hGBA-3, hGBA-4, hGBA-5, hGBA-7, hGBA-8 HCDR1
       Sequence

<400> 7

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

<210> 8
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-6, hGBA-9 HCDR1 Sequence

```
<400>  8

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


<210>  9
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-1 HCDR2 Sequence

<400>  9

Gly Asn Ile Tyr Pro Gly Ala Ser Asp Thr Arg Tyr Ala
1               5                   10


<210>  10
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-2 HCDR2 Sequence

<400>  10

Gly Asn Ile Tyr Pro Gly Asp Ala Asp Thr Arg Tyr Ala
1               5                   10


<210>  11
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-3 HCDR2 Sequence

<400>  11

Gly Ile Ile Tyr Pro Gly Ala Ser Asp Thr Asn Tyr Ala
1               5                   10


<210>  12
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-4 HCDR2 Sequence

<400>  12

Gly Ile Ile Tyr Pro Gly Asp Ala Tyr Thr Arg Tyr Ser
1               5                   10


<210>  13
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-5 HCDR2 Sequence
```

```
<400>  13

Gly Ile Ile Tyr Pro Gly Ala Ala Tyr Thr Arg Tyr Ala
1               5                   10


<210>  14
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-6 HCDR2 Sequence

<400>  14

Gly Asn Ile Tyr Pro Gly Ala Ser Tyr Thr Arg Tyr Ser
1               5                   10


<210>  15
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-7 HCDR2 Sequence

<400>  15

Gly Asn Ile Tyr Pro Gly Glu Ala Tyr Thr Arg Tyr Ser
1               5                   10


<210>  16
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-8 HCDR1 Sequence

<400>  16

Gly Asn Ile Tyr Pro Ser Glu Ser Tyr Thr Asn Tyr Ala
1               5                   10


<210>  17
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-9 HCDR2 Sequence

<400>  17

Gly Ile Ile Tyr Pro Ser Ala Ala Tyr Thr Arg Tyr Ala
1               5                   10


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

<220>
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```
<223>  hGBA-1, hGBA-5 HCDR3 Sequence

<400>  18

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


<210>  19
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-2 HCDR3 Sequence

<400>  19

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


<210>  20
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-3 HCDR3 Sequence

<400>  20

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


<210>  21
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-4 HCDR3 Sequence

<400>  21

Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Ala
1               5                   10


<210>  22
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-6 HCDR3 Sequence

<400>  22

Thr Arg Gln Trp Arg Gly Asn Ser Phe Asp Tyr
1               5                   10


<210>  23
<211>  11
<212>  PRT
<213>  Artificial Sequence
```

<220>
<223> hGBA-7, hGBA-8 HCDR3 Sequence

<400> 23

Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr
1   5   10

<210> 24
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-9 HCDR3 Sequence

<400> 24

Thr Arg Met Trp Arg Gly Asn Ser Phe Asp Tyr
1   5   10

<210> 25
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-1, hGBA-3, hGBA-5, hGBA-6, hGBA-8 LCDR1 Sequence

<400> 25

Lys Ser Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
1   5   10   15

Ala

<210> 26
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-4 LCDR1 Sequence

<400> 26

Lys Ser Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
1   5   10   15

Thr

<210> 27
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-7 LCDR1 Sequence

<400> 27

Lys Ser Ser Gln Ser Val Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
1   5   10   15

Thr

<210> 28
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-9 LCDR1 Sequence

<400> 28

Lys Ser Ser Gln Ser Val Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
1   5   10   15

Ala

<210> 29
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-1, hGBA-3, hGBA-6, hGBA-7, hGBA-8 LCDR3 Sequence

<400> 29

Gln Asn Asp Tyr Ser Tyr Pro Phe Thr
1   5

<210> 30
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-4 LCDR3 Sequence

<400> 30

Gln Asn Asp Tyr Ser Tyr Pro Leu Thr
1   5

<210> 31
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-5, hGBA-9 LCDR3 Sequence

<400> 31

Gln Gln Asp Tyr Ser Tyr Pro Phe Thr
1   5

<210> 32

<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-1 VH Sequence

<400> 32

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20   25   30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45

Gly Asn Ile Tyr Pro Gly Ala Ser Asp Thr Arg Tyr Ala Pro Ser Phe
    50   55   60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65   70   75   80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85   90   95

Ala Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 33
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-1, hGBA-2, hGBA-6 , hGBA-8 VL Sequence

