

ANTIBODY THAT BINDS TO C3bBb

FIELD OF THE INVENTION

5 The present invention relates to anti-C3bBb antibodies and methods of using the same.

BACKGROUND OF THE INVENTION

10 The complement system is crucially involved in the disease biology of age related macular degeneration (AMD) (Cell Mol Life Sci 2021 May;78(10):4487-4505). The alternative pathway C3 convertase (C3bBb) is a key amplifying factor of the complement cascade and it is formed by binding of Factor B (FB) to the C3b fragment of complement component C3 and subsequent cleavage by plasma serine protease Factor D (FD) under release of a fragment Ba. The remaining Bb fragment bound to C3b forms the functional C3 convertase C3bBb. C3bBb is relatively
15 unstable with a half-life of a few minutes making it an unsuitable target for antibody generation.

Due to the central role of the alternative pathway in various pathologies, there is still a need for developing potent inhibitors acting at various complement components within this proteolytic cascade.

20 SUMMARY OF THE INVENTION

The present invention relates to an antibody that specifically binds to human C3bBb.

25 The invention further relates to an antibody that binds to human C3bBb, wherein the antibody:

- binds to wild-type human C3bBb, and/or
- binds to recombinant human C3bBb, which comprises the Bb subunit of a recombinant Factor B (FB) protein, which comprises a D279G mutation and optionally mutations K350N and/or a M458I; and/or
- 30 - inhibits the alternative pathway; and/or
- is an agonist or antagonist of C3bBb activity; and/or

- specifically binds to cynomolgus C3bBb and human C3bBb, and/or
- specifically binds to African green monkey C3bBb and human C3bBb, and/or
- binds with an affinity of ≤ 10 nM at 37 °C as measured by SPR, and/or
- 5 - does not compete with properdin for C3bBb binding, and/or
- does not stabilize C3 convertase.

In one aspect, the invention relates to an antibody that specifically binds to wild-type human C3bBb.

10 In another aspect, the invention relates to an antibody that specifically binds to recombinant human C3bBb, wherein the C3bBb comprises the Bb subunit of a recombinant FB protein that comprises a D279G and optionally further mutations K350N and/or M458I. In one embodiment the antibody specifically binds to human C3bBb comprising the Bb subunit of a recombinant FB protein according to SEQ ID NO: 492. In one embodiment the antibody specifically binds to human C3bBb
15 comprising the Bb subunit of a recombinant FB protein according to SEQ ID NO: 493.

In another aspect, the invention relates to an antibody that specifically binds to an epitope of human C3bBb that includes amino acid residues of the C3b subunit and amino acid residues of the Bb subunit of human FB. In one embodiment the
20 antibody of the invention specifically binds to human C3bBb, wherein the antibody does not specifically bind to the (isolated) C3b subunit of C3bBb, and wherein the antibody does not specifically bind to the (isolated) Bb subunit of C3bBb.

In another aspect, the invention relates to an antibody that binds to human C3bBb, wherein the antibody comprises the heavy and light chain CDRs of an
25 antibody selected from Table D1. In one embodiment the antibody comprises the heavy and light chain variable domains of an antibody selected from Table D1.

In one embodiment, the antibody comprises a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:449; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:450; and (c) CDR-H3
30 comprising the amino acid sequence of SEQ ID NO:451, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:452; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:453; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:454 (corresponding to antibody #1, P1AG9426); or a heavy chain variable domain (VH)

- (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:455; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:456; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:457, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:458; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:459; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:460 (corresponding to antibody #2, P1AG9376); or a heavy chain variable domain (VH)
- (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:461; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:462; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:463, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:464; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:465; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:466 (corresponding to antibody #3, P1AG9372); or a heavy chain variable domain (VH)
- (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:467; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:468; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:469, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:470; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:471; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:472 (corresponding to antibody #4, P1AG9420); or a heavy chain variable domain (VH)
- (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:473; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:474; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:475, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:476; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:477; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:478 (corresponding to antibody #5, P1AG9391); or a heavy chain variable domain (VH)
- (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:479; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:480; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:481, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:482; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:483; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:484 (corresponding to antibody #6, P1AH1205); or a heavy chain variable domain (VH)
- (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:485; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:486; and (c) CDR-H3

comprising the amino acid sequence of SEQ ID NO:487, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:488; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:489; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:490 (corresponding to antibody #7, P1AH1199).

In one embodiment, the antibody comprises a VH domain comprising SEQ ID NO:1 and a VL domain comprising SEQ ID NO:2 (corresponding to antibody #1, P1AG9426); or a VH domain comprising SEQ ID NO:3 and a VL domain comprising SEQ ID NO:4 (corresponding to antibody #2, P1AG9376); or a VH domain comprising SEQ ID NO:5 and a VL domain comprising SEQ ID NO:6 (corresponding to antibody #3, P1AG9372); or a VH domain comprising SEQ ID NO:7 and a VL domain comprising SEQ ID NO:8 (corresponding to antibody #4, P1AG9420); or a VH domain comprising SEQ ID NO:9 and a VL domain comprising SEQ ID NO:10 (corresponding to antibody #5, P1AG9391); or a VH domain comprising SEQ ID NO:11 and a VL domain comprising SEQ ID NO:12 (corresponding to antibody #6, P1AH1205); or a VH domain comprising SEQ ID NO:13 and a VL domain comprising SEQ ID NO:14 (corresponding to antibody #7, P1AH1199).

Also, the invention relates to an antibody that competes for binding to wild-type human C3bBb with the antibodies of the invention.

The invention also relates to an antibody that competes for binding to recombinant human C3bBb comprising the Bb subunit of a recombinant FB protein that comprises a D279G and optionally further mutations K350N and/or M458I with the antibody of the invention.

Another aspect of the invention is an isolated nucleic acid encoding the antibody of the invention.

The invention also relates to a host cell comprising the nucleic acid of the invention.

Further, the invention relates to a method of producing an antibody that binds to human C3bBb comprising culturing the host cell of the invention under conditions suitable for the expression of the antibody.

In another aspect, the invention relates to a pharmaceutical composition comprising the antibody of the invention.

In a further aspect, the invention relates to an antibody of the invention for use as a medicament.

Antibodies of the invention are suitable to inhibit the alternative pathway by binding to C3bBb. Antibodies of the invention may be capable of inhibiting the alternative pathway without stabilizing C3bBb upon binding, thus avoiding accumulation of C3bBb. Furthermore, antibodies of the invention may be specific for the C3bBb complex but not exhibit prominent antigen binding to its individual subunits.

The antibodies disclosed herein may be suitable for therapy, particularly treatment of ocular vascular diseases.

The antibodies of the invention provide several valuable properties that allow their therapeutic application, like high affinities, and a high stability advantageous for long duration. Also, the antibodies of the invention are advantageous to be provided in high concentrations liquid formulations with a viscosity suitable for ocular application.

DESCRIPTION OF THE FIGURES

Figure 1: The left image shows the trimeric complex formed between the P1AF8499 Fab fragment and C3bBb. The epitope bound by P1AF8499 Fab fragment comprises amino acids from both components, C3b and Bb (right image).

Figure 2: Binding of antibody P1AG9426 (#1) to wild-type human C3bBb complex. Sensorgram generated as described in Example 14.

DETAILED DESCRIPTION OF THE INVENTION

1. Definitions

An “acceptor human framework” for the purposes herein is a framework comprising the amino acid sequence of a light chain variable domain (VL) framework or a heavy chain variable domain (VH) framework derived from a human immunoglobulin framework or a human consensus framework, as defined below. An acceptor human framework “derived from” a human immunoglobulin framework or a human consensus framework may comprise the same amino acid sequence thereof, or it may contain amino acid sequence changes. In some aspects, the number

of amino acid changes are 10 or less, 9 or less, 8 or less, 7 or less, 6 or less, 5 or less, 4 or less, 3 or less, or 2 or less. In some aspects, the VL acceptor human framework is identical in sequence to the VL human immunoglobulin framework sequence or human consensus framework sequence.

5 “Affinity” refers to the strength of the sum total of noncovalent interactions between a single binding site of a molecule (e.g., an antibody) and its binding partner (e.g., an antigen). Unless indicated otherwise, as used herein, “binding affinity” refers to intrinsic binding affinity which reflects a 1:1 interaction between members of a binding pair (e.g., antibody and antigen). The affinity of a molecule X for its
10 partner Y can generally be represented by the dissociation constant (K_D). Affinity can be measured by common methods known in the art, including those described herein. Specific illustrative and exemplary methods for measuring binding affinity are described in the following. Antibodies that bind to human C3bBb have a dissociation constant (K_D) of $\leq 1\mu\text{M}$, $\leq 100\text{ nM}$, $\leq 10\text{ nM}$, $\leq 1\text{ nM}$, $\leq 0.1\text{ nM}$,
15 $\leq 0.01\text{ nM}$, or $\leq 0.001\text{ nM}$, in one embodiment 10^{-6} M or less, in one embodiment 10^{-7} M or less, in one embodiment 10^{-8} M or less, in one embodiment from 10^{-8} M to 10^{-13} M , in one embodiment from 10^{-9} M to 10^{-13} M). An antibody is said to “specifically bind” to human C3bBb when the antibody has a K_D of $1\mu\text{M}$ or less. In certain aspects, an anti-human C3bBb antibody binds to an epitope of human
20 C3bBb that is conserved among human C3bBb from different species.

The components of the innate immune system, i.e. the different elements from the classical and alternative pathways are referred to herein according to their standard meaning in the art and the termini used herein include recombinant variants of the respective natural components of the innate immune system that maintain
25 functionality and may include variants comprising tags and/or labels.

In brief, the term “C3bBb” as used herein refers to the alternative pathway C3 convertase that is formed by binding of C3 fragment (“C3b”) to Factor B (“FB”) and subsequent cleavage by plasma serine protease Factor D (“FD”) under release of a fragment Ba. The term “C3b” as used herein refers to the larger of two elements
30 resulting from the alternative pathway cleavage of complement component 3 (C3), the other one being C3a. The term “C3 convertase” refers to the serine proteases of the complement system and may refer to the alternative pathway C3 convertase (C3bBb) or the classical and lectin pathway C3 convertase (C4bC2b). The term “human Factor B” or “FB” refers to complement factor B encoded in humans by the
35 CFB gene. The term “human Factor D” refers to complement factor D encoded in

humans by the CFD gene. The term “C5 convertase” as used herein refers to the alternative pathway C5 convertase (C3bBbC3b).

5 The term “antibody screening” refers to techniques used to identify antibodies specifically binding to a target antigen. Various techniques for identifying antibodies are known in the art, such as administration of an immunogenic target antigen to a transgenic animal, hybridoma-based methods, or isolating variable domain sequences selected from phage-display libraries. The term “phage library panning” refers to an affinity selection technique used to identify phage display variants with desired binding properties towards a target antigen.

10 The term “antibody” herein is used in the broadest sense and encompasses various antibody structures, including but not limited to monoclonal antibodies, polyclonal antibodies, multispecific antibodies (e.g., bispecific antibodies), and antibody fragments so long as they exhibit the desired antigen-binding activity.

15 An “antibody fragment” refers to a molecule other than an intact antibody that comprises a portion of an intact antibody that binds the antigen to which the intact antibody binds. Examples of antibody fragments include but are not limited to Fv, Fab, Fab', Fab'-SH, F(ab')₂; diabodies; linear antibodies; single-chain antibody molecules (e.g., scFv, and scFab); single domain antibodies (dAbs); and multispecific antibodies formed from antibody fragments. For a review of certain antibody fragments, see Holliger and Hudson, Nature Biotechnology 23:1126-1136 (2005).

20 The term “epitope” denotes the site on an antigen, either proteinaceous or non-proteinaceous, to which an anti-human C3bBb antibody binds. The epitope bound by antibodies of the invention comprises non-contiguous amino acids and hence is a conformational epitope.

25 Screening for antibodies binding to a particular epitope (i.e., those binding to the same epitope) can be done using methods routine in the art such as, e.g., without limitation, alanine scanning, peptide blots (see Meth. Mol. Biol. 248 (2004) 443-463), peptide cleavage analysis, epitope excision, epitope extraction, chemical modification of antigens (see Prot. Sci. 9 (2000) 487-496), cross-blocking (see “Antibodies”, Harlow and Lane (Cold Spring Harbor Press, Cold Spring Harb., NY). In certain embodiments used herein, an epitope of an antibody is identified by cryogenic electron microscopy.

Also, competitive binding can be used to easily determine whether an antibody competes for binding to human C3bBb with a reference anti-human C3bBb antibody of the invention. For example, an “antibody that competes for binding with” a reference anti-human C3bBb antibody of the invention refers to an antibody that blocks binding of the reference anti-human C3bBb antibody to its antigen in a competition assay by 50% or more, and conversely, the reference antibody blocks binding of the antibody to its antigen in a competition assay by 50% or more.

In some aspects, two antibodies are deemed to compete for binding to human C3bBb if a 1-, 5-, 10-, 20- or 100-fold excess of one antibody inhibits binding of the other by at least 50%, at least 75%, at least 90% or even 99% or more as measured in a competitive binding assay (see, e.g., Junghans et al., Cancer Res. 50 (1990) 1495-1502).

The “class” of an antibody refers to the type of constant domain or constant region possessed by its heavy chain. There are five major classes of antibodies: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2. In certain aspects, the antibody is of the IgG1 isotype. In certain aspects, the antibody is of the IgG1 isotype with the P329G, L234A and L235A mutation to reduce Fc-region effector function. In other aspects, the antibody is of the IgG2 isotype. In certain aspects, the antibody is of the IgG4 isotype with the S228P mutation in the hinge region to improve stability of IgG4 antibody. The heavy chain constant domains that correspond to the different classes of immunoglobulins are called α , δ , ϵ , γ , and μ , respectively. The light chain of an antibody may be assigned to one of two types, called kappa (κ) and lambda (λ), based on the amino acid sequence of its constant domain. The terms “constant region derived from human origin” or “human constant region” as used in the current application denotes a constant heavy chain region of a human antibody of the subclass IgG1, IgG2, IgG3, or IgG4 and/or a constant light chain kappa or lambda region. Such constant regions are well known in the state of the art and e.g. described by Kabat, E.A., et al., Sequences of Proteins of Immunological Interest, 5th ed., Public Health Service, National Institutes of Health, Bethesda, MD (1991) (see also e.g. Johnson, G., and Wu, T.T., Nucleic Acids Res. 28 (2000) 214-218; Kabat, E.A., et al., Proc. Natl. Acad. Sci. USA 72 (1975) 2785-2788). Unless otherwise specified herein, numbering of amino acid residues in the constant region is according to the EU numbering system, also called the EU index of Kabat, as described in Kabat, E.A. et al., Sequences of Proteins of Immunological

Interest, 5th ed., Public Health Service, National Institutes of Health, Bethesda, MD (1991), NIH Publication 91-3242.

5 “Effector functions” refer to those biological activities attributable to the Fc region of an antibody, which vary with the antibody isotype. Examples of antibody effector functions include: C1q binding and complement dependent cytotoxicity (CDC); Fc receptor binding; antibody-dependent cell-mediated cytotoxicity (ADCC); phagocytosis; down regulation of cell surface receptors (e.g., B cell receptor); and B cell activation.

10 An “effective amount” of an agent, e.g., a pharmaceutical composition, refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic or prophylactic result.

15 The term “Fc region” herein is used to define a C-terminal region of an immunoglobulin heavy chain that contains at least a portion of the constant region. The term includes native sequence Fc regions and variant Fc regions. In one aspect, a human IgG heavy chain Fc region extends from Cys226, or from Pro230, to the carboxyl-terminus of the heavy chain. However, antibodies produced by host cells may undergo post-translational cleavage of one or more, particularly one or two, amino acids from the C-terminus of the heavy chain. Therefore an antibody produced by a host cell by expression of a specific nucleic acid molecule encoding a full-length heavy chain may include the full-length heavy chain, or it may include a cleaved variant of the full-length heavy chain. This may be the case where the final two C-terminal amino acids of the heavy chain are glycine (G446) and lysine (K447, EU numbering system). Therefore, the C-terminal lysine (Lys447), or the C-terminal glycine (Gly446) and lysine (Lys447), of the Fc region may or may not be present.

20 Amino acid sequences of heavy chains including an Fc region are denoted herein without C-terminal glycine-lysine dipeptide if not indicated otherwise. In one aspect, a heavy chain including an Fc region as specified herein, comprised in an antibody according to the invention, comprises an additional C-terminal glycine-lysine dipeptide (G446 and K447, EU numbering system). In one aspect, a heavy chain including an Fc region as specified herein, comprised in an antibody according to the invention, comprises an additional C-terminal glycine residue (G446, numbering according to EU index). Unless otherwise specified herein, numbering of amino acid residues in the Fc region or constant region is according to the EU numbering system, also called the EU index, as described in Kabat et al., Sequences of Proteins of

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Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD, 1991.

“Framework” or “FR” refers to variable domain residues other than complementary determining regions (CDRs). The FR of a variable domain generally consists of four FR domains: FR1, FR2, FR3, and FR4. Accordingly, the CDR and FR sequences generally appear in the following sequence in VH (or VL): FR1-CDR-H1(CDR-L1)-FR2- CDR-H2(CDR-L2)-FR3- CDR-H3(CDR-L3)-FR4.

The terms “full length antibody”, “intact antibody”, and “whole antibody” are used herein interchangeably to refer to an antibody having a structure substantially similar to a native antibody structure or having heavy chains that contain an Fc region as defined herein.

The terms “host cell”, “host cell line”, and “host cell culture” are used interchangeably and refer to cells into which exogenous nucleic acid has been introduced, including the progeny of such cells. Host cells include “transformants” and “transformed cells”, which include the primary transformed cell and progeny derived therefrom without regard to the number of passages. Progeny may not be completely identical in nucleic acid content to a parent cell, but may contain mutations. Mutant progeny that have the same function or biological activity as screened or selected for in the originally transformed cell are included herein.

A “human antibody” is one which possesses an amino acid sequence which corresponds to that of an antibody produced by a human or a human cell or derived from a non-human source that utilizes human antibody repertoires or other human antibody-encoding sequences. This definition of a human antibody specifically excludes a humanized antibody comprising non-human antigen-binding residues.

A “human consensus framework” is a framework which represents the most commonly occurring amino acid residues in a selection of human immunoglobulin VL or VH framework sequences. Generally, the selection of human immunoglobulin VL or VH sequences is from a subgroup of variable domain sequences. Generally, the subgroup of sequences is a subgroup as in Kabat et al., Sequences of Proteins of Immunological Interest, Fifth Edition, NIH Publication 91-3242, Bethesda MD (1991), vols. 1-3. In one aspect, for the VL, the subgroup is subgroup kappa I as in Kabat et al., supra. In one aspect, for the VH, the subgroup is subgroup III as in Kabat et al., supra.

The term “hypervariable region” or “HVR” as used herein refers to each of the regions of an antibody variable domain which are hypervariable in sequence and which determine antigen binding specificity, for example “complementarity determining regions” (“CDRs”).

5 Generally, antibodies comprise six CDRs: three in the VH (CDR-H1, CDR-H2, CDR-H3), and three in the VL (CDR-L1, CDR-L2, CDR-L3). Exemplary CDRs herein include:

- 10 a) hypervariable loops occurring at amino acid residues 26-32 (L1), 50-52 (L2), 91-96 (L3), 26-32 (H1), 53-55 (H2), and 96-101 (H3) (Chothia and Lesk, J. Mol. Biol. 196:901-917 (1987));
- b) CDRs occurring at amino acid residues 24-34 (L1), 50-56 (L2), 89-97 (L3), 31-35b (H1), 50-65 (H2), and 95-102 (H3) (Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD (1991)); and
- 15 c) antigen contacts occurring at amino acid residues 27c-36 (L1), 46-55 (L2), 89-96 (L3), 30-35b (H1), 47-58 (H2), and 93-101 (H3) (MacCallum et al. J. Mol. Biol. 262: 732-745 (1996)).

 Unless otherwise indicated, the CDRs are determined according to Kabat et al., supra. One of skill in the art will understand that the CDR designations can also
20 be determined according to Chothia, supra, McCallum, supra, or any other scientifically accepted nomenclature system.

 An “individual” or “subject” is a mammal. Mammals include, but are not limited to, domesticated animals (e.g., cows, sheep, cats, dogs, and horses), primates (e.g., humans and non-human primates such as monkeys), rabbits, and rodents (e.g.,
25 mice and rats). In certain aspects, the individual or subject is a human.

 An “isolated” antibody is one which has been separated from a component of its natural environment. In some aspects, an antibody is purified to greater than 95% or 99% purity as determined by, for example, electrophoretic (e.g., SDS-PAGE, isoelectric focusing (IEF), capillary electrophoresis) or chromatographic (e.g., ion
30 exchange or reverse phase HPLC) methods. For a review of methods for assessment of antibody purity, see, e.g., Flatman et al., J. Chromatogr. B 848:79-87 (2007).

 The term “nucleic acid molecule” or “polynucleotide” includes any compound and/or substance that comprises a polymer of nucleotides. Each

nucleotide is composed of a base, specifically a purine- or pyrimidine base (i.e. cytosine (C), guanine (G), adenine (A), thymine (T) or uracil (U)), a sugar (i.e. deoxyribose or ribose), and a phosphate group. Often, the nucleic acid molecule is described by the sequence of bases, whereby said bases represent the primary structure (linear structure) of a nucleic acid molecule. The sequence of bases is typically represented from 5' to 3'. Herein, the term nucleic acid molecule encompasses deoxyribonucleic acid (DNA) including e.g., complementary DNA (cDNA) and genomic DNA, ribonucleic acid (RNA), in particular messenger RNA (mRNA), synthetic forms of DNA or RNA, and mixed polymers comprising two or more of these molecules. The nucleic acid molecule may be linear or circular. In addition, the term nucleic acid molecule includes both, sense and antisense strands, as well as single stranded and double stranded forms. Moreover, the herein described nucleic acid molecule can contain naturally occurring or non-naturally occurring nucleotides. Examples of non-naturally occurring nucleotides include modified nucleotide bases with derivatized sugars or phosphate backbone linkages or chemically modified residues. Nucleic acid molecules also encompass DNA and RNA molecules which are suitable as a vector for direct expression of an antibody of the invention in vitro and/or in vivo, e.g., in a host or patient. Such DNA (e.g., cDNA) or RNA (e.g., mRNA) vectors, can be unmodified or modified. For example, mRNA can be chemically modified to enhance the stability of the RNA vector and/or expression of the encoded molecule so that mRNA can be injected into a subject to generate the antibody in vivo (see e.g., Stadler et al, Nature Medicine 2017, published online 12 June 2017, doi:10.1038/nm.4356 or EP 2 101 823 B1).

An "isolated" nucleic acid refers to a nucleic acid molecule that has been separated from a component of its natural environment. An isolated nucleic acid includes a nucleic acid molecule contained in cells that ordinarily contain the nucleic acid molecule, but the nucleic acid molecule is present extrachromosomally or at a chromosomal location that is different from its natural chromosomal location.

"Isolated nucleic acid encoding an anti-human C3bBb antibody" refers to one or more nucleic acid molecules encoding anti-human C3bBb antibody heavy and light chains (or fragments thereof), including such nucleic acid molecule(s) in a single vector or separate vectors, and such nucleic acid molecule(s) present at one or more locations in a host cell.

The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the

individual antibodies comprising the population are identical and/or bind the same epitope, except for possible variant antibodies, e.g., containing naturally occurring mutations or arising during production of a monoclonal antibody preparation, such variants generally being present in minor amounts. In contrast to polyclonal antibody preparations, which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody of a monoclonal antibody preparation is directed against a single determinant on an antigen. Thus, the modifier “monoclonal” indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies in accordance with the present invention may be made by a variety of techniques, including but not limited to the hybridoma method, recombinant DNA methods, phage-display methods, and methods utilizing transgenic animals containing all or part of the human immunoglobulin loci, such methods and other exemplary methods for making monoclonal antibodies being described herein.

The term “package insert” is used to refer to instructions customarily included in commercial packages of therapeutic products, that contain information about the indications, usage, dosage, administration, combination therapy, contraindications and/or warnings concerning the use of such therapeutic products.

“Percent (%) amino acid sequence identity” with respect to a reference polypeptide sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the reference polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity for the purposes of the alignment. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, Clustal W, Megalign (DNASTAR) software or the FASTA program package. Those skilled in the art can determine appropriate parameters for aligning sequences, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. Alternatively, the percent identity values can be generated using the sequence comparison computer program ALIGN-2. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc., and the source code has been filed with user documentation in the U.S. Copyright

Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087 and is described in WO 2001/007611.

Unless otherwise indicated, for purposes herein, percent amino acid sequence identity values are generated using the ggsearch program of the FASTA package version 36.3.8c or later with a BLOSUM50 comparison matrix. The FASTA program package was authored by W. R. Pearson and D. J. Lipman (1988), "Improved Tools for Biological Sequence Analysis", PNAS 85:2444-2448; W. R. Pearson (1996) "Effective protein sequence comparison" Meth. Enzymol. 266:227-258; and Pearson et. al. (1997) Genomics 46:24-36 and is publicly available from www.fasta.bioch.virginia.edu/fasta_www2/fasta_down.shtml or www.ebi.ac.uk/Tools/sss/fasta. Alternatively, a public server accessible at fasta.bioch.virginia.edu/fasta_www2/index.cgi can be used to compare the sequences, using the ggsearch (global protein:protein) program and default options (BLOSUM50; open: -10; ext: -2; Ktup = 2) to ensure a global, rather than local, alignment is performed. Percent amino acid identity is given in the output alignment header.

The term "pharmaceutical composition" or "pharmaceutical formulation" refers to a preparation which is in such form as to permit the biological activity of an active ingredient contained therein to be effective, and which contains no additional components which are unacceptably toxic to a subject to which the pharmaceutical composition would be administered.

A "pharmaceutically acceptable carrier" refers to an ingredient in a pharmaceutical composition or formulation, other than an active ingredient, which is nontoxic to a subject. A pharmaceutically acceptable carrier includes, but is not limited to, a buffer, excipient, stabilizer, or preservative.

As used herein, "treatment" (and grammatical variations thereof such as "treat" or "treating") refers to clinical intervention in an attempt to alter the natural course of a disease in the individual being treated, and can be performed either for prophylaxis or during the course of clinical pathology. Desirable effects of treatment include, but are not limited to, preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, preventing metastasis, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. In some aspects, antibodies of the invention are used to delay development of a disease or to slow the progression of a disease.

The term “variable region” or “variable domain” refers to the domain of an antibody heavy or light chain that is involved in binding the antibody to antigen. The variable domains of the heavy chain and light chain (VH and VL, respectively) of a native antibody generally have similar structures, with each domain comprising four conserved framework regions (FRs) and three complementary determining regions (CDRs). (See, e.g., Kindt et al. *Kuby Immunology*, 6th ed., W.H. Freeman and Co., page 91 (2007).) A single VH or VL domain may be sufficient to confer antigen-binding specificity. Furthermore, antibodies that bind a particular antigen may be isolated using a VH or VL domain from an antibody that binds the antigen to screen a library of complementary VL or VH domains, respectively. See, e.g., Portolano et al., *J. Immunol.* 150:880-887 (1993); Clarkson et al., *Nature* 352:624-628 (1991).

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

2. Detailed description of the embodiments of the invention

In one aspect, the invention is based, in part, on the provision of antibodies that specifically bind to human C3bBb that were obtained upon screening using a stabilized C3bBb complex. In certain aspects, antibodies that bind to human C3bBb are provided. Antibodies of the invention are useful, e.g., for the diagnosis, prevention or treatment of diseases, such as ocular diseases, e.g. age related macular degeneration.

A. Exemplary Anti-C3bBb Antibodies

In one aspect, the invention provides an antibody that specifically binds to human C3bBb. In another aspect, the invention provides an antibody that specifically binds to human C3bBb comprising a Bb subunit of factor B (FB) with a D279G mutation. In one embodiment, the antibody binds to human C3bBb comprising a Bb subunit of factor B (FB) with an amino acid sequence of SEQ ID NO: 492.

In another aspect, the invention provides an antibody that specifically binds to human C3bBb comprising a Bb subunit of factor B (FB) with D279G, K350N and M458I mutations. In one embodiment, the antibody binds to human C3bBb

comprising a Bb subunit of factor B (FB) with an amino acid sequence of SEQ ID NO: 493.

In another aspect, the invention provides an antibody that binds to human C3bBb, wherein the antibody:

- 5 - binds to wild-type human C3bBb, and/or
- binds to recombinant human C3bBb, which comprises the Bb subunit of a recombinant Factor B (FB) protein, which comprises a D279G mutation and optionally mutations K350N and/or a M458I; and/or
- inhibits the alternative pathway; and/or
- 10 - is an agonist or antagonist of C3bBb activity; and/or
- specifically binds to cynomolgus C3bBb and human C3bBb, and/or
- specifically binds to African green monkey C3bBb and human C3bBb, and/or
- binds with an affinity of ≤ 10 nM at 37 °C as measured by SPR.

15 Antibodies of the invention may be provided by screening using a stabilized C3bBb that was provided using a recombinant FB protein with a D279G and optionally, further mutations K350N and/or M458I. Wild type C3bBb is a rapidly decaying molecule, which requires stabilization to be used for antibody screening purposes. The inventors of the present invention were able to increase the half life of
20 the C3bBb complex from about 5 minutes to 11 hours, which allowed for using the stabilized complex for antibody generation in a phage library panning.

 Hence, antibodies of the invention specifically bind to stabilized C3bBb, particularly to C3bBb comprising the Bb subunit of factor B (FB) with a D279G mutation and optionally mutations K350N and/or a M458I. In one embodiment, the
25 antibodies of the invention specifically bind to stabilized C3bBb comprising the Bb subunit of factor B (FB) with D279G, K350N and M458I mutations (preferably of FB with an amino acid sequence of SEQ ID NO: 493).

 Hence, one aspect of the invention is an antibody that binds to human C3bBb comprising the Bb subunit of recombinant factor B (FB) with D279G,
30 K350N and M458I mutations (preferably of FB with an amino acid sequence of SEQ ID NO: 493) that inhibits the alternative pathway.

 Also, antibodies of the invention specifically bind to wild-type human C3bBb (Example 14) and are capable of inhibiting the alternative pathway (Example 9).

The antibodies of the invention bind to an epitope on human C3bBb that includes amino acid residues of the C3b subunit and amino acid residues of the Bb subunit of human C3bBb. This may be achieved by screening antibodies using a stabilized C3bBb as target antigen, e.g. by a method as described herein.

5 The epitope of antibodies of the invention may be identified by methods known in the art, e.g., by cryogenic electron microscopy. P1AF8499 (#20, see Examples 2 and 4) of the invention was analyzed by cryogenic electron microscopy of the trimeric complex of the antibody with C3bBb (Example 4). As indicated in Figure 1, the epitope is a conformational epitope including amino acid residues of
10 the C3b subunit and amino acid residues of the Bb subunit of human C3bBb, which results in that the antibodies specifically bind to C3bBb while showing no relevant binding activity to its subunits C3b and Bb. Cryogenic electron microscopy was used to identify amino acids that are bound by the antibody of the invention (Table E5 of Example 4).

15 In one aspect of the invention, the antibody binds to an epitope comprising the following amino acid residues on wild-type human C3bBb as detected by cryogenic electron microscopy, preferably with a method according to Example 4:

- C3b subunit: Arg444, Lys534, Gly539, Ser540, Val524, Lys544, Gly546, Gln547, Ser548, Arg551, Gln557, Gln558, Thr560, Lys562, Glu564,
20 Glu758, Pro759, Lys761, Asn762, Ile764, Leu768, Asn770, Asp797, and
- Bb subunit: Tyr465, Lys473, Ile474, Ser475, Ile477, Gly482, His483, Lys513, Val514, Ser515, Lys520, Arg521, Asp522, Glu610, and Lys613.

 In one embodiment the antibody binds to the same or an overlapping epitope than the epitope bound by antibody having a VH domain of SEQ ID NO: 39 and a
25 VL domain of SEQ ID NO: 30.

 Screening of antibodies binding to human C3bBb was done with phage library panning and further engineering of the directly generated antibodies resulting in a plurality of antibodies that were identified to bind to a stabilized C3bBb. Amino acid sequences of VH and VL domains of the antibodies are indicated in Table D1.

Table D1: amino acid sequence numbers of variable heavy chain and variable light chain domains of anti-C3bBb antibodies

#	identifier		VH (SEQ ID NO:)	VL (SEQ ID NO:)
1	P1AG9426	IgG	1	2
2	P1AG9376	IgG	3	4
3	P1AG9372	IgG	5	6
4	P1AG9420	IgG	7	8
5	P1AG9391	IgG	9	10
6	P1AH1205	Fab	11	12
7	P1AH1199	Fab	13	14
8	C3bBb.P045.072	Fab	15	16
9	C3bBb.P045.236	Fab	17	18
10	C3bBb.P045.225	Fab	19	20
11	C3bBb.P048.152	Fab	21	22
12	C3bBb.P048.061	Fab	23	24
13	C3bBb.P048.127	Fab	25	26
14	C3bBb.P048.241	Fab	27	28
15	C3bBb.P048.230	Fab	29	30
16	C3bBb.P048.204	Fab	31	32
17	C3bBb.P048.333	Fab	33	34
18	C3bBb.P053.095	Fab	35	36
19	C3bBb.P055.015	Fab	37	38
20	P1AF8499	Fab	39	40
21	GQ-5_1	Fab	41	42
22	GQ-11_1	Fab	43	44
23	PT5622.F19	Fab	45	46
24	PT5624.P06	Fab	47	48
25	PT5624.M09	Fab	49	50
26	PT5626.M10	Fab	51	52
27	PT5626.C10	Fab	53	54
28	PT5628.E16	Fab	55	56
29	PT5630.D05	Fab	57	58
30	PT5630.A20	Fab	59	60
31	PT5632.A13	Fab	61	62
32	PT5634.N13	Fab	63	64
33	PT5634.M24	Fab	65	66

34	PT5636.P22	Fab	67	68
35	PT5625.G07	Fab	69	70
36	PT5627.M20	Fab	71	72
37	PT5627.M12	Fab	73	74
38	PT5629.F09	Fab	75	76
39	PT5629.H08	Fab	77	78
40	PT5631.D21	Fab	79	80
41	PT5633.I03	Fab	81	82
42	PT5635.C08	Fab	83	84
43	PT5639.G15	Fab	85	86
44	PT5622.A20	Fab	87	88
45	PT5622.C12	Fab	89	90
46	PT5622.G24	Fab	91	92
47	PT5622.I20	Fab	93	94
48	PT5622.J24	Fab	95	96
49	PT5624.A21	Fab	97	98
50	PT5624.B10	Fab	99	100
51	PT5624.N05	Fab	101	102
52	PT5624.P11	Fab	103	104
53	PT5626.A12	Fab	105	106
54	PT5626.N08	Fab	107	108
55	PT5626.N18	Fab	109	110
56	PT5626.O09	Fab	111	112
57	PT5628.B13	Fab	113	114
58	PT5628.C21	Fab	115	116
59	PT5628.E12	Fab	117	118
60	PT5628.I07	Fab	119	120
61	PT5628.P14	Fab	121	122
62	PT5630.G05	Fab	123	124
63	PT5630.K04	Fab	125	126
64	PT5630.M11	Fab	127	128
65	PT5630.N06	Fab	129	130
66	PT5630.O08	Fab	131	132
67	PT5632.A10	Fab	133	134
68	PT5632.A15	Fab	135	136
69	PT5632.B15	Fab	137	138
70	PT5632.D11	Fab	139	140
71	PT5632.J23	Fab	141	142
72	PT5634.A17	Fab	143	144
73	PT5634.A21	Fab	145	146
74	PT5634.K10	Fab	147	148
75	PT5634.M16	Fab	149	150

76	PT5634.N11	Fab	151	152
77	PT5634.P19	Fab	153	154
78	PT5636.A16	Fab	155	156
79	PT5636.D21	Fab	157	158
80	PT5636.M03	Fab	159	160
81	PT5636.N13	Fab	161	162
82	PT5636.P11	Fab	163	164
83	PT5636.P15	Fab	165	166
84	PT5638.C06	Fab	167	168
85	PT5638.C20	Fab	169	170
86	PT5638.E14	Fab	171	172
87	PT5638.J23	Fab	173	174
88	PT5638.O14	Fab	175	176
89	PT5638.P12	Fab	177	178
90	PT5623.E21	Fab	179	180
91	PT5623.F17	Fab	181	182
92	PT5623.G08	Fab	183	184
93	PT5623.H05	Fab	185	186
94	PT5623.O08	Fab	187	188
95	PT5625.A05	Fab	189	190
96	PT5625.B14	Fab	191	192
97	PT5625.C15	Fab	193	194
98	PT5625.G05	Fab	195	196
99	PT5625.L22	Fab	197	198
100	PT5625.O14	Fab	199	200
101	PT5627.I21	Fab	201	202
102	PT5629.F04	Fab	203	204
103	PT5629.L22	Fab	205	206
104	PT5629.L24	Fab	207	208
105	PT5629.M15	Fab	209	210
106	PT5631.H06	Fab	211	212
107	PT5631.K12	Fab	213	214
108	PT5631.N17	Fab	215	216
109	PT5631.P07	Fab	217	218
110	PT5633.E09	Fab	219	220
111	PT5633.G19	Fab	221	222
112	PT5635.F04	Fab	223	224
113	PT5635.L21	Fab	225	226
114	PT5635.O15	Fab	227	228
115	PT5637.B23	Fab	229	230
116	PT5637.C20	Fab	231	232
117	PT5637.K09	Fab	233	234

118	PT5637.L15	Fab	235	236
119	PT5637.M03	Fab	237	238
120	PT5637.P15	Fab	239	240
121	PT5639.B15	Fab	241	242
122	PT5639.P05	Fab	243	244
123	PT5625.G07 22.F19 2	Fab	245	246
124	PT5625.G07 24.M09 1	Fab	247	248
125	PT5625.G07 24.P06 2	Fab	249	250
126	PT5625.G07 26.C10 1	Fab	251	252
127	PT5625.G07 26.M10 2	Fab	253	254
128	PT5625.G07 28.E16 1	Fab	255	256
129	PT5625.G07 30.A20 1	Fab	257	258
130	PT5625.G07 32.A13 2	Fab	259	260
131	PT5625.G07 34.M24 1	Fab	261	262
132	PT5625.G07 34.N13 3	Fab	263	264
133	PT5625.G07 36.P22 1	Fab	265	266
134	PT5627.M20 24.M09 1	Fab	267	268
135	PT5627.M20 24.P06 1	Fab	269	270
136	PT5627.M20 26.C10 1	Fab	271	272
137	PT5627.M20 26.M10 2	Fab	273	274
138	PT5627.M20 28.E16 2	Fab	275	276
139	PT5627.M20 30.D05 1	Fab	277	278
140	PT5627.M20 32.A13 1	Fab	279	280
141	PT5627.M20 34.M24 2	Fab	281	282
142	PT5627.M20 34.N13 4	Fab	283	284
143	PT5627.M20 36.P22 1	Fab	285	286
144	PT5627.M12 22.F19 1	Fab	287	288
145	PT5627.M12 24.M09 1	Fab	289	290
146	PT5627.M12 26.M10 2	Fab	291	292
147	PT5627.M12 32.A13 2	Fab	293	294
148	PT5627.M12 34.M24 2	Fab	295	296
149	PT5627.M12 34.N13 1	Fab	297	298
150	PT5629.F09 26.C10 1	Fab	299	300
151	PT5629.F09 28.E16 1	Fab	301	302
152	PT5629.F09 30.A20 1	Fab	303	304
153	PT5629.F09 30.D05 1	Fab	305	306
154	PT5629.F09 32.A13 3	Fab	307	308
155	PT5629.F09 36.P22 2	Fab	309	310
156	PT5629.H08 22.F19 4	Fab	311	312
157	PT5629.H08 24.M09 4	Fab	313	314
158	PT5629.H08 24.P06 2	Fab	315	316
159	PT5629.H08 26.C10 1	Fab	317	318