<400> 33

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

```
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85                  90                  95


Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110


Lys




<210>  34
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-2 VH Sequence

<400>  34

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Asn Ile Tyr Pro Gly Asp Ala Asp Thr Arg Tyr Ala Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Met Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  35
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-3 VH Sequence

<400>  35

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

```
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Tyr Pro Gly Ala Ser Asp Thr Asn Tyr Ala Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Ile Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  36
<211>  113
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-3 VL Sequence

<400>  36

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85                  90                  95


Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110


Lys
```

```
<210>  37
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-4 VH Sequence

<400>  37

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Tyr Pro Gly Asp Ala Tyr Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Ala Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  38
<211>  113
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-4 VL Sequence

<400>  38

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60
```

```
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85                  90                  95


Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110


Lys



<210>  39
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-5 VH Sequence

<400>  39

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Tyr Pro Gly Ala Ala Tyr Thr Arg Tyr Ala Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  40
<211>  113
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-5 VL Sequence

<400>  40
```

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
                85   90   95

Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100   105   110

Lys

<210> 41
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-6 VH Sequence

<400> 41

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45

Gly Asn Ile Tyr Pro Gly Ala Ser Tyr Thr Arg Tyr Ser Pro Ser Phe
    50   55   60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65   70   75   80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85   90   95

Thr Arg Gln Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 42
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-7 VH Sequence

<400> 42

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20   25   30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45

Gly Asn Ile Tyr Pro Gly Glu Ala Tyr Thr Arg Tyr Ser Pro Ser Phe
    50   55   60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65   70   75   80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85   90   95

Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 43
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-7 VL Sequence

<400> 43

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85   90   95

Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100   105   110

Lys

<210> 44
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-8 VH Sequence

<400> 44

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20   25   30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45

Gly Asn Ile Tyr Pro Ser Glu Ser Tyr Thr Asn Tyr Ala Pro Ser Phe
    50   55   60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65   70   75   80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85   90   95

Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 45
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-9 VH Sequence

```
<400>  45

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Tyr Pro Ser Ala Ala Tyr Thr Arg Tyr Ala Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Thr Arg Met Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210>  46
<211>  113
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-9 VL Sequence

<400>  46

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asn Ser
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
                85                  90                  95
```

```
Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110

Lys


<210>  47
<211>  448
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  IMAB362 HC full

<400>  47

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Arg Pro Gly Ala
1               5                   10                  15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Ile Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Asn Ile Tyr Pro Ser Asp Ser Tyr Thr Asn Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

Thr Arg Ser Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

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

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

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

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

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

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

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


His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240


Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255


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


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


Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300


Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320


Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335


Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350


Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365


Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380


Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400


Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415


Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430


Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210>  48
<211>  220
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  IMAB362 Light Chain full
```

```
<400>  48

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1               5                   10                  15


Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
                85                  90                  95


Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile
            100                 105                 110


Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115                 120                 125


Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130                 135                 140


Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145                 150                 155                 160


Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175


Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190


Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205


Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220


<210>  49
<211>  448
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-1 Heavy Chain Sequence

<400>  49

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
```

```
1               5                   10                  15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Asn Ile Tyr Pro Gly Ala Ser Asp Thr Arg Tyr Ala Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

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

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

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

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

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

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

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
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Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210>  50
<211>  220
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-1, hGBA-2, hGBA-6, hGBA-8 Light Chain Sequence

<400>  50

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20                  25                  30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
```

65   70   75   80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85   90   95

Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100   105   110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115   120   125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130   135   140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145   150   155   160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165   170   175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180   185   190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195   200   205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210   215   220

<210> 51
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-2 Heavy Chain Sequence

<400> 51

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20   25   30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45

Gly Asn Ile Tyr Pro Gly Asp Ala Asp Thr Arg Tyr Ala Pro Ser Phe
    50   55   60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65   70   75   80

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Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Met Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

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

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

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

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

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
```

355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405 410 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 52
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-3 Heavy Chain Sequence

<400> 52

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Ala Ser Asp Thr Asn Tyr Ala Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ile Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

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

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

```
Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160


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


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


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


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


His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240


Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255


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


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


Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300


Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320


Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335


Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350


Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365


Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380


Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400


Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415


Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
```

            420   425   430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435   440   445

<210> 53
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-3 Light Chain Sequence