160	PT5629.H08 26.M10 1	Fab	319	320
161	PT5629.H08 28.E16 2	Fab	321	322
162	PT5629.H08 30.A20 2	Fab	323	324
163	PT5629.H08 30.D05 1	Fab	325	326
164	PT5629.H08 32.A13 1	Fab	327	328
165	PT5629.H08 34.M24 2	Fab	329	330
166	PT5629.H08 34.N13 2	Fab	331	332
167	PT5629.H08 36.P22 4	Fab	333	334
168	PT5631.D21 22.F19 2	Fab	335	336
169	PT5631.D21 24.M09 1	Fab	337	338
170	PT5631.D21 24.P06 4	Fab	339	340
171	PT5631.D21 26.C10 1	Fab	341	342
172	PT5631.D21 26.M10 4	Fab	343	344
173	PT5631.D21 28.E16 3	Fab	345	346
174	PT5631.D21 30.A20 4	Fab	347	348
175	PT5631.D21 30.D05 1	Fab	349	350
176	PT5631.D21 32.A13 4	Fab	351	352
177	PT5631.D21 34.M24 4	Fab	353	354
178	PT5631.D21 34.N13 2	Fab	355	356
179	PT5631.D21 36.P22 3	Fab	357	358
180	PT5633.I03 22.F19 1	Fab	359	360
181	PT5633.I03 24.M09 1	Fab	361	362
182	PT5633.I03 24.P06 4	Fab	363	364
183	PT5633.I03 26.C10 1	Fab	365	366
184	PT5633.I03 26.M10 4	Fab	367	368
185	PT5633.I03 28.E16 4	Fab	369	370
186	PT5633.I03 30.A20 1	Fab	371	372
187	PT5633.I03 30.D05 1	Fab	373	374
188	PT5633.I03 32.A13 1	Fab	375	376
189	PT5633.I03 34.M24 2	Fab	377	378
190	PT5633.I03 34.N13 1	Fab	379	380
191	PT5633.I03 36.P22 2	Fab	381	382
192	PT5635.C08 22.F19 1	Fab	383	384
193	PT5635.C08 24.M09 1	Fab	385	386
194	PT5635.C08 24.P06 1	Fab	387	388
195	PT5635.C08 26.C10 1	Fab	389	390
196	PT5635.C08 26.M10 2	Fab	391	392
197	PT5635.C08 28.E16 1	Fab	393	394
198	PT5635.C08 30.A20 1	Fab	395	396
199	PT5635.C08 30.D05 3	Fab	397	398
200	PT5635.C08 32.A13 3	Fab	399	400
201	PT5635.C08 34.M24 2	Fab	401	402

202	PT5635.C08 34.N13 1	Fab	403	404
203	PT5635.C08 36.P22 1	Fab	405	406
204	PT5639.G15 22.F19 2	Fab	407	408
205	PT5639.G15 24.P06 1	Fab	409	410
206	PT5639.G15 24.M09 4	Fab	411	412
207	PT5639.G15 26.M10 3	Fab	413	414
208	PT5639.G15 28.E16 1	Fab	415	416
209	PT5639.G15 30.A20 1	Fab	417	418
210	PT5639.G15 30.D05 1	Fab	419	420
211	PT5639.G15 34.N13 4	Fab	421	422
212	PT5639.G15 34.M24 3	Fab	423	424
213	PT5639.G15 36.P22 3	Fab	425	426
214	PT5625.G07 30.D05 1	Fab	427	428
215	PT5627.M12 26.C10 1	Fab	429	430
216	PT5627.M12 30.A20 2	Fab	431	432
217	PT5629.F09 34.N13 3	Fab	433	434

Antibodies derived from antibody screening

Each one of the 217 antibodies disclosed herein are disclosed as an invention, being defined by their 6 CDRs as derived from the amino acid sequences of their VH domain amino acid sequence and their VL amino acid sequence as indicated in Table D1. Alternatively, the antibodies of the invention are characterized by a VH domain having the VH amino acid sequence indicated in Table D1, and a VL domain having the VL amino acid sequence as indicated in Table D1.

One aspect of the invention is an antibody that specifically binds to human C3bBb comprising a set of six CDRs of any one of the antibodies of Table D1. In one embodiment the antibody comprises a variable light chain amino acid sequence and a variable heavy chain amino acid sequence of any one of the antibodies of Table D1.

In one aspect the invention refers to an antibody selected from antibody #1 to antibody #217 as indicated in the first column of Table D1, wherein the antibody comprises a set of six CDRs as derived from the amino acid sequences of its respective VH domain amino acid sequence and its respective VL amino acid sequence as indicated in Table D1. In one embodiment, the antibody comprises a variable light chain amino acid sequence and a variable heavy chain amino acid sequence of any one of the antibodies of Table D1.

In one aspect the invention refers to an antibody selected from antibody #1 to antibody #122 as indicated in the first column of Table D1, wherein the antibody comprises a set of six CDRs as derived from the amino acid sequences of its respective VH domain amino acid sequence and its respective VL amino acid sequence as indicated in Table D1. In one embodiment, the antibody comprises a variable light chain amino acid sequence and a variable heavy chain amino acid sequence of any one of the antibodies of Table D1.

In one aspect the invention refers to an antibody selected from antibody #1 to antibody #7 and #22 to #217 as indicated in the first column of Table D1, wherein the antibody comprises a set of six CDRs as derived from the amino acid sequences of its respective VH domain amino acid sequence and its respective VL amino acid sequence as indicated in Table D1. In one embodiment, the antibody comprises a variable light chain amino acid sequence and a variable heavy chain amino acid sequence of any one of the antibodies of Table D1.

In one aspect the invention refers to an antibody selected from antibody #1 to antibody #7 and #22 to #122 as indicated in the first column of Table D1, wherein the antibody comprises a set of six CDRs as derived from the amino acid sequences of its respective VH domain amino acid sequence and its respective VL amino acid sequence as indicated in Table D1. In one embodiment, the antibody comprises a variable light chain amino acid sequence and a variable heavy chain amino acid sequence of any one of the antibodies of Table D1.

In one aspect the invention refers to an antibody selected from antibody #1 to antibody #7 as indicated in the first column of Table D1, wherein the antibody comprises a set of six CDRs as derived from the amino acid sequences of its respective VH domain amino acid sequence and its respective VL amino acid sequence as indicated in Table D1. In one embodiment, the antibody comprises a variable light chain amino acid sequence and a variable heavy chain amino acid sequence of any one of the antibodies of Table D1.

In one aspect the invention refers to an antibody derived from the antibody #22 as indicated in the first column of Table D1.

Another aspect of the invention is an antibody that specifically binds to human C3bBb comprising a set of VH and VL domains of any one of the antibodies of Table D1.

In one embodiment, the antibody comprises a set of six CDRs of any one of the antibodies of Table E4. In another embodiment, the antibody comprises a set of VH and VL domains of any one of the antibodies of Table E4.

Individual antibodies

5 Antibody P1AG9426

In another aspect, the invention provides an antibody comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:449; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:450; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:451; (d) CDR-L1 comprising the amino acid
10 sequence of SEQ ID NO:452; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:453; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:454 (corresponding to antibody #1, P1AG9426).

In another aspect, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VH of SEQ ID NO:1. In another embodiment, an anti-C3bBb
15 antibody comprises one or more of the CDR sequences of the VL of SEQ ID NO:2. In another embodiment, an anti-C3bBb antibody comprises the CDR sequences of the VH of SEQ ID NO:1 and the CDR sequences of the VL of SEQ ID NO:2.

In a further aspect, an anti-C3bBb antibody comprises the CDR-H1, CDR-H2 and CDR-H3 amino acid sequences of the VH domain of SEQ ID NO:1 and the
20 CDR-L1, CDR-L2 and CDR-L3 amino acid sequences of the VL domain of SEQ ID NO:2.

In one aspect, an anti-C3bBb antibody comprises one or more of the heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:1 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%,
25 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:1. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:1 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence
30 of the VH domain of SEQ ID NO:1. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:1 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:1. In another aspect, the anti-

C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:1 and a framework of at least of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:1.

5 In one aspect, an anti-C3bBb antibody comprises one or more of the light chain CDR amino acid sequences of the VL domain of SEQ ID NO:2 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:2. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:2
10 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:2. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:2 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:2. In another aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:2 and a framework of at least particularly of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:2.

20 In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:449; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:450; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:451; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:452; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:453; and
25 (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:454, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:1, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:2. In one aspect,
30 the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:1. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:449; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:450; (c) CDR-H3 comprising the amino acid sequence
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of SEQ ID NO:451; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:452; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:453; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:454, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:1, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:2; wherein the antibody specifically binds to human C3bBb. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:1. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2. In one aspect, the antibody binds to C3bBb having a dissociation constant (KD) that is up to 10 fold reduced or up to 10 fold increased when compared to the dissociation constant (KD) of an antibody comprising a VH sequence of SEQ ID NO:1 and a VL sequence of SEQ ID NO:2.

15 In another aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:1. In one aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2. In certain aspects, a VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:1. In certain aspects, substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VH sequence in SEQ ID NO:1, including post-translational modifications of that sequence. In a particular aspect, the VH comprises one, two or three CDRs selected from: (a) CDR-H1, comprising the amino acid sequence of SEQ ID NO:449, (b) CDR-H2, comprising the amino acid sequence of SEQ ID NO:450, and (c) CDR-H3, comprising the amino acid sequence of SEQ ID NO:451. In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a light chain variable domain (VL) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:2. In one aspect, an anti-C3bBb antibody comprises a light chain variable domain (VL) sequence having at least 95% sequence identity to the amino acid sequence of SEQ

5 ID NO:2. In certain aspects, a VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:2. In certain aspects, the substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VL sequence in SEQ ID NO:2, including post-translational modifications of that sequence. In a particular aspect, the VL comprises one, two or three CDRs selected from: (a) CDR-L1, comprising the amino acid sequence of SEQ ID NO:452, (b) CDR-L2, comprising the amino acid sequence of SEQ ID NO:453, and (c) CDR-L3, comprising the amino acid sequence of SEQ ID NO:454.

15 In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a VH sequence as in any of the aspects provided above, and a VL sequence as in any of the aspects provided above. In one aspect, the antibody comprises the VH and VL sequences in SEQ ID NO:1 and SEQ ID NO:2, respectively, including post-translational modifications of those sequences.

20 In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a heavy chain amino acid sequence of SEQ OF NO:435 and a light chain amino acid sequence of SEQ ID NO:436.

25 In one aspect, an antibody is provided that comprises a VH domain as described above and the heavy chain constant domain amino acid sequences as comprised in SEQ ID NO:435, and a VL domain as described above and the light chain constant domain amino acid sequences as comprised in SEQ ID NO:436.

Antibody P1AG9376

30 In another aspect, the invention provides an antibody comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:455; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:456; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:457; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:458; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:459; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:460 (corresponding to antibody #2, P1AG9376).

In another aspect, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VH of SEQ ID NO:3. In another embodiment, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VL of SEQ ID NO:4. In another embodiment, an anti-C3bBb antibody comprises the CDR sequences of the VH of SEQ ID NO:3 and the CDR sequences of the VL of SEQ ID NO:4.

In a further aspect, an anti-C3bBb antibody comprises the CDR-H1, CDR-H2 and CDR-H3 amino acid sequences of the VH domain of SEQ ID NO:3 and the CDR-L1, CDR-L2 and CDR-L3 amino acid sequences of the VL domain of SEQ ID NO:4.

In one aspect, an anti-C3bBb antibody comprises one or more of the heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:3 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:3. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:3 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:3. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:3 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:3. In another aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:3 and a framework of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:3.

In one aspect, an anti-C3bBb antibody comprises one or more of the light chain CDR amino acid sequences of the VL domain of SEQ ID NO:4 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:4. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:4 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:4. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:4 and a framework of at least 95% sequence identity to the framework amino

acid sequence of the VL domain of SEQ ID NO:4. In another aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:4 and a framework of at least particularly of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:4.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:455; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:456; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:457; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:458; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:459; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:460, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:3, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:4. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:3. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:4.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:455; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:456; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:457; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:458; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:459; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:460, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:3, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:4; wherein the antibody specifically binds to human C3bBb. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:3. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:4. In one aspect, the antibody binds to C3bBb having a dissociation constant (KD) that is up to 10 fold reduced or up to 10 fold increased when compared to the dissociation constant (KD) of an antibody comprising a VH sequence of SEQ ID NO:3 and a VL sequence of SEQ ID NO:4.

In another aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:3. In one aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:4. In certain aspects, a VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:3. In certain aspects, substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VH sequence in SEQ ID NO:3, including post-translational modifications of that sequence. In a particular aspect, the VH comprises one, two or three CDRs selected from: (a) CDR-H1, comprising the amino acid sequence of SEQ ID NO:455, (b) CDR-H2, comprising the amino acid sequence of SEQ ID NO:456, and (c) CDR-H3, comprising the amino acid sequence of SEQ ID NO:457. In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a light chain variable domain (VL) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:4. In one aspect, an anti-C3bBb antibody comprises a light chain variable domain (VL) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:4. In certain aspects, a VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:4. In certain aspects, the substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VL sequence in SEQ ID NO:4, including post-translational modifications of that sequence. In a particular aspect, the VL comprises one, two or three CDRs selected from: (a) CDR-L1, comprising the amino acid sequence of SEQ ID NO:458, (b) CDR-L2, comprising the amino acid sequence of SEQ ID NO:459, and (c) CDR-L3, comprising the amino acid sequence of SEQ ID NO:460.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a VH sequence as in any of the aspects provided above, and a VL sequence as in any of the aspects provided above. In one aspect, the antibody comprises the VH and VL sequences in SEQ ID NO:3 and SEQ ID NO:4, respectively, including post-translational modifications of those sequences.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a heavy chain amino acid sequence of SEQ OF NO:437 and a light chain amino acid sequence of SEQ ID NO:438.

In one aspect, an antibody is provided that comprises a VH domain as described above and the heavy chain constant domain amino acid sequences as comprised in SEQ ID NO:437, and a VL domain as described above and the light chain constant domain amino acid sequences as comprised in SEQ ID NO:438.

Antibody P1AG9372

In another aspect, the invention provides an antibody comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:461; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:462; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:463; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:464; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:465; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:466 (corresponding to antibody #3, P1AG9372).

In another aspect, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VH of SEQ ID NO:5. In another embodiment, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VL of SEQ ID NO:6. In another embodiment, an anti-C3bBb antibody comprises the CDR sequences of the VH of SEQ ID NO:5 and the CDR sequences of the VL of SEQ ID NO:6.

In a further aspect, an anti-C3bBb antibody comprises the CDR-H1, CDR-H2 and CDR-H3 amino acid sequences of the VH domain of SEQ ID NO:5 and the CDR-L1, CDR-L2 and CDR-L3 amino acid sequences of the VL domain of SEQ ID NO:6.

In one aspect, an anti-C3bBb antibody comprises one or more of the heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:5 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of

the VH domain of SEQ ID NO:5. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:5 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:5. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:5 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:5. In another aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:5 and a framework of at least of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:5.

In one aspect, an anti-C3bBb antibody comprises one or more of the light chain CDR amino acid sequences of the VL domain of SEQ ID NO:6 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:6. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:6 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:6. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:6 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:6. In another aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:6 and a framework of at least particularly of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:6.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:461; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:462; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:463; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:464; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:465; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:466, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:5, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100% sequence identity to the amino acid sequence of SEQ ID NO:6. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:5. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6.

5 In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:461; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:462; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:463; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:464; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:465; and
10 (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:466, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:5, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:6; wherein the
15 antibody specifically binds to human C3bBb. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:5. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6. In one aspect, the antibody binds to C3bBb having a dissociation constant (KD) that is up to 10 fold reduced or up to 10 fold increased when compared
20 to the dissociation constant (KD) of an antibody comprising a VH sequence of SEQ ID NO:5 and a VL sequence of SEQ ID NO:6.

 In another aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:5.
25 In one aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6. In certain aspects, a VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference
30 sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:5. In certain aspects, substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VH sequence in SEQ ID
35 NO:5, including post-translational modifications of that sequence. In a particular aspect, the VH comprises one, two or three CDRs selected from: (a) CDR-H1,

comprising the amino acid sequence of SEQ ID NO:461, (b) CDR-H2, comprising the amino acid sequence of SEQ ID NO:462, and (c) CDR-H3, comprising the amino acid sequence of SEQ ID NO:463. In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a light chain variable domain (VL) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:6. In one aspect, an anti-C3bBb antibody comprises a light chain variable domain (VL) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6. In certain aspects, a VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:6. In certain aspects, the substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VL sequence in SEQ ID NO:6, including post-translational modifications of that sequence. In a particular aspect, the VL comprises one, two or three CDRs selected from: (a) CDR-L1, comprising the amino acid sequence of SEQ ID NO:464, (b) CDR-L2, comprising the amino acid sequence of SEQ ID NO:465, and (c) CDR-L3, comprising the amino acid sequence of SEQ ID NO:466.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a VH sequence as in any of the aspects provided above, and a VL sequence as in any of the aspects provided above. In one aspect, the antibody comprises the VH and VL sequences in SEQ ID NO:5 and SEQ ID NO:6, respectively, including post-translational modifications of those sequences.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a heavy chain amino acid sequence of SEQ OF NO:439 and a light chain amino acid sequence of SEQ ID NO:440.

In one aspect, an antibody is provided that comprises a VH domain as described above and the heavy chain constant domain amino acid sequences as comprised in SEQ ID NO:439, and a VL domain as described above and the light chain constant domain amino acid sequences as comprised in SEQ ID NO:440.

Antibody P1AG9420

In another aspect, the invention provides an antibody comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:467; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:468; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:469; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:470; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:471; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:472 (corresponding to antibody #4, P1AG9420).

In another aspect, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VH of SEQ ID NO:7. In another embodiment, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VL of SEQ ID NO:8. In another embodiment, an anti-C3bBb antibody comprises the CDR sequences of the VH of SEQ ID NO:7 and the CDR sequences of the VL of SEQ ID NO:8.

In a further aspect, an anti-C3bBb antibody comprises the CDR-H1, CDR-H2 and CDR-H3 amino acid sequences of the VH domain of SEQ ID NO:7 and the CDR-L1, CDR-L2 and CDR-L3 amino acid sequences of the VL domain of SEQ ID NO:8.

In one aspect, an anti-C3bBb antibody comprises one or more of the heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:7 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:7. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:7 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:7. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:7 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:7. In another aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:7 and a framework of at least of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:7.

In one aspect, an anti-C3bBb antibody comprises one or more of the light chain CDR amino acid sequences of the VL domain of SEQ ID NO:8 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of

the VL domain of SEQ ID NO:8. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:8 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:8. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:8 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:8. In another aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:8 and a framework of at least particularly of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:8.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:467; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:468; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:469; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:470; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:471; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:472, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:7, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:8. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:467; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:468; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:469; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:470; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:471; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:472, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:7, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:8; wherein the antibody specifically binds to human C3bBb. In one aspect, the VH domain has at

least 95% sequence identity to the amino acid sequence of SEQ ID NO:7. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8. In one aspect, the antibody binds to C3bBb having a dissociation constant (KD) that is up to 10 fold reduced or up to 10 fold increased when compared to the dissociation constant (KD) of an antibody comprising a VH sequence of SEQ ID NO:7 and a VL sequence of SEQ ID NO:8.

In another aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:7.

10 In one aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8. In certain aspects, a VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference

15 sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:7. In certain aspects, substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VH sequence in SEQ ID

20 NO:7, including post-translational modifications of that sequence. In a particular aspect, the VH comprises one, two or three CDRs selected from: (a) CDR-H1, comprising the amino acid sequence of SEQ ID NO:467, (b) CDR-H2, comprising the amino acid sequence of SEQ ID NO:468, and (c) CDR-H3, comprising the amino acid sequence of SEQ ID NO:469. In another aspect, an anti-C3bBb antibody is

25 provided, wherein the antibody comprises a light chain variable domain (VL) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:8. In one aspect, an anti-C3bBb antibody comprises a light chain variable domain (VL) sequence having at least 95% sequence identity to the amino acid sequence of SEQ

30 ID NO:8. In certain aspects, a VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been

35 substituted, inserted and/or deleted in SEQ ID NO:8. In certain aspects, the substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VL sequence in SEQ ID

NO:8, including post-translational modifications of that sequence. In a particular aspect, the VL comprises one, two or three CDRs selected from: (a) CDR-L1, comprising the amino acid sequence of SEQ ID NO:470, (b) CDR-L2, comprising the amino acid sequence of SEQ ID NO:471, and (c) CDR-L3, comprising the amino acid sequence of SEQ ID NO:472.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a VH sequence as in any of the aspects provided above, and a VL sequence as in any of the aspects provided above. In one aspect, the antibody comprises the VH and VL sequences in SEQ ID NO:7 and SEQ ID NO:8, respectively, including post-translational modifications of those sequences.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a heavy chain amino acid sequence of SEQ OF NO:441 and a light chain amino acid sequence of SEQ ID NO:442.

In one aspect, an antibody is provided that comprises a VH domain as described above and the heavy chain constant domain amino acid sequences as comprised in SEQ ID NO:441, and a VL domain as described above and the light chain constant domain amino acid sequences as comprised in SEQ ID NO:442.

Antibody P1AG9391

In another aspect, the invention provides an antibody comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:473; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:474; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:475; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:476; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:477; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:478 (corresponding to antibody #5, P1AG9391).

In another aspect, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VH of SEQ ID NO:9. In another embodiment, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VL of SEQ ID NO:10. In another embodiment, an anti-C3bBb antibody comprises the CDR sequences of the VH of SEQ ID NO:9 and the CDR sequences of the VL of SEQ ID NO:10.

In a further aspect, an anti-C3bBb antibody comprises the CDR-H1, CDR-H2 and CDR-H3 amino acid sequences of the VH domain of SEQ ID NO:9 and the

CDR-L1, CDR-L2 and CDR-L3 amino acid sequences of the VL domain of SEQ ID NO:10.

5 In one aspect, an anti-C3bBb antibody comprises one or more of the heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:9 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:9. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:9 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:9. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:9 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:9. In another aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:9 and a framework of at least of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:9.

20 In one aspect, an anti-C3bBb antibody comprises one or more of the light chain CDR amino acid sequences of the VL domain of SEQ ID NO:10 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:10. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:10 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:10. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:10 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:10. In another aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:10 and a framework of at least particularly of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:10.

35 In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:473; (b) CDR-H2 comprising the amino

acid sequence of SEQ ID NO:474; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:475; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:476; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:477; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:478, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:9, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:10. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:9. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:10.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:473; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:474; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:475; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:476; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:477; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:478, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:9, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:10; wherein the antibody specifically binds to human C3bBb. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:9. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:10. In one aspect, the antibody binds to C3bBb having a dissociation constant (KD) that is up to 10 fold reduced or up to 10 fold increased when compared to the dissociation constant (KD) of an antibody comprising a VH sequence of SEQ ID NO:9 and a VL sequence of SEQ ID NO:10.

In another aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:9. In one aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:10. In certain aspects, a VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference

sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:9. In certain aspects, substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VH sequence in SEQ ID NO:9, including post-translational modifications of that sequence. In a particular aspect, the VH comprises one, two or three CDRs selected from: (a) CDR-H1, comprising the amino acid sequence of SEQ ID NO:473, (b) CDR-H2, comprising the amino acid sequence of SEQ ID NO:474, and (c) CDR-H3, comprising the amino acid sequence of SEQ ID NO:475. In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a light chain variable domain (VL) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:10. In one aspect, an anti-C3bBb antibody comprises a light chain variable domain (VL) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:10. In certain aspects, a VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:10. In certain aspects, the substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VL sequence in SEQ ID NO:10, including post-translational modifications of that sequence. In a particular aspect, the VL comprises one, two or three CDRs selected from: (a) CDR-L1, comprising the amino acid sequence of SEQ ID NO:476, (b) CDR-L2, comprising the amino acid sequence of SEQ ID NO:477, and (c) CDR-L3, comprising the amino acid sequence of SEQ ID NO:478.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a VH sequence as in any of the aspects provided above, and a VL sequence as in any of the aspects provided above. In one aspect, the antibody comprises the VH and VL sequences in SEQ ID NO:9 and SEQ ID NO:10, respectively, including post-translational modifications of those sequences.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a heavy chain amino acid sequence of SEQ OF NO:443 and a light chain amino acid sequence of SEQ ID NO:444.

In one aspect, an antibody is provided that comprises a VH domain as described above and the heavy chain constant domain amino acid sequences as comprised in SEQ ID NO:443, and a VL domain as described above and the light chain constant domain amino acid sequences as comprised in SEQ ID NO:444.

5 Antibody P1AH1205

In another aspect, the invention provides an antibody comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:479; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:480; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:481; (d) CDR-L1 comprising the amino acid
10 sequence of SEQ ID NO:482; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:483; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:484 (corresponding to antibody #6, P1AH1205).

In another aspect, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VH of SEQ ID NO:11. In another embodiment, an anti-C3bBb
15 antibody comprises one or more of the CDR sequences of the VL of SEQ ID NO:12. In another embodiment, an anti-C3bBb antibody comprises the CDR sequences of the VH of SEQ ID NO:11 and the CDR sequences of the VL of SEQ ID NO:12.

In a further aspect, an anti-C3bBb antibody comprises the CDR-H1, CDR-H2 and CDR-H3 amino acid sequences of the VH domain of SEQ ID NO:11 and the
20 CDR-L1, CDR-L2 and CDR-L3 amino acid sequences of the VL domain of SEQ ID NO:12.

In one aspect, an anti-C3bBb antibody comprises one or more of the heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:11 and a
25 framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:11. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:11 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%,
30 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:11. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:11 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:11. In another aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid

sequences of the VH domain of SEQ ID NO:11 and a framework of at least of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:11.

5 In one aspect, an anti-C3bBb antibody comprises one or more of the light chain CDR amino acid sequences of the VL domain of SEQ ID NO:12 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:12. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:12 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:12. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:12 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:12. In another aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:12 and a framework of at least particularly of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:12.

20 In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:479; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:480; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:481; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:482; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:483; and 25 (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:484, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:11, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:12. In one aspect, 30 the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:11. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:12.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:479; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:480; (c) CDR-H3 comprising the amino acid sequence 35

of SEQ ID NO:481; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:482; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:483; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:484, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:11, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:12; wherein the antibody specifically binds to human C3bBb. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:11. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:12. In one aspect, the antibody binds to C3bBb having a dissociation constant (KD) that is up to 10 fold reduced or up to 10 fold increased when compared to the dissociation constant (KD) of an antibody comprising a VH sequence of SEQ ID NO:11 and a VL sequence of SEQ ID NO:12.

In another aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:11. In one aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:12. In certain aspects, a VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:11. In certain aspects, substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VH sequence in SEQ ID NO:11, including post-translational modifications of that sequence. In a particular aspect, the VH comprises one, two or three CDRs selected from: (a) CDR-H1, comprising the amino acid sequence of SEQ ID NO:479, (b) CDR-H2, comprising the amino acid sequence of SEQ ID NO:480, and (c) CDR-H3, comprising the amino acid sequence of SEQ ID NO:481. In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a light chain variable domain (VL) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:12. In one aspect, an anti-C3bBb antibody comprises a light chain variable domain (VL) sequence having at least 95% sequence identity to the amino acid sequence of SEQ

5 ID NO:12. In certain aspects, a VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:12. In certain aspects, the substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VL sequence in SEQ ID NO:12, including post-translational modifications of that sequence. In a particular aspect, the VL comprises one, two or three CDRs selected from: (a) CDR-L1, comprising the amino acid sequence of SEQ ID NO:482, (b) CDR-L2, comprising the amino acid sequence of SEQ ID NO:483, and (c) CDR-L3, comprising the amino acid sequence of SEQ ID NO:484.

15 In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a VH sequence as in any of the aspects provided above, and a VL sequence as in any of the aspects provided above. In one aspect, the antibody comprises the VH and VL sequences in SEQ ID NO:11 and SEQ ID NO:12, respectively, including post-translational modifications of those sequences.

20 In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a heavy chain amino acid sequence of SEQ OF NO:445 and a light chain amino acid sequence of SEQ ID NO:446.

25 In one aspect, an antibody is provided that comprises a VH domain as described above and the heavy chain constant domain amino acid sequences as comprised in SEQ ID NO:445, and a VL domain as described above and the light chain constant domain amino acid sequences as comprised in SEQ ID NO:446.

Antibody P1AH1199

30 In another aspect, the invention provides an antibody comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:485; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:486; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:487; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:488; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:489; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:490 (corresponding to antibody #7, P1AH1199).

In another aspect, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VH of SEQ ID NO:13. In another embodiment, an anti-C3bBb antibody comprises one or more of the CDR sequences of the VL of SEQ ID NO:14. In another embodiment, an anti-C3bBb antibody comprises the CDR sequences of the VH of SEQ ID NO:13 and the CDR sequences of the VL of SEQ ID NO:14.

In a further aspect, an anti-C3bBb antibody comprises the CDR-H1, CDR-H2 and CDR-H3 amino acid sequences of the VH domain of SEQ ID NO:13 and the CDR-L1, CDR-L2 and CDR-L3 amino acid sequences of the VL domain of SEQ ID NO:14.

In one aspect, an anti-C3bBb antibody comprises one or more of the heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:13 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:13. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:13 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:13. In one aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:13 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:13. In another aspect, the anti-C3bBb antibody comprises the three heavy chain CDR amino acid sequences of the VH domain of SEQ ID NO:13 and a framework of at least of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:13.

In one aspect, an anti-C3bBb antibody comprises one or more of the light chain CDR amino acid sequences of the VL domain of SEQ ID NO:14 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:14. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:14 and a framework of at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:14. In one aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ

ID NO:14 and a framework of at least 95% sequence identity to the framework amino acid sequence of the VL domain of SEQ ID NO:14. In another aspect, the anti-C3bBb antibody comprises the three light chain CDR amino acid sequences of the VL domain of SEQ ID NO:14 and a framework of at least particularly of at least 98% sequence identity to the framework amino acid sequence of the VH domain of SEQ ID NO:14.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:485; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:486; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:487; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:488; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:489; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:490, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:13, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:14. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:13. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:14.

In one aspect, the anti-C3bBb antibody comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:485; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:486; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:487; (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:488; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:489; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:490, and a VH domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:13, and a VL domain having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:14; wherein the antibody specifically binds to human C3bBb. In one aspect, the VH domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:13. In one aspect, the VL domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:14. In one aspect, the antibody binds to C3bBb having a dissociation constant (KD) that is up to 10 fold reduced or up to 10 fold increased when compared to the dissociation constant (KD) of an antibody comprising a VH sequence of SEQ ID NO:13 and a VL sequence of SEQ ID NO:14.

In another aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:13.

5 In one aspect, an anti-C3bBb antibody comprises a heavy chain variable domain (VH) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:14. In certain aspects, a VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-C3bBb antibody comprising that sequence retains the ability

10 to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:13. In certain aspects, substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VH sequence in SEQ ID NO:13, including post-translational modifications of that sequence. In a particular

15 aspect, the VH comprises one, two or three CDRs selected from: (a) CDR-H1, comprising the amino acid sequence of SEQ ID NO:485, (b) CDR-H2, comprising the amino acid sequence of SEQ ID NO:486, and (c) CDR-H3, comprising the amino acid sequence of SEQ ID NO:487. In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a light chain variable domain (VL)

20 sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:14. In one aspect, an anti-C3bBb antibody comprises a light chain variable domain (VL) sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:14. In certain aspects, a VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference

25 sequence, but an anti-C3bBb antibody comprising that sequence retains the ability to bind to C3bBb. In certain aspects, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:14. In certain aspects, the substitutions, insertions, or deletions occur in regions outside the CDRs (i.e., in the FRs). Optionally, the anti-C3bBb antibody comprises the VL sequence in SEQ ID NO:14, including post-translational modifications of that sequence. In a particular

30 aspect, the VL comprises one, two or three CDRs selected from: (a) CDR-L1, comprising the amino acid sequence of SEQ ID NO:488, (b) CDR-L2, comprising the amino acid sequence of SEQ ID NO:489, and (c) CDR-L3, comprising the amino acid sequence of SEQ ID NO:490.

35

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a VH sequence as in any of the aspects provided above, and a VL sequence as in any of the aspects provided above. In one aspect, the antibody comprises the VH and VL sequences in SEQ ID NO:13 and SEQ ID NO:14, respectively, including post-translational modifications of those sequences.

In another aspect, an anti-C3bBb antibody is provided, wherein the antibody comprises a heavy chain amino acid sequence of SEQ OF NO:447 and a light chain amino acid sequence of SEQ ID NO:448.

In one aspect, an antibody is provided that comprises a VH domain as described above and the heavy chain constant domain amino acid sequences as comprised in SEQ ID NO:447, and a VL domain as described above and the light chain constant domain amino acid sequences as comprised in SEQ ID NO:448.

Further aspects and embodiments

In a further aspect of the invention, an anti-human C3bBb antibody according to any of the above aspects is a monoclonal antibody, including a chimeric, humanized or human antibody. In one aspect, an anti-human C3bBb antibody is an antibody fragment, e.g., a Fv, Fab, Fab', scFv, diabody, or F(ab')₂ fragment.

In another aspect, the antibody is a full length antibody, e.g., an intact IgG1 antibody or other antibody class or isotype as defined herein. In one embodiment the antibody is a full length IgG1 antibody.

In one embodiment, the antibody is a monovalent antibody. In one embodiment, the antibody is a bivalent antibody. In one embodiment, the antibody is a trivalent antibody. In one embodiment, the antibody is a tetravalent antibody.

In a further aspect, an anti-human C3bBb antibody according to any of the above aspects may incorporate any of the features, singly or in combination, as described in Sections 1-8 below:

1. Antibody Affinity

In certain aspects, an antibody provided herein has a dissociation constant (KD) of $\leq 1\mu\text{M}$, $\leq 100\text{ nM}$, $\leq 10\text{ nM}$, $\leq 1\text{ nM}$, $\leq 0.1\text{ nM}$, $\leq 0.01\text{ nM}$, or $\leq 0.001\text{ nM}$. In certain embodiments, an antibody provided herein has a dissociation constant (KD) 10^{-6} M or less, in one embodiment 10^{-7} M or less, in one embodiment 10^{-8} M

or less, in one embodiment from 10^{-8} M to 10^{-13} M, in one embodiment from 10^{-9} M to 10^{-13} M.

5 In one embodiment the antibody binds human C3bBb at about 37°C with an affinity of ≤ 300 pM as measured by SPR. In one embodiment the antibody binds human C3bBb at about 37°C with an affinity of about 1 to 300 pM as measured by SPR. In one embodiment the antibody binds human C3bBb at about 37°C with an affinity of about 1 to about 200 pM as measured by SPR.

10 In one embodiment the antibody binds human C3bBb at about 25°C with an affinity of ≤ 100 pM as measured by SPR. In one embodiment the antibody binds human C3bBb at about 25°C with an affinity of about 1 to 100 pM as measured by SPR. In one embodiment the antibody binds human C3bBb at about 25°C with an affinity of ≤ 50 pM as measured by SPR.

In one aspect, KD is measured using a BIACORE® surface plasmon resonance assay. In one embodiment KD is measured as described in Example 5.

15 2. Antibody Fragments

In certain aspects, an antibody provided herein is an antibody fragment.

20 In one aspect, the antibody fragment is a Fab, Fab', Fab'-SH, or F(ab')₂ fragment, in particular a Fab fragment. Papain digestion of intact antibodies produces two identical antigen-binding fragments, called "Fab" fragments containing each the heavy- and light-chain variable domains (VH and VL, respectively) and also the constant domain of the light chain (CL) and the first constant domain of the heavy chain (CH1). The term "Fab fragment" thus refers to an antibody fragment comprising a light chain comprising a VL domain and a CL domain, and a heavy chain fragment comprising a VH domain and a CH1 domain. "Fab' fragments" differ from Fab fragments by the addition of residues at the carboxy terminus of the CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH are Fab' fragments in which the cysteine residue(s) of the constant domains bear a free thiol group. Pepsin treatment yields an F(ab')₂ fragment that has two antigen-binding sites (two Fab fragments) and a part of the Fc region. For discussion of Fab and F(ab')₂ fragments comprising salvage receptor binding epitope residues and having increased in vivo half-life, see U.S. Patent No. 5,869,046.

30

In another aspect, the antibody fragment is a diabody, a triabody or a tetrabody. "Diabodies" are antibody fragments with two antigen-binding sites that may be bivalent or bispecific. See, for example, EP 404,097; WO 1993/01161; Hudson et al., Nat. Med. 9:129-134 (2003); and Hollinger et al., Proc. Natl. Acad. Sci. USA 90: 6444-6448 (1993). Triabodies and tetrabodies are also described in Hudson et al., Nat. Med. 9:129-134 (2003).

In a further aspect, the antibody fragment is a single chain Fab fragment. A "single chain Fab fragment" or "scFab" is a polypeptide consisting of an antibody heavy chain variable domain (VH), an antibody heavy chain constant domain 1 (CH1), an antibody light chain variable domain (VL), an antibody light chain constant domain (CL) and a linker, wherein said antibody domains and said linker have one of the following orders in N-terminal to C-terminal direction: a) VH-CH1-linker-VL-CL, b) VL-CL-linker-VH-CH1, c) VH-CL-linker-VL-CH1 or d) VL-CH1-linker-VH-CL. In particular, said linker is a polypeptide of at least 30 amino acids, preferably between 32 and 50 amino acids. Said single chain Fab fragments are stabilized via the natural disulfide bond between the CL domain and the CH1 domain. In addition, these single chain Fab fragments might be further stabilized by generation of interchain disulfide bonds via insertion of cysteine residues (e.g., position 44 in the variable heavy chain and position 100 in the variable light chain according to Kabat numbering).

In another aspect, the antibody fragment is single-chain variable fragment (scFv). A "single-chain variable fragment" or "scFv" is a fusion protein of the variable domains of the heavy (VH) and light chains (VL) of an antibody, connected by a linker. In particular, the linker is a short polypeptide of 10 to 25 amino acids and is usually rich in glycine for flexibility, as well as serine or threonine for solubility, and can either connect the N-terminus of the VH with the C-terminus of the VL, or vice versa. This protein retains the specificity of the original antibody, despite removal of the constant regions and the introduction of the linker. For a review of scFv fragments, see, e.g., Plückthun, in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenberg and Moore eds., (Springer-Verlag, New York), pp. 269-315 (1994); see also WO 93/16185; and U.S. Patent Nos. 5,571,894 and 5,587,458.

In another aspect, the antibody fragment is a single-domain antibody. "Single-domain antibodies" are antibody fragments comprising all or a portion of the heavy chain variable domain or all or a portion of the light chain variable domain

of an antibody. In certain aspects, a single-domain antibody is a human single-domain antibody (Domantis, Inc., Waltham, MA; see, e.g., U.S. Patent No. 6,248,516 B1).

5 Antibody fragments can be made by various techniques, including but not limited to proteolytic digestion of an intact antibody as well as recombinant production by recombinant host cells (e.g., *E. coli*), as described herein.