<400> 53

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85   90   95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100   105   110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115   120   125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130   135   140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145   150   155   160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165   170   175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180   185   190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195   200   205

```
Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220


<210>  54
<211>  448
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-4 Heavy Chain Sequence

<400>  54

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Tyr Pro Gly Asp Ala Tyr Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Ala Trp Gly Gln Gly Thr
            100                 105                 110


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


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


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


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


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


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


Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220
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His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210>  55
<211>  220
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-4 Light Chain Sequence

<400>  55

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15
```

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85   90   95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100   105   110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115   120   125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130   135   140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145   150   155   160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165   170   175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180   185   190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195   200   205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210   215   220

<210> 56
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-5 Heavy Chain Sequence

<400> 56

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr

```
            20                  25                  30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Tyr Pro Gly Ala Ala Tyr Thr Arg Tyr Ala Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

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

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

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

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

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300
```

```
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320


Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335


Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350


Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365


Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380


Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400


Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415


Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430


Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210>  57
<211>  220
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-5 Light Chain Sequence

<400>  57

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
```

85 90 95

Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
115 120 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135 140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145 150 155 160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
165 170 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
180 185 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
195 200 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 58
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-6 Heavy Chain Sequence

<400> 58

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Asn Ile Tyr Pro Gly Ala Ser Tyr Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

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Thr Arg Gln Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

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

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

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

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

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
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    370                 375                 380


Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400


Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415


Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430


Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210>  59
<211>  448
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-7 Heavy Chain Sequence

<400>  59

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Asn Ile Tyr Pro Gly Glu Ala Tyr Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


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


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


Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160
```

```
Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
```

```
        435                 440                 445


<210>  60
<211>  220
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-7 Light Chain Sequence

<400>  60

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asn Ser
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn
                85                  90                  95


Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110


Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115                 120                 125


Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130                 135                 140


Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145                 150                 155                 160


Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175


Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190


Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205


Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220
```

```
<210>  61
<211>  448
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  hGBA-8 Heavy Chain Sequence

<400>  61

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Asn Ile Tyr Pro Ser Glu Ser Tyr Thr Asn Tyr Ala Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Thr Arg Leu Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


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


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


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


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


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


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


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


His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240
```

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245   250   255

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290   295   300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305   310   315   320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325   330   335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340   345   350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355   360   365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370   375   380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385   390   395   400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405   410   415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420   425   430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435   440   445

<210> 62
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-9 Heavy Chain Sequence

<400> 62

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

```
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Tyr Pro Ser Ala Ala Tyr Thr Arg Tyr Ala Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65              70                  75                      80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Thr Arg Met Trp Arg Gly Asn Ser Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

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

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

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

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

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225             230                 235                     240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300
```

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305   310   315   320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325   330   335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340   345   350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355   360   365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370   375   380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385   390   395   400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405   410   415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420   425   430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435   440   445

<210> 63
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<223> hGBA-9 Light Chain Sequence

<400> 63

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
                85   90   95

```
Asp Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110


Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115                 120                 125


Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130                 135                 140


Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145                 150                 155                 160


Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175


Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190


Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205


Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220


<210>  64
<211>  330
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Constant heavy chain - CH1 + Fc domain

<400>  64

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15


Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30


Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45


Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60


Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80


Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95


Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
```

```
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225                 230                 235                 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210>  65
<211>  107
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Constant light chain region

<400>  65
```

```
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1               5                   10                  15


Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
            20                  25                  30


Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
        35                  40                  45


Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
    50                  55                  60


Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65                  70                  75                  80


Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
                85                  90                  95


Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105


<210>  66
<211>  330
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Constant heavy chain region CH1 and Fc region with reduced Fc
       gamma R binding having the L234A/L235A mutations

<400>  66

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15


Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30


Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45


Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60


Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80


Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95


Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110


Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125
```

```
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140


Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160


Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175


Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190


His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205


Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220


Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225                 230                 235                 240


Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255


Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270


Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285


Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300


Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320


Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210>  67
<211>  330
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Constant heavy chain region CH1 and Fc region having the
       L234A/L235A/P329G mutations in the constant heavy chain region
       CH1 and Fc region with even further reduced Fc gamma R binding

<400>  67

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15
```

```
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225                 230                 235                 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285
```

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290   295   300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305   310   315   320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325   330

<210> 68
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> N-terminal extracellular domain of CLDN18.2, independent of glycosylation

<400> 68

Asp Gln Trp Ser Thr Gln Asp Leu Tyr Asn
1   5   10

<210> 69
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> N-terminal extracellular domain of CLDN18.2, mainly unglycosylated

<400> 69

Asn Asn Pro Val Thr Ala Val Phe Asn Tyr Gln
1   5   10

<210> 70
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> N-terminal extracellular domain of CLDN18.2, unglycosylated

<400> 70

Ser Thr Gln Asp Leu Tyr Asn Asn Pro Val Thr Ala Val Phe
1   5   10

<210> 71
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> pan-CLDN18 peptide

<400> 71

Thr Asn Phe Trp Met Ser Thr Ala Asn Met Tyr Thr Gly
1   5   10