3. Chimeric and Humanized Antibodies

10 In certain aspects, an antibody provided herein is a chimeric antibody. Certain chimeric antibodies are described, e.g., in U.S. Patent No. 4,816,567; and Morrison et al., Proc. Natl. Acad. Sci. USA, 81:6851-6855 (1984)). In one example, a chimeric antibody comprises a non-human variable region (e.g., a variable region derived from a mouse, rat, hamster, rabbit, or non-human primate, such as a monkey) and a human constant region. In a further example, a chimeric antibody is a “class switched” antibody in which the class or subclass has been changed from that of the parent antibody. Chimeric antibodies include antigen-binding fragments thereof.

15 In certain aspects, a chimeric antibody is a humanized antibody. Typically, a non-human antibody is humanized to reduce immunogenicity to humans, while retaining the specificity and affinity of the parental non-human antibody. Generally, a humanized antibody comprises one or more variable domains in which the CDRs (or portions thereof) are derived from a non-human antibody, and FRs (or portions thereof) are derived from human antibody sequences. A humanized antibody optionally will also comprise at least a portion of a human constant region. In some aspects, some FR residues in a humanized antibody are substituted with corresponding residues from a non-human antibody (e.g., the antibody from which the CDR residues are derived), e.g., to restore or improve antibody specificity or affinity.

20 Humanized antibodies and methods of making them are reviewed, e.g., in Almagro and Fransson, Front. Biosci. 13:1619-1633 (2008), and are further described, e.g., in Riechmann et al., Nature 332:323-329 (1988); Queen et al., Proc. Nat'l Acad. Sci. USA 86:10029-10033 (1989); US Patent Nos. 5, 821,337, 7,527,791, 6,982,321, and 7,087,409; Kashmiri et al., Methods 36:25-34 (2005) (describing specificity determining region (SDR) grafting); Padlan, Mol. Immunol. 28:489-498 (1991) (describing “resurfacing”); Dall’Acqua et al., Methods 36:43-60 (2005) (describing “FR shuffling”); and Osbourn et al., Methods 36:61-68 (2005)

and Klimka et al., Br. J. Cancer, 83:252-260 (2000) (describing the “guided selection” approach to FR shuffling).

Human framework regions that may be used for humanization include but are not limited to: framework regions selected using the “best-fit” method (see, e.g.,
5 Sims et al. J. Immunol. 151:2296 (1993)); framework regions derived from the consensus sequence of human antibodies of a particular subgroup of light or heavy chain variable regions (see, e.g., Carter et al. Proc. Natl. Acad. Sci. USA, 89:4285 (1992); and Presta et al. J. Immunol., 151:2623 (1993)); human mature (somatically mutated) framework regions or human germline framework regions (see, e.g.,
10 Almagro and Fransson, Front. Biosci. 13:1619-1633 (2008)); and framework regions derived from screening FR libraries (see, e.g., Baca et al., J. Biol. Chem. 272:10678-10684 (1997) and Rosok et al., J. Biol. Chem. 271:22611-22618 (1996)).

4. Human Antibodies

In certain aspects, an antibody provided herein is a human antibody. Human
15 antibodies can be produced using various techniques known in the art. Human antibodies are described generally in van Dijk and van de Winkel, Curr. Opin. Pharmacol. 5: 368-74 (2001) and Lonberg, Curr. Opin. Immunol. 20:450-459 (2008).

Human antibodies may be prepared by administering an immunogen to a transgenic animal that has been modified to produce intact human antibodies or intact
20 antibodies with human variable regions in response to antigenic challenge. Such animals typically contain all or a portion of the human immunoglobulin loci, which replace the endogenous immunoglobulin loci, or which are present extrachromosomally or integrated randomly into the animal’s chromosomes. In such transgenic mice, the endogenous immunoglobulin loci have generally been
25 inactivated. For review of methods for obtaining human antibodies from transgenic animals, see Lonberg, Nat. Biotech. 23:1117-1125 (2005). See also, e.g., U.S. Patent Nos. 6,075,181 and 6,150,584 describing XENOMOUSE™ technology; U.S. Patent No. 5,770,429 describing HUMAB® technology; U.S. Patent No. 7,041,870 describing K-M MOUSE® technology, and U.S. Patent Application Publication No.
30 US 2007/0061900, describing VELOCIMOUSE® technology). Human variable regions from intact antibodies generated by such animals may be further modified, e.g., by combining with a different human constant region.

Human antibodies can also be made by hybridoma-based methods. Human myeloma and mouse-human heteromyeloma cell lines for the production of human

monoclonal antibodies have been described. (See, e.g., Kozbor J. Immunol., 133: 3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, pp. 51-63 (Marcel Dekker, Inc., New York, 1987); and Boerner et al., J. Immunol., 147: 86 (1991).) Human antibodies generated via human B-cell
5 hybridoma technology are also described in Li et al., Proc. Natl. Acad. Sci. USA, 103:3557-3562 (2006). Additional methods include those described, for example, in U.S. Patent No. 7,189,826 (describing production of monoclonal human IgM antibodies from hybridoma cell lines) and Ni, Xiandai Mianyixue, 26(4):265-268 (2006) (describing human-human hybridomas). Human hybridoma technology
10 (Trioma technology) is also described in Vollmers and Brandlein, Histology and Histopathology, 20(3):927-937 (2005) and Vollmers and Brandlein, Methods and Findings in Experimental and Clinical Pharmacology, 27(3):185-91 (2005).

Human antibodies may also be generated by isolating variable domain sequences selected from human-derived phage display libraries. Such variable
15 domain sequences may then be combined with a desired human constant domain. Techniques for selecting human antibodies from antibody libraries are described below.

5. Library-Derived Antibodies

In certain aspects, an antibody provided herein is derived from a library.
20 Antibodies of the invention may be isolated by screening combinatorial libraries for antibodies with the desired activity or activities. Methods for screening combinatorial libraries are reviewed, e.g., in Lerner et al. in Nature Reviews 16:498-508 (2016). For example, a variety of methods are known in the art for generating phage display libraries and screening such libraries for antibodies possessing the
25 desired binding characteristics. Such methods are reviewed, e.g., in Frenzel et al. in mAbs 8:1177-1194 (2016); Bazan et al. in Human Vaccines and Immunotherapeutics 8:1817-1828 (2012) and Zhao et al. in Critical Reviews in Biotechnology 36:276-289 (2016) as well as in Hoogenboom et al. in Methods in Molecular Biology 178:1-37 (O'Brien et al., ed., Human Press, Totowa, NJ, 2001)
30 and in Marks and Bradbury in Methods in Molecular Biology 248:161-175 (Lo, ed., Human Press, Totowa, NJ, 2003).

In certain phage display methods, repertoires of VH and VL genes are separately cloned by polymerase chain reaction (PCR) and recombined randomly in phage libraries, which can then be screened for antigen-binding phage as described

in Winter et al. in *Annual Review of Immunology* 12: 433-455 (1994). Phage typically display antibody fragments, either as single-chain Fv (scFv) fragments or as Fab fragments. Libraries from immunized sources provide high-affinity antibodies to the immunogen without the requirement of constructing hybridomas.

5 Alternatively, the naive repertoire can be cloned (e.g., from human) to provide a single source of antibodies to a wide range of non-self and also self antigens without any immunization as described by Griffiths et al. in *EMBO Journal* 12: 725-734 (1993). Furthermore, naive libraries can also be made synthetically by cloning

10 unarranged V-gene segments from stem cells, and using PCR primers containing random sequence to encode the highly variable CDR3 regions and to accomplish rearrangement in vitro, as described by Hoogenboom and Winter in *Journal of Molecular Biology* 227: 381-388 (1992). Patent publications describing human antibody phage libraries include, for example: US Patent Nos. 5,750,373; 7,985,840; 7,785,903 and 8,679,490 as well as US Patent Publication Nos. 2005/0079574,

15 2007/0117126, 2007/0237764 and 2007/0292936.

Further examples of methods known in the art for screening combinatorial libraries for antibodies with a desired activity or activities include ribosome and mRNA display, as well as methods for antibody display and selection on bacteria, mammalian cells, insect cells or yeast cells. Methods for yeast surface display are

20 reviewed, e.g., in Scholler et al. in *Methods in Molecular Biology* 503:135-56 (2012) and in Cherf et al. in *Methods in Molecular biology* 1319:155-175 (2015) as well as in Zhao et al. in *Methods in Molecular Biology* 889:73-84 (2012). Methods for ribosome display are described, e.g., in He et al. in *Nucleic Acids Research* 25:5132-5134 (1997) and in Hanes et al. in *PNAS* 94:4937-4942 (1997).

25 Antibodies or antibody fragments isolated from human antibody libraries are considered human antibodies or human antibody fragments herein.

6. Multispecific Antibodies

In certain aspects, an antibody provided herein is a multispecific antibody, e.g., a bispecific antibody. "Multispecific antibodies" are monoclonal antibodies that

30 have binding specificities for at least two different sites, i.e., different epitopes on different antigens or different epitopes on the same antigen. In certain aspects, the multispecific antibody has three or more binding specificities. In certain aspects, one of the binding specificities is for human C3bBb and the other specificity is for any other antigen. In certain aspects, bispecific antibodies may bind to two (or more)

different epitopes of human C3bBb. Multispecific (e.g., bispecific) antibodies may also be used to localize cytotoxic agents or cells to cells which express human C3bBb. Multispecific antibodies may be prepared as full length antibodies or antibody fragments.

5 Techniques for making multispecific antibodies include, but are not limited to, recombinant co-expression of two immunoglobulin heavy chain-light chain pairs having different specificities (see Milstein and Cuello, *Nature* 305: 537 (1983)) and “knob-in-hole” engineering (see, e.g., U.S. Patent No. 5,731,168, and Atwell et al., *J. Mol. Biol.* 270:26 (1997)). Multi-specific antibodies may also be made by
10 engineering electrostatic steering effects for making antibody Fc-heterodimeric molecules (see, e.g., WO 2009/089004); cross-linking two or more antibodies or fragments (see, e.g., US Patent No. 4,676,980, and Brennan et al., *Science*, 229: 81 (1985)); using leucine zippers to produce bi-specific antibodies (see, e.g., Kostelny et al., *J. Immunol.*, 148(5):1547-1553 (1992) and WO 2011/034605); using the
15 common light chain technology for circumventing the light chain mis-pairing problem (see, e.g., WO 98/50431); using “diabody” technology for making bispecific antibody fragments (see, e.g., Hollinger et al., *Proc. Natl. Acad. Sci. USA*, 90:6444-6448 (1993)); and using single-chain Fv (sFv) dimers (see, e.g., Gruber et al., *J. Immunol.*, 152:5368 (1994)); and preparing trispecific antibodies as described,
20 e.g., in Tutt et al. *J. Immunol.* 147: 60 (1991).

Engineered antibodies with three or more antigen binding sites, including for example, “Octopus antibodies”, or DVD-Ig are also included herein (see, e.g., WO 2001/77342 and WO 2008/024715). Other examples of multispecific antibodies with three or more antigen binding sites can be found in WO 2010/115589, WO
25 2010/112193, WO 2010/136172, WO 2010/145792, and WO 2013/026831. The bispecific antibody or antigen binding fragment thereof also includes a “Dual Acting FAb” or “DAF” comprising an antigen binding site that binds to human C3bBb as well as another different antigen, or two different epitopes of human C3bBb (see, e.g., US 2008/0069820 and WO 2015/095539).

30 Multi-specific antibodies may also be provided in an asymmetric form with a domain crossover in one or more binding arms of the same antigen specificity, i.e. by exchanging the VH/VL domains (see e.g., WO 2009/080252 and WO 2015/150447), the CH1/CL domains (see e.g., WO 2009/080253) or the complete Fab arms (see e.g., WO 2009/080251, WO 2016/016299, also see Schaefer et al,
35 PNAS, 108 (2011) 1187-1191, and Klein et al., *MAbs* 8 (2016) 1010-20). In one

aspect, the multispecific antibody comprises a cross-Fab fragment. The term “cross-Fab fragment” or “xFab fragment” or “crossover Fab fragment” refers to a Fab fragment, wherein either the variable regions or the constant regions of the heavy and light chain are exchanged. A cross-Fab fragment comprises a polypeptide chain composed of the light chain variable region (VL) and the heavy chain constant region 1 (CH1), and a polypeptide chain composed of the heavy chain variable region (VH) and the light chain constant region (CL). Asymmetrical Fab arms can also be engineered by introducing charged or non-charged amino acid mutations into domain interfaces to direct correct Fab pairing. See e.g., WO 2016/172485.

Various further molecular formats for multispecific antibodies are known in the art and are included herein (see e.g., Spiess et al., *Mol Immunol* 67 (2015) 95-106).

A particular type of multispecific antibodies, also included herein, are bispecific antibodies designed to simultaneously bind to a surface antigen on a target cell, e.g., a tumor cell, and to an activating, invariant component of the T cell receptor (TCR) complex, such as CD3, for retargeting of T cells to kill target cells. Hence, in certain aspects, an antibody provided herein is a multispecific antibody, particularly a bispecific antibody, wherein one of the binding specificities is for human C3bBb and the other is for CD3.

Examples of bispecific antibody formats that may be useful for this purpose include, but are not limited to, the so-called “BiTE” (bispecific T cell engager) molecules wherein two scFv molecules are fused by a flexible linker (see, e.g., WO 2004/106381, WO 2005/061547, WO 2007/042261, and WO 2008/119567, Nagorsen and Bäuerle, *Exp Cell Res* 317, 1255-1260 (2011)); diabodies (Holliger et al., *Prot Eng* 9, 299-305 (1996)) and derivatives thereof, such as tandem diabodies (“TandAb”; Kipriyanov et al., *J Mol Biol* 293, 41-56 (1999)); “DART” (dual affinity retargeting) molecules which are based on the diabody format but feature a C-terminal disulfide bridge for additional stabilization (Johnson et al., *J Mol Biol* 399, 436-449 (2010)), and so-called triomabs, which are whole hybrid mouse/rat IgG molecules (reviewed in Seimetz et al., *Cancer Treat Rev* 36, 458-467 (2010)). Particular T cell bispecific antibody formats included herein are described in WO 2013/026833, WO 2013/026839, WO 2016/020309; Bacac et al., *Oncoimmunology* 5(8) (2016) e1203498.

7. Antibody Variants

In certain aspects, amino acid sequence variants of the antibodies provided herein are contemplated. For example, it may be desirable to alter the binding affinity and/or other biological properties of the antibody. Amino acid sequence variants of an antibody may be prepared by introducing appropriate modifications into the nucleotide sequence encoding the antibody, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of residues within the amino acid sequences of the antibody. Any combination of deletion, insertion, and substitution can be made to arrive at the final construct, provided that the final construct possesses the desired characteristics, e.g., antigen-binding.

a) Substitution, Insertion, and Deletion Variants

In certain aspects, antibody variants having one or more amino acid substitutions are provided. Sites of interest for substitutional mutagenesis include the CDRs and FRs. Conservative substitutions are shown in Table D2 under the heading of “preferred substitutions”. More substantial changes are provided in Table 1 under the heading of “exemplary substitutions”, and as further described below in reference to amino acid side chain classes. Amino acid substitutions may be introduced into an antibody of interest and the products screened for a desired activity, e.g., retained/improved antigen binding, decreased immunogenicity, or improved ADCC or CDC.

Table D2: amino acid substitutions

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala (A)	Val; Leu; Ile	Val
Arg (R)	Lys; Gln; Asn	Lys
Asn (N)	Gln; His; Asp, Lys; Arg	Gln
Asp (D)	Glu; Asn	Glu
Cys (C)	Ser; Ala	Ser
Gln (Q)	Asn; Glu	Asn
Glu (E)	Asp; Gln	Asp
Gly (G)	Ala	Ala
His (H)	Asn; Gln; Lys; Arg	Arg

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ile (I)	Leu; Val; Met; Ala; Phe; Norleucine	Leu
Leu (L)	Norleucine; Ile; Val; Met; Ala; Phe	Ile
Lys (K)	Arg; Gln; Asn	Arg
Met (M)	Leu; Phe; Ile	Leu
Phe (F)	Trp; Leu; Val; Ile; Ala; Tyr	Tyr
Pro (P)	Ala	Ala
Ser (S)	Thr	Thr
Thr (T)	Val; Ser	Ser
Trp (W)	Tyr; Phe	Tyr
Tyr (Y)	Trp; Phe; Thr; Ser	Phe
Val (V)	Ile; Leu; Met; Phe; Ala; Norleucine	Leu

Amino acids may be grouped according to common side-chain properties:

- 5

(1) hydrophobic: Norleucine, Met, Ala, Val, Leu, Ile;

(2) neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;

(3) acidic: Asp, Glu;

(4) basic: His, Lys, Arg;

(5) residues that influence chain orientation: Gly, Pro;

(6) aromatic: Trp, Tyr, Phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for a member of another class.

10

One type of substitutional variant involves substituting one or more hypervariable region residues of a parent antibody (e.g., a humanized or human antibody). Generally, the resulting variant(s) selected for further study will have modifications (e.g., improvements) in certain biological properties (e.g., increased affinity, reduced immunogenicity) relative to the parent antibody and/or will have

15

substantially retained certain biological properties of the parent antibody. An exemplary substitutional variant is an affinity matured antibody, which may be

conveniently generated, e.g., using phage display-based affinity maturation techniques such as those described herein. Briefly, one or more CDR residues are mutated and the variant antibodies displayed on phage and screened for a particular biological activity (e.g., binding affinity).

5 Alterations (e.g., substitutions) may be made in CDRs, e.g., to improve antibody affinity. Such alterations may be made in CDR “hotspots”, i.e., residues encoded by codons that undergo mutation at high frequency during the somatic maturation process (see, e.g., Chowdhury, *Methods Mol. Biol.* 207:179-196 (2008)), and/or residues that contact antigen, with the resulting variant VH or VL being tested
10 for binding affinity. Affinity maturation by constructing and reselecting from secondary libraries has been described, e.g., in Hoogenboom et al. in *Methods in Molecular Biology* 178:1-37 (O’Brien et al., ed., Human Press, Totowa, NJ, (2001).) In some aspects of affinity maturation, diversity is introduced into the variable genes chosen for maturation by any of a variety of methods (e.g., error-prone PCR, chain
15 shuffling, or oligonucleotide-directed mutagenesis). A secondary library is then created. The library is then screened to identify any antibody variants with the desired affinity. Another method to introduce diversity involves CDR-directed approaches, in which several CDR residues (e.g., 4-6 residues at a time) are randomized. CDR residues involved in antigen binding may be specifically
20 identified, e.g., using alanine scanning mutagenesis or modeling. CDR-H3 and CDR-L3 in particular are often targeted.

 In certain aspects, substitutions, insertions, or deletions may occur within one or more CDRs so long as such alterations do not substantially reduce the ability of the antibody to bind antigen. For example, conservative alterations (e.g.,
25 conservative substitutions as provided herein) that do not substantially reduce binding affinity may be made in the CDRs. Such alterations may, for example, be outside of antigen contacting residues in the CDRs. In certain variant VH and VL sequences provided above, each CDR either is unaltered, or contains no more than one, two or three amino acid substitutions.

30 A useful method for identification of residues or regions of an antibody that may be targeted for mutagenesis is called “alanine scanning mutagenesis” as described by Cunningham and Wells (1989) *Science*, 244:1081-1085. In this method, a residue or group of target residues (e.g., charged residues such as arg, asp, his, lys, and glu) are identified and replaced by a neutral or negatively charged amino
35 acid (e.g., alanine or polyalanine) to determine whether the interaction of the

antibody with antigen is affected. Further substitutions may be introduced at the amino acid locations demonstrating functional sensitivity to the initial substitutions. Alternatively, or additionally, a crystal structure of an antigen-antibody complex may be used to identify contact points between the antibody and antigen. Such contact residues and neighboring residues may be targeted or eliminated as candidates for substitution. Variants may be screened to determine whether they contain the desired properties.

Amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from one residue to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include an antibody with an N-terminal methionyl residue. Other insertional variants of the antibody molecule include the fusion to the N- or C-terminus of the antibody to an enzyme (e.g., for ADEPT (antibody directed enzyme prodrug therapy)) or a polypeptide which increases the serum half-life of the antibody.

b) Glycosylation variants

In certain aspects, an antibody provided herein is altered to increase or decrease the extent to which the antibody is glycosylated. Addition or deletion of glycosylation sites to an antibody may be conveniently accomplished by altering the amino acid sequence such that one or more glycosylation sites is created or removed.

Where the antibody comprises an Fc region, the oligosaccharide attached thereto may be altered. Native antibodies produced by mammalian cells typically comprise a branched, biantennary oligosaccharide that is generally attached by an N-linkage to Asn297 of the CH2 domain of the Fc region. See, e.g., Wright et al. TIBTECH 15:26-32 (1997). The oligosaccharide may include various carbohydrates, e.g., mannose, N-acetyl glucosamine (GlcNAc), galactose, and sialic acid, as well as a fucose attached to a GlcNAc in the “stem” of the biantennary oligosaccharide structure. In some aspects, modifications of the oligosaccharide in an antibody of the invention may be made in order to create antibody variants with certain improved properties.

In one aspect, antibody variants are provided having a non-fucosylated oligosaccharide, i.e. an oligosaccharide structure that lacks fucose attached (directly or indirectly) to an Fc region. Such non-fucosylated oligosaccharide (also referred to as “afucosylated” oligosaccharide) particularly is an N-linked oligosaccharide

which lacks a fucose residue attached to the first GlcNAc in the stem of the biantennary oligosaccharide structure. In one aspect, antibody variants are provided having an increased proportion of non-fucosylated oligosaccharides in the Fc region as compared to a native or parent antibody. For example, the proportion of non-fucosylated oligosaccharides may be at least about 20%, at least about 40%, at least about 60%, at least about 80%, or even about 100% (i.e. no fucosylated oligosaccharides are present). The percentage of non-fucosylated oligosaccharides is the (average) amount of oligosaccharides lacking fucose residues, relative to the sum of all oligosaccharides attached to Asn 297 (e. g. complex, hybrid and high mannose structures) as measured by MALDI-TOF mass spectrometry, as described in WO 2006/082515, for example. Asn297 refers to the asparagine residue located at about position 297 in the Fc region (EU numbering of Fc region residues); however, Asn297 may also be located about ± 3 amino acids upstream or downstream of position 297, i.e., between positions 294 and 300, due to minor sequence variations in antibodies. Such antibodies having an increased proportion of non-fucosylated oligosaccharides in the Fc region may have improved Fc γ RIIIa receptor binding and/or improved effector function, in particular improved ADCC function. See, e.g., US 2003/0157108; US 2004/0093621.

Examples of cell lines capable of producing antibodies with reduced fucosylation include Lec13 CHO cells deficient in protein fucosylation (Ripka et al. Arch. Biochem. Biophys. 249:533-545 (1986); US 2003/0157108; and WO 2004/056312, especially at Example 11), and knockout cell lines, such as alpha-1,6-fucosyltransferase gene, FUT8, knockout CHO cells (see, e.g., Yamane-Ohnuki et al. Biotech. Bioeng. 87:614-622 (2004); Kanda, Y. et al., Biotechnol. Bioeng., 94(4):680-688 (2006); and WO 2003/085107), or cells with reduced or abolished activity of a GDP-fucose synthesis or transporter protein (see, e.g., US2004259150, US2005031613, US2004132140, US2004110282).

In a further aspect, antibody variants are provided with bisected oligosaccharides, e.g., in which a biantennary oligosaccharide attached to the Fc region of the antibody is bisected by GlcNAc. Such antibody variants may have reduced fucosylation and/or improved ADCC function as described above. Examples of such antibody variants are described, e.g., in Umana et al., Nat Biotechnol 17, 176-180 (1999); Ferrara et al., Biotechn Bioeng 93, 851-861 (2006); WO 99/54342; WO 2004/065540, WO 2003/011878.

Antibody variants with at least one galactose residue in the oligosaccharide attached to the Fc region are also provided. Such antibody variants may have improved CDC function. Such antibody variants are described, e.g., in WO 1997/30087; WO 1998/58964; and WO 1999/22764.

5 **c) Fc region variants**

In certain aspects, one or more amino acid modifications may be introduced into the Fc region of an antibody provided herein, thereby generating an Fc region variant. The Fc region variant may comprise a human Fc region sequence (e.g., a human IgG1, IgG2, IgG3 or IgG4 Fc region) comprising an amino acid modification
10 (e.g., a substitution) at one or more amino acid positions.

In certain aspects, the invention contemplates an antibody variant that possesses some but not all effector functions, which make it a desirable candidate for applications in which the half life of the antibody in vivo is important yet certain effector functions (such as complement-dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC)) are unnecessary or deleterious. In
15 vitro and/or in vivo cytotoxicity assays can be conducted to confirm the reduction/depletion of CDC and/or ADCC activities. For example, Fc receptor (FcR) binding assays can be conducted to ensure that the antibody lacks FcγR binding (hence likely lacking ADCC activity), but retains FcRn binding ability. The primary cells for mediating ADCC, NK cells, express FcγRIII only, whereas
20 monocytes express FcγRI, FcγRII and FcγRIII. FcR expression on hematopoietic cells is summarized in Table 3 on page 464 of Ravetch and Kinet, Annu. Rev. Immunol. 9:457-492 (1991). Non-limiting examples of in vitro assays to assess ADCC activity of a molecule of interest is described in U.S. Patent No. 5,500,362
25 (see, e.g., Hellstrom, I. et al. Proc. Nat'l Acad. Sci. USA 83:7059-7063 (1986)) and Hellstrom, I et al., Proc. Nat'l Acad. Sci. USA 82:1499-1502 (1985); 5,821,337 (see Bruggemann, M. et al., J. Exp. Med. 166:1351-1361 (1987)). Alternatively, non-radioactive assays methods may be employed (see, for example, ACTITM non-radioactive cytotoxicity assay for flow cytometry (CellTechnology, Inc. Mountain
30 View, CA; and CytoTox 96® non-radioactive cytotoxicity assay (Promega, Madison, WI). Useful effector cells for such assays include peripheral blood mononuclear cells (PBMC) and Natural Killer (NK) cells. Alternatively, or additionally, ADCC activity of the molecule of interest may be assessed in vivo, e.g., in a animal model such as that disclosed in Clynes et al. Proc. Nat'l Acad. Sci. USA
35 95:652-656 (1998). C1q binding assays may also be carried out to confirm that the

antibody is unable to bind C1q and hence lacks CDC activity. See, e.g., C1q and C3c binding ELISA in WO 2006/029879 and WO 2005/100402. To assess complement activation, a CDC assay may be performed (see, for example, Gazzano-Santoro et al., J. Immunol. Methods 202:163 (1996); Cragg, M.S. et al., Blood 101:1045-1052 (2003); and Cragg, M.S. and M.J. Glennie, Blood 103:2738-2743 (2004)). FcRn binding and in vivo clearance/half life determinations can also be performed using methods known in the art (see, e.g., Petkova, S.B. et al., Int'l. Immunol. 18(12):1759-1769 (2006); WO 2013/120929 A1).

Antibodies with reduced effector function include those with substitution of one or more of Fc region residues 238, 265, 269, 270, 297, 327 and 329 (U.S. Patent No. 6,737,056). Such Fc mutants include Fc mutants with substitutions at two or more of amino acid positions 265, 269, 270, 297 and 327, including the so-called "DANA" Fc mutant with substitution of residues 265 and 297 to alanine (US Patent No. 7,332,581).

Certain antibody variants with improved or diminished binding to FcRs are described. (See, e.g., U.S. Patent No. 6,737,056; WO 2004/056312, and Shields et al., J. Biol. Chem. 9(2): 6591-6604 (2001).)

In certain aspects, an antibody variant comprises an Fc region with one or more amino acid substitutions which improve ADCC, e.g., substitutions at positions 298, 333, and/or 334 of the Fc region (EU numbering of residues).

In certain aspects, an antibody variant comprises an Fc region with one or more amino acid substitutions which diminish FcγR binding, e.g., substitutions at positions 234 and 235 of the Fc region (EU numbering of residues). In one aspect, the substitutions are L234A and L235A (LALA). In certain aspects, the antibody variant further comprises D265A and/or P329G in an Fc region derived from a human IgG1 Fc region. In one aspect, the substitutions are L234A, L235A and P329G (LALA-PG) in an Fc region derived from a human IgG1 Fc region. (See, e.g., WO 2012/130831). In another aspect, the substitutions are L234A, L235A and D265A (LALA-DA) in an Fc region derived from a human IgG1 Fc region.

In some aspects, alterations are made in the Fc region that result in altered (i.e., either improved or diminished) C1q binding and/or Complement Dependent Cytotoxicity (CDC), e.g., as described in US Patent No. 6,194,551, WO 99/51642, and Idusogie et al. J. Immunol. 164: 4178-4184 (2000).

Antibodies with increased half lives and improved binding to the neonatal Fc receptor (FcRn), which is responsible for the transfer of maternal IgGs to the fetus (Guyer et al., J. Immunol. 117:587 (1976) and Kim et al., J. Immunol. 24:249 (1994)), are described in US2005/0014934 (Hinton et al.). Those antibodies
5 comprise an Fc region with one or more substitutions therein which improve binding of the Fc region to FcRn. Such Fc variants include those with substitutions at one or more of Fc region residues: 238, 252, 254, 256, 265, 272, 286, 303, 305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434, e.g., substitution of Fc region residue 434 (See, e.g., US Patent No. 7,371,826; Dall'Acqua, W.F., et
10 al. J. Biol. Chem. 281 (2006) 23514-23524).

Studies of the human Fc-human FcRn complex have shown that residues I253, S254, H435, and Y436 are crucial for the interaction (Firan, M., et al., Int. Immunol. 13 (2001) 993; Shields, R.L., et al., J. Biol. Chem. 276 (2001) 6591-6604). In Yeung, Y.A., et al. (J. Immunol. 182 (2009) 7667-7671) various mutants of
15 residues 248 to 259 and 301 to 317 and 376 to 382 and 424 to 437 have been reported and examined.

In certain aspects, an antibody variant comprises an Fc region with one or more amino acid substitutions, which reduce FcRn binding, e.g., substitutions at positions 253, and/or 310, and/or 435 of the Fc-region (EU numbering of residues).
20 In certain aspects, the antibody variant comprises an Fc region with the amino acid substitutions at positions 253, 310 and 435. In one aspect, the substitutions are I253A, H310A and H435A in an Fc region derived from a human IgG1 Fc-region. See, e.g., Grevys, A., et al., J. Immunol. 194 (2015) 5497-5508.

In certain aspects, an antibody variant comprises an Fc region with one or
25 more amino acid substitutions, which reduce FcRn binding, e.g., substitutions at positions 310, and/or 433, and/or 436 of the Fc region (EU numbering of residues). In certain aspects, the antibody variant comprises an Fc region with the amino acid substitutions at positions 310, 433 and 436. In one aspect, the substitutions are H310A, H433A and Y436A in an Fc region derived from a human IgG1 Fc-region.
30 (See, e.g., WO 2014/177460 A1).

In certain aspects, an antibody variant comprises an Fc region with one or more amino acid substitutions which increase FcRn binding, e.g., substitutions at positions 252, and/or 254, and/or 256 of the Fc region (EU numbering of residues). In certain aspects, the antibody variant comprises an Fc region with amino acid
35 substitutions at positions 252, 254, and 256. In one aspect, the substitutions are

M252Y, S254T and T256E in an Fc region derived from a human IgG1 Fc-region. See also Duncan & Winter, Nature 322:738-40 (1988); U.S. Patent No. 5,648,260; U.S. Patent No. 5,624,821; and WO 94/29351 concerning other examples of Fc region variants.

5 The C-terminus of the heavy chain of the antibody as reported herein can be a complete C-terminus ending with the amino acid residues PGK. The C-terminus of the heavy chain can be a shortened C-terminus in which one or two of the C terminal amino acid residues have been removed. In one preferred aspect, the C-terminus of the heavy chain is a shortened C-terminus ending PG. In one aspect of all aspects as
10 reported herein, an antibody comprising a heavy chain including a C-terminal CH3 domain as specified herein, comprises the C-terminal glycine-lysine dipeptide (G446 and K447, EU index numbering of amino acid positions). In one aspect of all aspects as reported herein, an antibody comprising a heavy chain including a C-terminal CH3 domain, as specified herein, comprises a C-terminal glycine residue (G446, EU index
15 numbering of amino acid positions).

d) Cysteine engineered antibody variants

 In certain aspects, it may be desirable to create cysteine engineered antibodies, e.g., THIOMAB™ antibodies, in which one or more residues of an antibody are substituted with cysteine residues. In particular aspects, the substituted
20 residues occur at accessible sites of the antibody. By substituting those residues with cysteine, reactive thiol groups are thereby positioned at accessible sites of the antibody and may be used to conjugate the antibody to other moieties, such as drug moieties or linker-drug moieties, to create an immunoconjugate, as described further herein. Cysteine engineered antibodies may be generated as described, e.g., in U.S.
25 Patent No. 7,521,541, 8,30,930, 7,855,275, 9,000,130, or WO 2016040856.

e) Antibody Derivatives

 In certain aspects, an antibody provided herein may be further modified to contain additional nonproteinaceous moieties that are known in the art and readily available. The moieties suitable for derivatization of the antibody include but are
30 not limited to water soluble polymers. Non-limiting examples of water soluble polymers include, but are not limited to, polyethylene glycol (PEG), copolymers of ethylene glycol/propylene glycol, carboxymethylcellulose, dextran, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1, 3-dioxolane, poly-1,3,6-trioxane, ethylene/maleic anhydride copolymer, polyaminoacids (either homopolymers or

random copolymers), and dextran or poly(n-vinyl pyrrolidone)polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide copolymers, polyoxyethylated polyols (e.g., glycerol), polyvinyl alcohol, and mixtures thereof. Polyethylene glycol propionaldehyde may have advantages in manufacturing due to its stability in water. The polymer may be of any molecular weight, and may be branched or unbranched. The number of polymers attached to the antibody may vary, and if more than one polymer are attached, they can be the same or different molecules. In general, the number and/or type of polymers used for derivatization can be determined based on considerations including, but not limited to, the particular properties or functions of the antibody to be improved, whether the antibody derivative will be used in a therapy under defined conditions, etc.

8. Immunoconjugates

The invention also provides immunoconjugates comprising an anti-human C3bBb antibody herein conjugated (chemically bonded) to one or more therapeutic agents such as cytotoxic agents, chemotherapeutic agents, drugs, growth inhibitory agents, toxins (e.g., protein toxins, enzymatically active toxins of bacterial, fungal, plant, or animal origin, or fragments thereof), or radioactive isotopes.

In one aspect, an immunoconjugate is an antibody-drug conjugate (ADC) in which an antibody is conjugated to one or more of the therapeutic agents mentioned above. The antibody is typically connected to one or more of the therapeutic agents using linkers. An overview of ADC technology including examples of therapeutic agents and drugs and linkers is set forth in Pharmacol Review 68:3-19 (2016).

In another aspect, an immunoconjugate comprises an antibody as described herein conjugated to an enzymatically active toxin or fragment thereof, including but not limited to diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolacca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes.

In another aspect, an immunoconjugate comprises an antibody as described herein conjugated to a radioactive atom to form a radioconjugate. A variety of radioactive isotopes are available for the production of radioconjugates. Examples

include At211, I131, I125, Y90, Re186, Re188, Sm153, Bi212, P32, Pb212 and radioactive isotopes of Lu. When the radioconjugate is used for detection, it may comprise a radioactive atom for scintigraphic studies, for example tc99m or I123, or a spin label for nuclear magnetic resonance (NMR) imaging (also known as magnetic resonance imaging, mri), such as iodine-123 again, iodine-131, indium-111, fluorine-19, carbon-13, nitrogen-15, oxygen-17, gadolinium, manganese or iron.

Conjugates of an antibody and cytotoxic agent may be made using a variety of bifunctional protein coupling agents such as N-succinimidyl-3-(2-pyridyldithio) propionate (SPDP), succinimidyl-4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCl), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as toluene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science 238:1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO 94/11026. The linker may be a "cleavable linker" facilitating release of a cytotoxic drug in the cell. For example, an acid-labile linker, peptidase-sensitive linker, photolabile linker, dimethyl linker or disulfide-containing linker (Chari et al., Cancer Res. 52:127-131 (1992); U.S. Patent No. 5,208,020) may be used.

The immunoconjugates or ADCs herein expressly contemplate, but are not limited to such conjugates prepared with cross-linker reagents including, but not limited to, BMPS, EMCS, GMBS, HBVS, LC-SMCC, MBS, MPBH, SBAP, SIA, SIAB, SMCC, SMPB, SMPH, sulfo-EMCS, sulfo-GMBS, sulfo-KMUS, sulfo-MBS, sulfo-SIAB, sulfo-SMCC, and sulfo-SMPB, and SVSB (succinimidyl-(4-vinylsulfone)benzoate) which are commercially available (e.g., from Pierce Biotechnology, Inc., Rockford, IL., U.S.A).

B. Recombinant Methods and Compositions

Antibodies may be produced using recombinant methods and compositions, e.g., as described in US 4,816,567. For these methods one or more isolated nucleic acid(s) encoding an antibody are provided.

In case of a native antibody or native antibody fragment two nucleic acids are required, one for the light chain or a fragment thereof and one for the heavy chain or a fragment thereof. Such nucleic acid(s) encode an amino acid sequence comprising the VL and/or an amino acid sequence comprising the VH of the antibody (e.g., the light and/or heavy chain(s) of the antibody). These nucleic acids can be on the same expression vector or on different expression vectors.

In case of a bispecific antibody with heterodimeric heavy chains four nucleic acids are required, one for the first light chain, one for the first heavy chain comprising the first heteromonomeric Fc-region polypeptide, one for the second light chain, and one for the second heavy chain comprising the second heteromonomeric Fc-region polypeptide. The four nucleic acids can be comprised in one or more nucleic acid molecules or expression vectors. Such nucleic acid(s) encode an amino acid sequence comprising the first VL and/or an amino acid sequence comprising the first VH including the first heteromonomeric Fc-region and/or an amino acid sequence comprising the second VL and/or an amino acid sequence comprising the second VH including the second heteromonomeric Fc-region of the antibody (e.g., the first and/or second light and/or the first and/or second heavy chains of the antibody). These nucleic acids can be on the same expression vector or on different expression vectors, normally these nucleic acids are located on two or three expression vectors, i.e. one vector can comprise more than one of these nucleic acids. Examples of these bispecific antibodies are CrossMabs (see, e.g., Schaefer, W. et al, PNAS, 108 (2011) 11187-11191). For example, one of the heteromonomeric heavy chain comprises the so-called "knob mutations" (T366W and optionally one of S354C or Y349C) and the other comprises the so-called "hole mutations" (T366S, L368A and Y407V and optionally Y349C or S354C) (see, e.g., Carter, P. et al., Immunotechnol. 2 (1996) 73) according to EU index numbering.

In one aspect, isolated nucleic acids encoding an antibody as used in the methods as reported herein are provided.

In one aspect, a method of making an anti-human C3bBb antibody is provided, wherein the method comprises culturing a host cell comprising nucleic acid(s) encoding the antibody, as provided above, under conditions suitable for expression of the antibody, and optionally recovering the antibody from the host cell (or host cell culture medium).

For recombinant production of an anti-human C3bBb antibody, nucleic acids encoding the antibody, e.g., as described above, are isolated and inserted into one or

more vectors for further cloning and/or expression in a host cell. Such nucleic acids may be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of the antibody) or produced by recombinant methods or
5 obtained by chemical synthesis.

Suitable host cells for cloning or expression of antibody-encoding vectors include prokaryotic or eukaryotic cells described herein. For example, antibodies may be produced in bacteria, in particular when glycosylation and Fc effector function are not needed. For expression of antibody fragments and polypeptides in
10 bacteria, see, e.g., US 5,648,237, US 5,789,199, and US 5,840,523. (See also Charlton, K.A., In: Methods in Molecular Biology, Vol. 248, Lo, B.K.C. (ed.), Humana Press, Totowa, NJ (2003), pp. 245-254, describing expression of antibody fragments in *E. coli*.) After expression, the antibody may be isolated from the bacterial cell paste in a soluble fraction and can be further purified.

15 In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for antibody-encoding vectors, including fungi and yeast strains whose glycosylation pathways have been “humanized”, resulting in the production of an antibody with a partially or fully human glycosylation pattern. See Gerngross, T.U., Nat. Biotech. 22 (2004) 1409-
20 1414; and Li, H. et al., Nat. Biotech. 24 (2006) 210-215.

Suitable host cells for the expression of (glycosylated) antibodies are also derived from multicellular organisms (invertebrates and vertebrates). Examples of invertebrate cells include plant and insect cells. Numerous baculoviral strains have been identified which may be used in conjunction with insect cells, particularly for
25 transfection of *Spodoptera frugiperda* cells.

Plant cell cultures can also be utilized as hosts. See, e.g., US 5,959,177, US 6,040,498, US 6,420,548, US 7,125,978, and US 6,417,429 (describing PLANTIBODIESTM technology for producing antibodies in transgenic plants).

30 Vertebrate cells may also be used as hosts. For example, mammalian cell lines that are adapted to grow in suspension may be useful. Other examples of useful mammalian host cell lines are monkey kidney CV1 line transformed by SV40 (COS-7); human embryonic kidney line (293 or 293T cells as described, e.g., in Graham, F.L. et al., J. Gen Virol. 36 (1977) 59-74); baby hamster kidney cells (BHK); mouse Sertoli cells (TM4 cells as described, e.g., in Mather, J.P., Biol. Reprod. 23 (1980)

243-252); monkey kidney cells (CV1); African green monkey kidney cells (VERO-76); human cervical carcinoma cells (HeLa); canine kidney cells (MDCK; buffalo rat liver cells (BRL 3A); human lung cells (W138); human liver cells (Hep G2); mouse mammary tumor (MMT 060562); TRI cells (as described, e.g., in Mather, J.P. et al., *Annals N.Y. Acad. Sci.* 383 (1982) 44-68); MRC 5 cells; and FS4 cells. Other useful mammalian host cell lines include Chinese hamster ovary (CHO) cells, including DHFR- CHO cells (Urlaub, G. et al., *Proc. Natl. Acad. Sci. USA* 77 (1980) 4216-4220); and myeloma cell lines such as Y0, NS0 and Sp2/0. For a review of certain mammalian host cell lines suitable for antibody production, see, e.g., Yazaki, P. and Wu, A.M., *Methods in Molecular Biology*, Vol. 248, Lo, B.K.C. (ed.), Humana Press, Totowa, NJ (2004), pp. 255-268.

In one aspect, the host cell is eukaryotic, e.g., a Chinese Hamster Ovary (CHO) cell or lymphoid cell (e.g., Y0, NS0, Sp20 cell).

C. Assays

Anti-C3bBb antibodies provided herein may be identified, screened for, or characterized for their physical/chemical properties and/or biological activities by various assays known in the art.

1. Binding assays and other assays

In one aspect, an antibody of the invention is tested for its antigen binding activity, e.g., by known methods such as ELISA, Western blot, etc.

In another aspect, competition assays may be used to identify an antibody that competes with an antibody of the invention for binding to C3bBb. In certain aspects, such a competing antibody binds to the same epitope (e.g., a linear or a conformational epitope) that is bound by an antibody of the invention. Detailed exemplary methods for mapping an epitope to which an antibody binds are provided in Morris (1996) "Epitope Mapping Protocols", in *Methods in Molecular Biology* vol. 66 (Humana Press, Totowa, NJ).

In an exemplary competition assay, immobilized C3bBb is incubated in a solution comprising a first labeled antibody that binds to C3bBb (e.g., an antibody of the invention) and a second unlabeled antibody that is being tested for its ability to compete with the first antibody for binding to C3bBb. The second antibody may be present in a hybridoma supernatant. As a control, immobilized C3bBb is incubated in a solution comprising the first labeled antibody but not the second

unlabeled antibody. After incubation under conditions permissive for binding of the first antibody to C3bBb, excess unbound antibody is removed, and the amount of label associated with immobilized C3bBb is measured. If the amount of label associated with immobilized C3bBb is substantially reduced in the test sample
5 relative to the control sample, then that indicates that the second antibody is competing with the first antibody for binding to C3bBb. See Harlow and Lane (1988) Antibodies: A Laboratory Manual ch.14 (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY).

2. Activity assays

10 In one aspect, assays are provided for identifying anti-C3bBb antibodies thereof having biological activity. Biological activity may include, e.g., inhibition modulating the formation, stability, activity and dissociation of C3 convertase protein complex as well as influencing the interaction with further proteins (e.g. Properdin or Complement Factor I). Antibodies having such biological activity in
15 vivo and/or in vitro are also provided.

In certain aspects, an antibody of the invention is tested for such biological activity.

D. Methods and Compositions for Diagnostics and Detection

20 In certain aspects, any of the anti-C3bBb antibodies provided herein is useful for detecting the presence of C3bBb in a biological sample. The term “detecting” as used herein encompasses quantitative or qualitative detection.

In one aspect, an anti-C3bBb antibody for use in a method of diagnosis or detection is provided. In a further aspect, a method of detecting the presence of C3bBb in a biological sample is provided. In certain aspects, the method comprises
25 contacting the biological sample with an anti-C3bBb antibody as described herein under conditions permissive for binding of the anti-C3bBb antibody to C3bBb, and detecting whether a complex is formed between the anti-C3bBb antibody and C3bBb. Such a method may be an in vitro or in vivo method. In one aspect, an anti-C3bBb antibody is used to select subjects eligible for therapy with an anti-C3bBb
30 antibody, e.g., where C3bBb is a biomarker for selection of patients.

In certain aspects, labeled anti-C3bBb antibodies are provided. Labels include, but are not limited to, labels or moieties that are detected directly (such as

fluorescent, chromophoric, electron-dense, chemiluminescent, and radioactive labels), as well as moieties, such as enzymes or ligands, that are detected indirectly, e.g., through an enzymatic reaction or molecular interaction. Exemplary labels include, but are not limited to, the radioisotopes ^{32}P , ^{14}C , ^{125}I , ^3H , and ^{131}I ,
5 fluorophores such as rare earth chelates or fluorescein and its derivatives, rhodamine and its derivatives, dansyl, umbelliferone, luciferases, e.g., firefly luciferase and bacterial luciferase (U.S. Patent No. 4,737,456), luciferin, 2,3-dihydrophthalazinediones, horseradish peroxidase (HRP), alkaline phosphatase, β -galactosidase, glucoamylase, lysozyme, saccharide oxidases, e.g., glucose oxidase,
10 galactose oxidase, and glucose-6-phosphate dehydrogenase, heterocyclic oxidases such as uricase and xanthine oxidase, coupled with an enzyme that employs hydrogen peroxide to oxidize a dye precursor such as HRP, lactoperoxidase, or microperoxidase, biotin/avidin, spin labels, bacteriophage labels, stable free radicals, and the like.

15 **E. Pharmaceutical Compositions**

In a further aspect, provided are pharmaceutical compositions comprising any of the antibodies provided herein, e.g., for use in any of the below therapeutic methods. In one aspect, a pharmaceutical composition comprises any of the antibodies provided herein and a pharmaceutically acceptable carrier. In another
20 aspect, a pharmaceutical composition comprises any of the antibodies provided herein and at least one additional therapeutic agent, e.g., as described below.

Pharmaceutical compositions (formulations) of an anti-C3bBb antibody as described herein can be prepared by combining the antibody with pharmaceutically acceptable carriers or excipients known to the skilled person. See, for example
25 Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980), Shire S., Monoclonal Antibodies: Meeting the Challenges in Manufacturing, Formulation, Delivery and Stability of Final Drug Product, 1st Ed., Woodhead Publishing (2015), §4 and Falconer R.J., Biotechnology Advances (2019), 37, 107412. Exemplary pharmaceutical compositions of an anti-C3bBb antibody as described herein are
30 lyophilized, aqueous, frozen, etc.

Pharmaceutically acceptable carriers are generally nontoxic to recipients at the dosages and concentrations employed, and include, but are not limited to: buffers

such as histidine, phosphate, citrate, acetate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride; benzethonium chloride; phenol, butyl or benzyl alcohol; 5 alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, 10 disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as polyethylene glycol (PEG).

15 The pharmaceutical composition herein may also contain more than one active ingredients as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Such active ingredients are suitably present in combination in amounts that are effective for the purpose intended.

20 The pharmaceutical compositions to be used for in vivo administration are generally sterile. Sterility may be readily accomplished, e.g., by filtration through sterile filtration membranes.

F. Therapeutic Methods and Routes of Administration

Any of the anti-C3bBb antibodies provided herein may be used in therapeutic methods.

25 In one aspect, an anti-C3bBb antibody for use as a medicament is provided. In further aspects, an anti-C3bBb antibody for use in treating an ocular disease is provided. In one embodiment the ocular disease is selected from AMD (in one embodiment wet AMD, dry AMD, intermediate AMD, advanced AMD, and geographic atrophy (GA), macular degeneration, macular edema, DME (in one 30 embodiment focal, non-center DME and diffuse, center-involved DME), retinopathy, diabetic retinopathy (DR) (in one embodiment proliferative DR (PDR), non-proliferative DR (NPDR), and high-altitude DR), other ischemia-related retinopathies, ROP, retinal vein occlusion (RVO) (in one embodiment central (CRVO) and branched (BRVO) forms), CNV (in one embodiment myopic CNV),

corneal neovascularization, diseases associated with corneal neovascularization, retinal neovascularization, diseases associated with retinal/choroidal neovascularization, central serous retinopathy (CSR), pathologic myopia, von Hippel-Lindau disease, histoplasmosis of the eye, FEVR, Coats' disease, Norrie Disease, retinal abnormalities associated with osteoporosis-pseudoglioma syndrome (OPPG), subconjunctival hemorrhage, rubeosis, ocular neovascular disease, neovascular glaucoma, retinitis pigmentosa (RP), hypertensive retinopathy, retinal angiomatous proliferation, macular telangiectasia, iris neovascularization, intraocular neovascularization, retinal degeneration, cystoid macular edema (CME), vasculitis, papilloedema, retinitis, including but not limited to CMV retinitis, ocular melanoma, retinal blastoma, conjunctivitis (in one embodiment infectious conjunctivitis and non-infectious (in one embodiment allergic) conjunctivitis), Leber congenital amaurosis (also known as Leber's congenital amaurosis or LCA), uveitis (including infectious and non-infectious uveitis), choroiditis (in one embodiment multifocal choroiditis), ocular histoplasmosis, blepharitis, dry eye, traumatic eye injury, Sjögren's disease, and other ophthalmic diseases wherein the disease or disease is associated with ocular neovascularization, vascular leakage, and/or retinal edema or retinal atrophy. In one embodiment the ocular disease is selected from AMD (in one embodiment wet AMD, dry AMD, intermediate AMD, advanced AMD, and geographic atrophy (GA)), macular degeneration, macular edema, DME (in one embodiment focal, non-center DME and diffuse, center-involved DME), retinopathy, diabetic retinopathy (DR) (in one embodiment proliferative DR (PDR), non-proliferative DR (NPDR), and high-altitude DR. In one embodiment the ocular disease is from AMD, in one embodiment wet AMD.

In certain aspects, an anti-C3bBb antibody for use in a method of treatment is provided. In certain aspects, the invention provides an anti-C3bBb antibody for use in a method of treating an individual having an ocular disease comprising administering to the individual an effective amount of the anti-C3bBb antibody. In one such aspect, the method further comprises administering to the individual an effective amount of at least one additional therapeutic agent (e.g., one, two, three, four, five, or six additional therapeutic agents), e.g., as described below.

In a further aspect, the invention provides for the use of an anti-C3bBb antibody in the manufacture or preparation of a medicament. In one aspect, the medicament is for treatment of an ocular disease. In a further aspect, the medicament is for use in a method of treating an ocular disease comprising administering to an individual having an ocular disease an effective amount of the medicament. In one

such aspect, the method further comprises administering to the individual an effective amount of at least one additional therapeutic agent, e.g., as described below. An “individual” according to any of the above aspects may be a human.

5 In a further aspect, the invention provides a method for treating an ocular disease. In one aspect, the method comprises administering to an individual having such ocular disease an effective amount of an anti-C3bBb antibody. In one such aspect, the method further comprises administering to the individual an effective amount of at least one additional therapeutic agent, as described below. An “individual” according to any of the above aspects may be a human.

10 In a further aspect, the invention provides pharmaceutical compositions comprising any of the anti-C3bBb antibodies provided herein, e.g., for use in any of the above therapeutic methods. In one aspect, a pharmaceutical composition comprises any of the anti-C3bBb antibodies provided herein and a pharmaceutically acceptable carrier. In another aspect, a pharmaceutical composition comprises any
15 of the anti-C3bBb antibodies provided herein and at least one additional therapeutic agent, e.g., as described below.

Antibodies of the invention can be administered alone or used in a combination therapy. For instance, the combination therapy includes administering an antibody of the invention and administering at least one additional therapeutic
20 agent (e.g. one, two, three, four, five, or six additional therapeutic agents). In certain aspects, the combination therapy comprises administering an antibody of the invention and administering at least one additional therapeutic agent, such as a VEGF-antagonist.

Any suitable AMD therapeutic agent can be administered as an additional
25 therapeutic agent in combination with an antibody that binds to human C3bBb as provided herein for treatment of an ocular disorder (e.g., AMD, DME, DR, RVO, or GA), including, but not limited to, a VEGF antagonist, for example, an anti-VEGF antibody (e.g., LUCENTIS® (ranibizumab), RTH-258 (formerly ESBA-1008, an anti-VEGF single-chain antibody fragment; Novartis), or a bispecific anti-VEGF
30 antibody (e.g., an anti-VEGF/anti-angiopoietin 2 bispecific antibody such as faricimab or zifibancimig; Roche)), a soluble VEGF receptor fusion protein (e.g., EYLEA® (aflibercept)), an anti-VEGF DARPIn® (e.g., abicipar pegol; Molecular Partners AG/Allergan), or an anti-VEGF aptamer (e.g., MACUGEN® (pegaptanib

sodium)); a platelet-derived growth factor (PDGF) antagonist, for example, an anti-PDGF antibody, an anti-PDGFR antibody (e.g., REGN2176-3), an anti-PDGF-BB pegylated aptamer (e.g., FOVISTA®; Ophthotech/Novartis), a soluble PDGFR receptor fusion protein, or a dual PDGF/VEGF antagonist (e.g., a small molecule inhibitor (e.g., DE-120 (Santen) or X-82 (TyrogeneX)) or a bispecific anti-PDGF/anti-VEGF antibody)); VISUDYNE® (verteporfin) in combination with photodynamic therapy; an antioxidant; a complement system antagonist, for example, a complement factor C5 antagonist (e.g., a small molecule inhibitor (e.g., ARC-1905; Ophthotech) or an anti-C5 antibody (e.g., LFG-316; Novartis), a properdin antagonist (e.g., an anti-properdin antibody, e.g., CLG-561; Alcon), or a complement factor D antagonist (e.g., an anti-complement factor D antibody, e.g., lampalizumab; Roche)); a C3 blocking peptide (e.g., APL-2, Appellis); a visual cycle modifier (e.g., emixustat hydrochloride); squalamine (e.g., OHR-102; Ohr Pharmaceutical); vitamin and mineral supplements (e.g., those described in the Age-Related Eye Disease Study 1 (AREDS1; zinc and/or antioxidants) and Study 2 (AREDS2; zinc, antioxidants, lutein, zeaxanthin, and/or omega-3 fatty acids)); a cell-based therapy, for example, NT-501 (Renexus); PH-05206388 (Pfizer), huCNS-SC cell transplantation (StemCells), CNTO-2476 (umbilical cord stem cell line; Janssen), OpRegen (suspension of RPE cells; Cell Cure Neurosciences), or MA09-hRPE cell transplantation (Ocata Therapeutics); a tissue factor antagonist (e.g., hIcon1; Iconic Therapeutics); an alpha-adrenergic receptor agonist (e.g., brimonidine tartrate; Allergan); a peptide vaccine (e.g., S-646240; Shionogi); an amyloid beta antagonist (e.g., an anti-beta amyloid monoclonal antibody, e.g., GSK-933776); an S1P antagonist (e.g., an anti-S1P antibody, e.g., iSONEP™; Lpath Inc); a ROBO4 antagonist (e.g., an anti-ROBO4 antibody, e.g., DS-7080a; Daiichi Sankyo); a lentiviral vector expressing endostatin and angiostatin (e.g., RetinoStat); and any combination thereof. In some instances, AMD therapeutic agents (including any of the preceding AMD therapeutic agents) can be co-formulated. For example, the anti-PDGFR antibody REGN2176-3 can be co-formulated with aflibercept (EYLEA®).

In some instances, such a co-formulation can be administered in combination with an antibody that binds to human C3bBb of the invention. In some instances, the ocular disorder is AMD (e.g., wet AMD).

Any suitable DME and/or DR therapeutic agent can be administered in combination with an antibody that binds to human C3bBb of the invention for treatment of an ocular disorder (e.g., AMD, DME, DR, RVO, or GA), including, but not limited, to a VEGF antagonist (e.g., LUCENTIS® or EYLEA®), a corticosteroid (e.g., a corticosteroid implant (e.g., OZURDEX® (dexamethasone intravitreal implant) or ILUVIEN® (fluocinolone acetonide intravitreal implant)) or a corticosteroid formulated for administration by intravitreal injection (e.g., triamcinolone acetonide)), or combinations thereof. In some instances, the ocular disorder is DME and/or DR.

An antibody that binds to human C3bBb as provided herein may be administered in combination with a therapy or surgical procedure for treatment of an ocular disorder (e.g., AMD, DME, DR, RVO, or GA), including, for example, laser photocoagulation (e.g., panretinal photocoagulation (PRP)), drusen lasering, macular hole surgery, macular translocation surgery, implantable miniature telescopes, PHI-motion angiography (also known as micro-laser therapy and feeder vessel treatment), proton beam therapy, microstimulation therapy, retinal detachment and vitreous surgery, scleral buckle, submacular surgery, transpupillary thermotherapy, photosystem I therapy, use of RNA interference (RNAi), extracorporeal rheopheresis (also known as membrane differential filtration and rheotherapy), microchip implantation, stem cell therapy, gene replacement therapy, ribozyme gene therapy (including gene therapy for hypoxia response element, Oxford Biomedica; Lentipak, Genetix; and PDEF gene therapy, GenVec), photoreceptor/retinal cells transplantation (including transplantable retinal epithelial cells, Diacrin, Inc.; retinal cell transplant, e.g., Astellas Pharma US, Inc., ReNeuron, CHA Biotech), acupuncture, and combinations thereof.

Such combination therapies noted above encompass combined administration (where two or more therapeutic agents are included in the same or separate formulations), and separate administration, in which case, administration of the antibody that binds to human C3bBb of the invention can occur prior to, simultaneously, and/or following, administration of the additional therapeutic agent or agents. In one embodiment, administration of the antibody that binds to human C3bBb of the invention and administration of an additional therapeutic agent occur

within about one, two, three, four, or five months, or within about one, two or three weeks, or within about one, two, three, four, five, or six days, of each other.