```
<210>  72
<211>  16
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  peptide sequence disclosed by WO2005/113587 against specific
       epitopes on CLDN18.2

<400>  72

Ala Leu Met Ile Val Gly Ile Val Leu Gly Ala Ile Gly Leu Leu Val
1               5                   10                  15


<210>  73
<211>  24
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  peptide sequence disclosed by WO2005/113587 against specific
       epitopes on CLDN18.2

<400>  73

Arg Ile Gly Ser Met Glu Asp Ser Ala Lys Ala Asn Met Thr Leu Thr
1               5                   10                  15


Ser Gly Ile Met Phe Ile Val Ser
            20


<210>  74
<211>  129
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Peptide including the first extracellular domain of CLDN18.2 with
       N- and C-terminal extensions

<400>  74

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1               5                   10                  15


Gly Ser Thr Gly Asp Ala Ala Gln Pro Ala Arg Arg Ala Arg Arg Thr
            20                  25                  30


Lys Leu Gly Thr Glu Leu Gly Ser Thr Pro Val Trp Trp Asn Ser Ala
        35                  40                  45


Asp Gly Arg Met Asp Gln Trp Ser Thr Gln Asp Leu Tyr Asn Asn Pro
    50                  55                  60


Val Thr Ala Val Phe Asn Tyr Gln Gly Leu Trp Arg Ser Cys Val Arg
65                  70                  75                  80


Glu Ser Ser Gly Phe Thr Glu Cys Arg Gly Tyr Phe Thr Leu Leu Gly
                85                  90                  95
```

```
Leu Pro Ala Met Leu Gln Ala Val Arg Ala Ala Ile Gln His Ser Gly
            100                 105                 110


Gly Arg Ser Arg Arg Ala Arg Thr Lys Thr His Leu Arg Arg Gly Ser
        115                 120                 125


Glu



<210>  75
<211>  15
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Overlapping peptides of CLDN18.2 within the first extracellular
       domain

<400>  75

Met Asp Gln Trp Ser Thr Gln Asp Leu Tyr Asn Asn Pro Val Thr
1               5                   10                  15


<210>  76
<211>  15
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Overlapping peptides of CLDN18.2 within the first extracellular
       domain

<400>  76

Leu Tyr Asn Asn Pro Val Thr Ala Val Phe Asn Tyr Gln Gly Leu
1               5                   10                  15


<210>  77
<211>  15
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Overlapping peptides of CLDN18.2 within the first extracellular
       domain

<400>  77

Val Phe Asn Tyr Gln Gly Leu Trp Arg Ser Cys Val Arg Glu Ser
1               5                   10                  15


<210>  78
<211>  15
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Overlapping peptides of CLDN18.2 within the first extracellular
       domain

<400>  78
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Gln Gly Leu Trp Arg Ser Cys Val Arg Glu Ser Ser Gly Phe Thr
1   5   10   15

<210> 79
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Overlapping peptides of CLDN18.2 within the first extracellular domain

<400> 79

Arg Ser Cys Val Arg Glu Ser Ser Gly Phe Thr Glu Cys Arg Gly
1   5   10   15

<210> 80
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Epitope of antibody of WO2013/167259 binding to C-terminal epitopes of CLDN18.2

<400> 80

Thr Glu Asp Glu Val Gln Ser Tyr Pro Ser Lys His Asp Tyr Val
1   5   10   15

<210> 81
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Epitope of antibody of WO2013/167259 binding to C-terminal epitopes of CLDN18.2

<400> 81

Glu Val Gln Ser Tyr Pro Ser Lys His Asp Tyr Val
1   5   10

<210> 82
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Consensus including IMAB362 HC CDR1

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> T or S

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> G or N

<400> 82

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Gly Tyr Xaa Phe Thr Ser Tyr Trp Ile Xaa
1               5                   10


<210>  83
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Consensus including IMAB362 HC CDR2


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  N or I

<220>
<221>  MISC_FEATURE
<222>  (6)..(6)
<223>  S or G

<220>
<221>  MISC_FEATURE
<222>  (7)..(7)
<223>  A, E or D

<220>
<221>  MISC_FEATURE
<222>  (8)..(8)
<223>  A or S

<220>
<221>  MISC_FEATURE
<222>  (9)..(9)
<223>  Y or D

<220>
<221>  MISC_FEATURE
<222>  (11)..(11)
<223>  N or R

<220>
<221>  MISC_FEATURE
<222>  (13)..(13)
<223>  A, N or S

<400>  83

Gly Xaa Ile Tyr Pro Xaa Xaa Xaa Xaa Thr Xaa Tyr Xaa
1               5                   10


<210>  84
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Consensus including IMAB362 HC CDR3


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  A or T
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<220>
<221>  MISC_FEATURE
<222>  (3)..(3)
<223>  L, M, I, S or Q

<220>
<221>  MISC_FEATURE
<222>  (11)..(11)
<223>  A or Y

<400>  84

Xaa Arg Xaa Trp Arg Gly Asn Ser Phe Asp Xaa
1               5                   10


<210>  85
<211>  30
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-1, hGBA-3 HCDR1 Sequence

<400>  85
ggctatagct ttacatcata ttggattgga                                        30


<210>  86
<211>  39
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-1 HCDR2 Sequence

<400>  86
gggaacattt accctggggc atcggatacg cgatacgca                              39


<210>  87
<211>  33
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-1 HCDR3 Sequence

<400>  87
gcgagacttt ggcgggggaa tagcttcgac tac                                    33


<210>  88
<211>  51
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-1 LCDR1 Sequence

<400>  88
aaaagctccc aaagcctatt gaactcggga aaccaaaaga attacttggc a                51


<210>  89
<211>  21
<212>  DNA
<213>  Artificial Sequence
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<220>
<223> hGBA-1 LCDR2 Sequence

<400> 89
tgggcaagca cccgagagag c   21

<210> 90
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-1 LCDR3 Sequence

<400> 90
caaaacgact attcataccc attcaca   27

<210> 91
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-2 HCDR1 Sequence

<400> 91
ggatattcat ttacaagcta ctggatcgga   30

<210> 92
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-2 HCDR2 Sequence

<400> 92
ggaaatatat accccggaga cgcggacacg agatacgca   39

<210> 93
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-2 HCDR3 Sequence

<400> 93
gcgcggatgt ggcgcggcaa tagctttgac tac   33

<210> 94
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-3 HCDR2 Sequence

<400> 94
gggatcatct atccgggggc atccgatacc aactatgcg   39

<210> 95
<211> 33

```
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-3 HCDR3 Sequence

<400>  95
gctaggattt ggcgaggaaa tagctttgat tat                                      33


<210>  96
<211>  51
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-3 LCDR1 Sequence

<400>  96
aagagctcgc aaagtttgct gaactccggg aaccaaaaga attacctggc a                  51


<210>  97
<211>  21
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-3 LCDR2 Sequence

<400>  97
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<210>  98
<211>  27
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-3 LCDR3 Sequence

<400>  98
caaaacgact actcctatcc gctgacc                                             27


<210>  99
<211>  30
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-4 HCDR1 Sequence

<400>  99
ggatactcat ttacatcata ctggatagga                                          30


<210>  100
<211>  39
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-4 HCDR2 Sequence

<400>  100
gggattatat accccggcga cgcttacact cgatattcg                                39
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<210> 101
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-4 HCDR3 Sequence

<400> 101
acgaggctat ggagggggaa tagctttgat gcc 33

<210> 102
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-4 LCDR1 Sequence

<400> 102
aagagctccc aaagcctatt gaactcggga aatcaaaaga attatctgac a 51

<210> 103
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-4 LCDR2 Sequence

<400> 103
tgggcctcga caagggagag c 21

<210> 104
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-4 LCDR3 Sequence

<400> 104
caaaatgact actcataccc gctgaca 27

<210> 105
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 HCDR1 Sequence

<400> 105
ggatatagct ttacgagcta ctggatcgga 30

<210> 106
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 HCDR2 Sequence

<400> 106
gggataatat accccggagc ggcatacacg agatatgcg   39

<210> 107
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 HCDR3 Sequence

<400> 107
gcgagactat ggcgcgggaa ctcatttgat tac   33

<210> 108
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 LCDR1 Sequence

<400> 108
aaatcatcgc aatcattgct aaattcgggg aaccaaaaga attatttggc a   51

<210> 109
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 LCDR2 Sequence

<400> 109
tgggcatcca cgagagaatc g   21

<210> 110
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 LCDR3 Sequence

<400> 110
caacaagatt attcataccc atttaca   27

<210> 111
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-6 HCDR1 Sequence

<400> 111
ggatatacat ttacatctta ctggatcgga   30

<210> 112
<211> 36
<212> DNA
<213> Artificial Sequence

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<220>
<223>  hGBA-6 HCDR2 Sequence

<400>  112
gggaacattt atcctggcgc gagctatacg cgctat                                 36


<210>  113
<211>  33
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-6 HCDR3 Sequence

<400>  113
acccggcaat ggaggggcaa tagctttgac tac                                    33


<210>  114
<211>  30
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-7 HCDR1 Sequence

<400>  114
ggatattcct ttacatcata ctggatcggc                                        30


<210>  115
<211>  39
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-7 HCDR2 Sequence

<400>  115
gggaacatat atcccggaga agcctatacg agatactcg                              39


<210>  116
<211>  33
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-7 HCDR3 Sequence

<400>  116
acgcgactat ggaggggaaa tagctttgac tat                                    33


<210>  117
<211>  51
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  hGBA-7 LCDR1 Sequence

<400>  117
aagagctccc aatcagtcct gaactctggg aatcaaaaga attacctgac a                51


<210>  118
<211>  21
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<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-7, h-GBA 9 LCDR2 Sequence

<400> 118
tgggcgagca cgagggagag c   21

<210> 119
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-7 LCDR3 Sequence

<400> 119
caaaatgatt attcataccc cttcaca   27

<210> 120
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-8 HCDR1 Sequence

<400> 120
ggatactcct ttacatcata ttggatcgga   30

<210> 121
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-8 HCDR2 Sequence

<400> 121
ggaaacatat atccgagcga atcatatacg aactacgcg   39

<210> 122
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-8 HCDR3 Sequence

<400> 122
acgaggctat ggagggggaa tagcttcgac tat   33

<210> 123
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-9 HCDR1 Sequence

<400> 123
ggatatacat tcacgagcta ctggatagga   30

<210> 124
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-9 HCDR2 Sequence

<400> 124
ggaatcatat atccttccgc ggcatatacg cgatatgcg 39

<210> 125
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-9 HCDR3 Sequence

<400> 125
acgcggatgt ggaggggaaa tagctttgat tac 33

<210> 126
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-9 LCDR1 Sequence

<400> 126
aagagctcgc aatcggtcct gaatagcggg aaccaaaaga attatctggc c 51

<210> 127
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-9 LCDR3 Sequence

<400> 127
caacaagact actcataccc atttaca 27

<210> 128
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-1 VH Sequence

<400> 128
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tcatgcaaag ggagcggcta tagctttaca tcatattgga ttggatgggt caggcaaatg 120

ccggggaagg ggctggaatg gatggggaac atttaccctg ggcatcgga tacgcgatac 180

gcacctagct ttcaagggca agtcacaatt tcggcggaca agagcatctc aacggcatac 240

ctgcaatggt cgagcttgaa ggcatctgat actgcaatgt actactgcgc gagactttgg 300

cgggggaata gcttcgacta ctgggggcag ggtaccctgg ttacggtctc gagc 354

<210> 129
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-1, h-GBA 2, h-GBA 6, h-GBA 8 VL Sequence

<400> 129
gacattgtga tgacgcaaag ccccgattcg ctggctgtat cgctagggga gcgcgctacg 60

atcaattgca aaagctccca aagcctattg aactcgggaa accaaaagaa ttacttggca 120

tggtatcaac aaaaaccggg gcaaccgccg aagctgctga tctattgggc aagcacccga 180

gagagcggtg tcccggaccg atttagcggg agcggatcgg gcaccgactt cacgctgaca 240

ataagctcat tgcaagccga ggatgtggcg gtctattatt gccaaaacga ctattcatac 300

ccattcacat tcgggcaagg taccaaggtc gagatcaag 339

<210> 130
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-2 VH Sequence

<400> 130
gaagtccaac tggtccaatc tggagcggaa gtcaagaagc ctggggagag cctgaaaatt 60

tcatgcaagg ggagcggata ttcatttaca agctactgga tcggatgggt ccggcaaatg 120

ccggggaagg gcttggaatg gatgggaaat atataccccg gagacgcgga cacgagatac 180

gcaccgagct ttcaagggca ggtcaccatt agcgctgata aatcgatttc aaccgcatat 240

ctgcaatggt catcgctgaa ggcctccgac accgcgatgt actattgcgc gcggatgtgg 300

cgcggcaata gctttgacta ctgggggcag ggtaccctcg tcacggtctc gagc 354

<210> 131
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-3 VH Sequence

<400> 131
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agctgcaaag gctccggcta tagctttaca tcatattgga tcggatgggt cagacaaatg 120

ccgggaaagg gacttgaatg gatggggatc atctatccgg gggcatccga taccaactat 180

gcgccgagct tccaagggca ggtcacgata tccgcggata aatcgattag caccgcatat 240

ctgcaatgga gctcgctgaa ggcatccgac accgcgatgt actactgcgc taggatttgg 300

cgaggaaata gctttgatta ttgggggcag ggtacccttg tcacggtctc gagc 354

<210> 132

<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-3 VL Sequence

<400> 132
gacattgtca tgacgcaaag ccccgactcg ctggccgtct cactgggggga gcgggcgaca 60

atcaactgca agagctcgca aagtttgctg aactccggga accaaaagaa ttacctggca 120

tggtatcaac aaaagccggg gcaacccccg aagctgctga tatattgggc atcaacgcgg 180

gaaagcggag tcccggatag atttagcgga tctggatcgg ggaccgactt cacgctgacg 240

atatctagcc ttcaagccga ggatgtggct gtatattatt gccaaaacga ctactcctat 300

ccgctgacct tcgggcaagg taccaaggtc gagatcaag 339

<210> 133
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-4 VH Sequence

<400> 133
gaagtccaac tagtccaaag cggagccgaa gtcaagaaac cgggggagag ccttaagatc 60

tcatgcaagg ggagcggata ctcatttaca tcatactgga taggatgggt cagacaaatg 120

cccggcaagg ggctggaatg gatggggatt atataccccg gcgacgctta cactcgatat 180

tcgccatcat tccaagggca ggtcacgata tcggccgata aatcgatatc cacggcatac 240

ctgcaatgga gctcactgaa agcatctgat acggcaatgt attattgcac gaggctatgg 300

agggggaata gctttgatgc ctgggggcag ggtaccctgg tcacggtctc gagc 354

<210> 134
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-4 VL Sequence

<400> 134
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atcaactgca agagctccca aagcctattg aactcgggaa atcaaaagaa ttatctgaca 120

tggtatcaac aaaagccggg gcaaccaccg aaactgctga tctattgggc ctcgacaagg 180

gagagcggag tcccggaccg cttctctgga tcgggaagcg ggactgactt cacgctgacc 240

ataagctcgc tgcaagccga ggacgtcgcc gtctattatt gccaaaatga ctactcatac 300

ccgctgacat ttggccaagg taccaaggtc gagatcaag 339

<210> 135
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 VH Sequence

<400> 135
gaggtgcaac tggtacaatc cggggcggaa gtgaagaagc cgggggaatc gctgaagata   60

agctgcaaag gctctggata tagctttacg agctactgga tcggatgggt caggcaaatg   120

ccggggaagg gactggaatg gatggggata atataccccg gagcggcata cacgagatat   180

gcgccgagct tccaagggca agtgacaata agcgcggaca aatcgattag cacggcatat   240

ctgcaatggt cctcgctgaa ggcgagcgat accgcaatgt actattgcgc gagactatgg   300

cgcgggaact catttgatta ctgggggcag ggtaccctag tgacggtctc gagc   354

<210> 136
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-5 VL Sequence

<400> 136
gacattgtca tgacgcaaag cccggatagc ctggctgtat cgctggggga gagagcgacg   60

atcaactgca aatcatcgca atcattgcta aattcgggga accaaaagaa ttatttggca   120

tggtatcaac aaaagccggg gcaaccgccg aaactgctga tttactgggc atccacgaga   180

gaatcgggag tcccggaccg atttagcgga tctgggagcg ggaccgattt cacgctgacc   240

attagctcgc tgcaagcgga ggatgtggcg gtctattact gccaacaaga ttattcatac   300

ccatttacat ttgggcaagg taccaaggtc gagatcaag   339

<210> 137
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-6 VH Sequence

<400> 137
gaagtacaat tggttcaatc gggggccgaa gtcaagaagc cgggggaatc gctgaagata   60

tcctgcaagg ggagcggata tacatttaca tcttactgga tcggatgggt cagacaaatg   120

cccggaaagg ggcttgaatg gatggggaac atttatcctg gcgcgagcta tacgcgctat   180

agcccgagct tccaagggca ggtcacgatt agcgccgaca agagcatttc gacggcatac   240

ctgcaatgga gctcgctgaa agcatcggat acggcaatgt attactgcac ccggcaatgg   300

aggggcaata gctttgacta ctgggggcag ggtaccctag tcacggtctc gagc   354

<210> 138
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-7 VH Sequence

<400> 138
gaagttcaat tggtccaatc tggagccgaa gtcaagaagc ccggagaatc gctgaagatt 60

agctgcaagg ggagcggata ttcctttaca tcatactgga tcggctgggt cagacaaatg 120

cccggaaagg gactggaatg gatggggaac atatatcccg gagaagccta tacgagatac 180

tcgccatcat ttcaaggaca ggtcaccata agcgcggaca agagcataag caccgcatac 240

ctgcaatgga gctcgctgaa ggcatcggac accgccatgt attactgcac gcgactatgg 300

aggggaaata gctttgacta ttgggggcag ggtaccttag tcacggtctc gagc 354

<210> 139
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-7 VL Sequence

<400> 139
gatatagtaa tgactcaatc acccgatagc ttggctgtga gcctgggaga aagagctaca 60

atcaactgca agagctccca atcagtcctg aactctggga atcaaaagaa ttacctgaca 120

tggtatcaac aaaagcccgg acaaccgccg aagctgctga tctactgggc gagcacgagg 180

gagagcggag tcccggatcg attttctggc tccgggagcg gaaccgactt cacactgact 240

attagctcgc tgcaagcgga ggacgtcgcc gtctactatt gccaaaatga ttattcatac 300

cccttcacat ttgggcaagg taccaaggtc gagatcaag 339

<210> 140
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-8 VH Sequence

<400> 140
gaggtgcaac tagtgcaatc gggggccgaa gtgaagaaac ctggggaatc gctgaagata 60

tcatgcaagg ggagcggata ctcctttaca tcatattgga tcggatgggt caggcaaatg 120

ccggggaagg ggctggaatg gatgggaaac atatatccga gcgaatcata tacgaactac 180

gcgccgagct ttcaaggaca agtcacgata tccgcggata aatcgatatc gaccgcatac 240

ctgcaatgga gctcgctgaa ggcttccgac actgcgatgt attactgcac gaggctatgg 300

agggggaata gcttcgacta ttgggggcag ggtaccctgg tgacggtctc gagc 354

<210> 141
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-9 VH Sequence

<400> 141
gaagtccaat tagtccaatc gggggccgag gtcaagaagc cgggggaatc gctcaagata 60

agctgcaagg gatcgggata tacattcacg agctactgga taggatgggt caggcaaatg   120

ccggggaagg ggctggaatg gatgggaatc atatatcctt ccgcggcata tacgcgatat   180

gcgccatcat ttcaaggaca ggtcacgata agcgccgaca agagcattag caccgcatac   240

ctgcaatggt cgagccttaa ggcatcggac accgcgatgt actactgcac gcggatgtgg   300

aggggaaata gctttgatta ctgggggcag ggtaccctag tcacggtctc gagc   354

<210> 142
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> hGBA-9 VL Sequence

<400> 142
gacatcgtca tgacgcaaag cccggactcg ctggcggtct cgctggggga gcgggccaca   60

ataaattgca agagctcgca atcggtcctg aatagcggga accaaaagaa ttatctggcc   120

tggtatcaac aaaagccggg gcaaccaccg aagctgctaa tctattgggc gagcacgagg   180

gagagcggag tccccgatcg atttagcgga tcgggaagcg ggaccgattt cacgctgacg   240

atttcgagcc tacaagccga ggatgtggcg gtctattact gccaacaaga ctactcatac   300

ccatttacat ttggacaagg taccaaggtc gagatcaag   339

<210> 143
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> RLPXTGG tag

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> X is any of the 20 natural amino acids

<400> 143

Arg Leu Pro Xaa Thr Gly Gly
1   5

<210> 144
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> GGGGSLPXTGG tag

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> X is any of the 20 natural amino acids

<400> 144

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Gly Gly Gly Gly Ser Leu Pro Xaa Thr Gly Gly
1               5                   10
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