5 An antibody of the invention (and any additional therapeutic agent) can be administered by any suitable means, including parenteral, intrapulmonary, and intranasal, and, if desired for local treatment, intralesional administration. Parenteral
infusions include intramuscular, intravenous, intraarterial, intraperitoneal, or subcutaneous administration. Dosing can be by any suitable route, e.g., by injections, such as intravenous or subcutaneous injections, depending in part on whether the administration is brief or chronic. Various dosing schedules including
10 but not limited to single or multiple administrations over various time-points, bolus administration, and pulse infusion are contemplated herein.

Antibodies of the invention would be formulated, dosed, and administered in a fashion consistent with good medical practice. Factors for consideration in this context include the particular disorder being treated, the particular mammal being
15 treated, the clinical condition of the individual patient, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. The antibody need not be, but is optionally formulated with one or more agents currently used to prevent or treat the disorder in question. The effective amount of such other agents depends
20 on the amount of antibody present in the pharmaceutical composition, the type of disorder or treatment, and other factors discussed above. These are generally used in the same dosages and with administration routes as described herein, or about from 1 to 99% of the dosages described herein, or in any dosage and by any route that is empirically/clinically determined to be appropriate.

25 For the prevention or treatment of disease, the appropriate dosage of an antibody of the invention (when used alone or in combination with one or more other additional therapeutic agents) will depend on the type of disease to be treated, the type of antibody, the severity and course of the disease, whether the antibody is administered for preventive or therapeutic purposes, previous therapy, the patient's
30 clinical history and response to the antibody, and the discretion of the attending physician. The antibody is suitably administered to the patient at one time or over a series of treatments. For repeated administrations over several days or longer, depending on the condition, the treatment would generally be sustained until a desired suppression of disease symptoms occurs. The progress of this therapy is
35 easily monitored by conventional techniques and assays.

3. Specific embodiments of the invention

In the following specific embodiments of the invention are listed.

1. An antibody that specifically binds to human C3bBb.
2. An antibody that binds to human C3bBb, wherein the antibody:
 - 5 - binds to wild-type human C3bBb; and/or
 - binds to recombinant human C3bBb, which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:491;
 - binds to recombinant human C3bBb, which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:492; and/or
 - 10 - binds to recombinant human C3bBb, which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:493; and/or
 - binds to recombinant human C3bBb, which comprises the Bb subunit of a recombinant Factor B (FB) protein, which comprises a D279G mutation and optionally mutations K350N and/or a M458I;
 - 15 - inhibits the alternative pathway; and/or
 - is an agonist or antagonist of C3bBb activity; and/or
 - specifically binds to cynomolgus C3bBb and human C3bBb, and/or
 - specifically binds to African green monkey C3bBb and human C3bBb, and/or
 - 20 - binds with an affinity of ≤ 300 pM at 37 °C as measured by SPR.
3. An antibody that specifically binds to recombinant human C3bBb comprising the Bb subunit of an FB protein with a D279G mutation and optionally further mutations K350N and/or M458I.
4. An antibody that specifically binds to recombinant human C3bBb which
25 comprises the Bb subunit of factor B (FB) according to SEQ ID NO:491.
5. An antibody that specifically binds to recombinant human C3bBb which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:492.
6. An antibody that specifically binds to recombinant human C3bBb which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:493.
- 30 7. An antibody that specifically binds to an epitope of human C3bBb that includes amino acid residues of the C3b subunit and amino acid residues of the Bb subunit of human C3bBb.
8. An antibody that binds to human C3bBb that binds to an epitope comprising the
35 following amino acid residues on C3bBb as detected by cryogenic electron microscopy:

- C3b subunit: Arg444, Lys534, Gly539, Ser540, Val524, Lys544, Gly546, Gln547, Ser548, Arg551, Gln557, Gln558, Thr560, Lys562, Glu564, Glu758, Pro759, Lys761, Asn762, Ile764, Leu768, Asn770, Asp797, and
 - Bb subunit: Tyr465, Lys473, Ile474, Ser475, Ile477, Gly482, His483, Lys513, Val514, Ser515, Lys520, Arg521, Asp522, Glu610, and Lys613.
- 5
9. An antibody that binds to the same or an overlapping epitope as an antibody having a VH domain of SEQ ID NO: 39 and a VL domain of SEQ ID NO: 40 (P1AF8499).
- 10
10. An antibody that binds to human C3bBb, wherein the antibody comprises the heavy and light chain CDRs of an antibody selected from Table D1.
11. An antibody that binds to human C3bBb, wherein the antibody comprises the heavy and light chain variable domains of an antibody selected from Table D1.
12. The antibody of one of the preceding embodiments, comprising a set of six CDRs, in one embodiment a set of a VH and a VL domain, as an antibody selected from antibody #1 to antibody #217 from Table D1.
- 15
13. The antibody of one of the preceding embodiments, comprising a set of six CDRs, in one embodiment a set of a VH and a VL domain, as an antibody selected from antibody #1 to antibody #122 from Table D1.
14. The antibody of one of the preceding embodiments, comprising a set of six CDRs, in one embodiment a set of a VH and a VL domain, as an antibody selected from antibody #1 to antibody #7 and antibody #22 to antibody #217 from Table D1.
- 20
15. The antibody of one of the preceding embodiments, comprising a set of six CDRs, in one embodiment a set of a VH and a VL domain, as an antibody selected from antibody #1 to antibody #7 from Table D1.
- 25
16. The antibody of one of the preceding embodiments, comprising
- i) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:449; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:450; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:451, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:452; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:453; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:454 (corresponding to antibody #1, P1AG9426);
 - 30
 - ii) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:455; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:456; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:457, and a light chain variable domain (VL)
 - 35

- comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:458; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:459; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:460 (corresponding to antibody #2, P1AG9376);
- 5 iii) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:461; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:462; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:463, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID
- 10 NO:464; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:465; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:466 (corresponding to antibody #3, P1AG9372);
- 15 iv) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:467; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:468; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:469, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID
- 20 NO:470; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:471; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:472 (corresponding to antibody #4, P1AG9420);
- 25 v) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:473; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:474; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:475, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID
- 30 NO:476; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:477; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:478 (corresponding to antibody #5, P1AG9391);
- 35 vi) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:479; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:480; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:481, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID
- NO:482; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:483; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:484 (corresponding to antibody #6, P1AH1205); or
- vii) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:485; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:486; and (c) CDR-H3 comprising the amino acid

- sequence of SEQ ID NO:487, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:488; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:489; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:490 (corresponding to to antibody #7, P1AH1199).
- 5
17. The antibody of any of the preceding embodiments, comprising a sequence selected from the group consisting of
- (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:1;
- 10 (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2; and
- (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).
18. The antibody of any of the preceding embodiments, comprising a sequence selected from the group consisting of
- 15 (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:3;
- (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:4; and
- (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).
- 20 19. The antibody of any of the preceding embodiments, comprising a sequence selected from the group consisting of
- (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:5;
- (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6; and
- 25 (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).
20. The antibody of any of the preceding embodiments, comprising a sequence selected from the group consisting of
- (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7;
- 30 (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; and
- (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).
21. The antibody of any of the preceding embodiments, comprising a sequence selected from the group consisting of
- 35 (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:9;

- (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:10; and
- (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).
22. The antibody of any of the preceding embodiments, comprising a sequence
5 selected from the group consisting of
- (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:11;
- (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:12; and
- 10 (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).
23. The antibody of any of the preceding embodiments, comprising a sequence selected from the group consisting of
- (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:13;
- 15 (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:14; and
- (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).
24. The antibody of one of the preceding embodiments, comprising
- 20 i) a VH domain comprising SEQ ID NO:1 and a VL domain comprising SEQ ID NO:2 (corresponding to antibody #1, P1AG9426);
- ii) a VH domain comprising SEQ ID NO:3 and a VL domain comprising SEQ ID NO:4 (corresponding to antibody #2, P1AG9376);
- iii) a VH domain comprising SEQ ID NO:5 and a VL domain comprising SEQ ID NO:6 (corresponding to antibody #3, P1AG9372);
- 25 iv) a VH domain comprising SEQ ID NO:7 and a VL domain comprising SEQ ID NO:8 (corresponding to antibody #4, P1AG9420);
- v) a VH domain comprising SEQ ID NO:9 and a VL domain comprising SEQ ID NO:10 (corresponding to antibody #5, P1AG9391);
- 30 vi) a VH domain comprising SEQ ID NO:11 and a VL domain comprising SEQ ID NO:12 (corresponding to antibody #6, P1AH1205); or
- vii) a VH domain comprising SEQ ID NO:13 and a VL domain comprising SEQ ID NO:14 (corresponding to antibody #7, P1AH1199).
25. The antibody of any of the preceding embodiments comprising a heavy chain of SEQ ID NO:435 and a light chain of SEQ ID NO:436.
- 35 26. The antibody of any of the preceding embodiments comprising a heavy chain of SEQ ID NO:437 and a light chain of SEQ ID NO:438.
27. The antibody of any of the preceding embodiments comprising a heavy chain of SEQ ID NO:439 and a light chain of SEQ ID NO:440.

28. The antibody of any of the preceding embodiments comprising a heavy chain of SEQ ID NO:441 and a light chain of SEQ ID NO:442.
29. The antibody of any of the preceding embodiments comprising a heavy chain of SEQ ID NO:443 and a light chain of SEQ ID NO:444.
- 5 30. The antibody of any of the preceding embodiments comprising a heavy chain of SEQ ID NO:445 and a light chain of SEQ ID NO:446.
31. The antibody of any of the preceding embodiments comprising a heavy chain of SEQ ID NO:447 and a light chain of SEQ ID NO:447.
- 10 32. The antibody of any one of the preceding embodiments, which is a monoclonal antibody.
33. The antibody of any one of the preceding embodiments, which is a human antibody.
34. The antibody of any one of the preceding embodiments, wherein the antibody comprises a VH domain with a VH3 framework and a VL domain with a V κ 1 framework.
- 15 35. The antibody of any one of the preceding embodiments, wherein the antibody comprises human constant regions of IgG isotype.
36. The antibody of any of the preceding embodiments, which is an antibody fragment that binds human C3bBb.
- 20 37. The antibody of any of the preceding embodiments, which is a full length IgG1 antibody.
38. The antibody of any of the preceding embodiments, wherein the antibody binds human C3bBb with an affinity of ≤ 300 pM as measured by SPR.
39. The antibody of any of the preceding embodiments, wherein the antibody is a multispecific antibody.
- 25 40. An antibody, which competes for binding to human C3bBb with the antibody of any one of the preceding embodiments.
41. An isolated nucleic acid encoding the antibody of any of the preceding embodiments.
- 30 42. A host cell comprising the nucleic acid of embodiment 42.
43. A method of producing an antibody that binds to human C3bBb comprising culturing the host cell of embodiment 42 under conditions suitable for the expression of the antibody.
44. The method of embodiment 43, further comprising recovering the antibody from the host cell.
- 35 45. An antibody produced by the method of embodiment 43.

46. A pharmaceutical composition comprising the antibody of any of embodiments
1 to 40 and a pharmaceutically acceptable carrier.
47. The pharmaceutical composition of embodiment 46, further comprising an
additional therapeutic agent.
548. The antibody of any one of embodiments 1 to 40 or the pharmaceutical
composition of any or embodiments 46 to 47 for use as a medicament.
49. The antibody of any one of embodiments 1 to 40 or the pharmaceutical
composition of any of embodiments 46 to 47 for use in treating an ocular disease.
50. Use of the antibody of any one of embodiments 1 to 40 or the pharmaceutical
composition of any of embodiments 46 to 47 in the manufacture of a medicament
for treatment of an ocular disease.
51. A method of treating an individual having an ocular disease comprising
administering to the individual an effective amount of the antibody of any one of
embodiments 1 to 40 or the pharmaceutical composition of any of embodiments
46 to 47.

DESCRIPTION OF THE AMINO ACID SEQUENCES

	#	identifier	domain	sequence
SEQ ID NO: 01	1	P1AG9426	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVIYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 02	1	P1AG9426	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 03	2	P1AG9376	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 04	2	P1AG9376	VL	AIQMTQSPSSLSASVGDRVTITCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSHDEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 05	3	P1AG9372	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 06	3	P1AG9372	VL	AIQMTQSPSSLSASVGDRVTITCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSHDEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK

SEQ ID NO: 07	4	P1AG9420	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRF TISRDEKNTL YLQMNSL RAEDTAVYYCARDWDYFDHWGQGTL VT VSS
SEQ ID NO: 08	4	P1AG9420	VL	AIQMTQSPSSLASVGDRTVITTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSHEEYTL TISSLQPEDFATYYCQQY RTPYTFGGGTKLEIK
SEQ ID NO: 09	5	P1AG9391	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRF TISRDNEKNTL YLQMNSL RAEDTAVYYCARDWEYFDNWGQGTL VT VSS
SEQ ID NO: 10	5	P1AG9391	VL	AIQMTQSPSSLASVGDRTVITTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPS RFSGSGSHEEYTL TISSLQPEDFATYYCQQ YRDTPTYTFGGGTKLEIK
SEQ ID NO: 11	6	P1AH1205	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRF TISRDNDKNTL YLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 12	6	P1AH1205	VL	AIQMTQSPSSLASVGDRTVITTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPERPS RFSGSGSHDEYTL TISSLQPEDFATYYCQQ YREEPTYTFGGGTKLEIK
SEQ ID NO: 13	7	P1AH1199	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRF TISRDNEKNTL YLQMNSL RAEDTAVYYCARDWEYFDNWGQGTL VT VSS
SEQ ID NO: 14	7	P1AH1199	VL	AIQMTQSPSSLASVGDRTVITTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPS RFSGSGSHEEYTL TISSLQPEDFATYYCQQ YRDTPTYTFGGGTKLEIK
SEQ ID NO: 15	8	C3bBb.P045.07 2	VH	KLQLVESGGGLVKPGGSLRLSCAASGRRF GVqDMSWVRQAPGKGLEWVGSISPKGDH KYLNTKFIGRFTISRDNKNTL YLQMNSLR AEDTAVYYCARDWGYFDQWGQGTL VTV SS
SEQ ID NO: 16	8	C3bBb.P045.07 2	VL	AIQMTQSPSSLASVGDRTVITTCGHSYWLS SEVAWYQQKPGKAPKLLIYDGNIGNVP SRFSGSGSHEDYTL TISSLQPEDFATYYCQ QYRYHPYTFGHGTVKVEIK
SEQ ID NO: 17	9	C3bBb.P045.23 6	VH	YGQLVESGGGLVKPGGSLRLSCAATGTLF SKqDMSWVRQAPGKGLEWVGSISPKGDH KYLNTKFIGRFTISRDNKNTL YLQMNSLR AEDTAVYYCAKDWGYFDHWGQGTL VTV SS
SEQ ID NO: 18	9	C3bBb.P045.23 6	VL	AIQMTQSPSSLASVGDRTVITTCGHSYWLS SEVAWYQQKPGKAPKLLIYDGNVQGSV PSRFSGSGSHEDYTL TISSLQPEDFATYYC QQYRYHPYTFGHGTVKVEIK
SEQ ID NO: 19	10	C3bBb.P045.22 5	VH	DPQLVESGGGLVKPGGSLRLSCAARGLHF NNTDMSWVRQAPGKGLEWVGSISPKGDH KYLNTKFIGRFTISRDNKNTL YLQMNSLR AEDTAVYYCARDWGYFDWWGQGTL VT VSS
SEQ ID NO: 20	10	C3bBb.P045.22 5	VL	AIQMTQSPSSLASVGDRTVITTCGHSYWLS SEVAWYQQKPGKAPKLLIYDGNLKGGV PSRFSGSGSHEDYTL TISSLQPEDFATYYC QQYRYHPYTFGHGTVKVEIK

SEQ ID NO: 21	11	C3bBb.P048.15 2	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKSGS KGYAQNVPRFTISRDNNDTL YLQMNS LRAEDTAVYYCARDIGFFDTWGQGT LVT VSS
SEQ ID NO: 22	11	C3bBb.P048.15 2	VL	HDIQMTQSPSSLSASVGDRVTITCDADFGI SNYLA WYQQKPGKAPKLLIFDAKYRAPE VPSRFGSGSGGSFTLTISLQPEDFATYYC QQYGVHPFTFGQGTKVEIK
SEQ ID NO: 23	12	C3bBb.P048.06 1	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKGGS TDINPKIGGRFTISRDNNDTL YLQMNSLR AEDTAVYYCARDIGFFDTWGQGT LVTVS S
SEQ ID NO: 24	12	C3bBb.P048.06 1	VL	AIQMTQSPSSLSASVGDRVTITCQGSWLIS NYLA WYQQKPGKAPKLLIFDAKYRAPEV PSRFGSGSGTDFTLTISLQPEDFATYYCQ QYGGRLTFGQGTKVEIK
SEQ ID NO: 25	13	C3bBb.P048.12 7	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKGGS TEYNTKVYGRFTISRDNNDTL YLQMNSL RAEDTAVYYCARDIGFFDTWGQGT LVT VSS
SEQ ID NO: 26	13	C3bBb.P048.12 7	VL	HQMTQSPSSLSASVGDRVTITCDGEWDIS NYLA WYQQKPGKAPKLLIFDAKYRAPEV PSRFGSGSGRDFTLTISLQPEDFATYYC QQYNRMFTFGQGTKVEIK
SEQ ID NO: 27	14	C3bBb.P048.24 1	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKGGS AWYNNNFTGRFTISRDNNDTL YLQMNS LRAEDTAVYYCARDIGFFDTWGQGT LVT VSS
SEQ ID NO: 28	14	C3bBb.P048.24 1	VL	HINQMTQSPSSLSASVGDRVTITCQAKWV ISNYLA WYQQKPGKAPKLLIFDAKYRAPE VPSRFGSGSGDFTLTISLQPEDFATYYC QQYDWWPYTFGQGTKVEIK
SEQ ID NO: 29	15	C3bBb.P048.23 0	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKGGS AWYNNKFHGRFTISRDNNDTL YLQMNS LRAEDTAVYYCARDIGFFDTWGQGT LVT VSS
SEQ ID NO: 30	15	C3bBb.P048.23 0	VL	HYIQMTQSPSSLSASVGDRVTITCQGNFI SNYLA WYQQKPGKAPKLLIFDAKYRAPE VPSRFGSGSGDDFTLTISLQPEDFATYY CQYDWWPYTFGQGTKVEIK
SEQ ID NO: 31	16	C3bBb.P048.20 4	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKGGS AWFNRFAGRFTISRDNNDTL YLQMNS LRAEDTAVYYCARDIGFFDTWGQGT LVT VSS
SEQ ID NO: 32	16	C3bBb.P048.20 4	VL	GHVQMTQSPSSLSASVGDRVTITCQAEDEI SNYLA WYQQKPGKAPKLLIFDAKYRAPE VPSRFGSGSDASFTLTISLQPEDFATYYC QQYDWWPYTFGQGTKVEIK
SEQ ID NO: 33	17	C3bBb.P048.33 3	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKGGS AWYNDKFKGRFTISRDNNDTL YLQMNS LRAEDTAVYYCARDIGFFDTWGQGT LVT VSS
SEQ ID NO: 34	17	C3bBb.P048.33 3	VL	HINQMTQSPSSLSASVGDRVTITCNSTEFIS NYLA WYQQKPGKAPKLLIFDAKYRAPEV PSRFGSGSDQEFTLTISLQPEDFATYYCQ QYDWWPYTFGQGTKVEIK

SEQ ID NO: 35	18	C3bBb.P053.095	VH	RKQLVESGGGLVQPGGSLRLSCAAHGSLV SRNDMSWVRQAPGKGLEWVGSISPKGDH KYYNTKFIDRF TISRDN SKNTL YLQMNSL RAEDTAVYYCAKDVDYMDLWGQGLVT VSS
SEQ ID NO: 36	18	C3bBb.P053.095	VL	AIQMTQSPSSLSASVGDRVTITCQASYWL NSELAWYQQKPGKAPKLLIFDGDQTWFG VPSRFGSGSGSHEDYTLTISSLQPEDFATYY CQQYRYTPYTFGQGTKLEIK
SEQ ID NO: 37	19	C3bBb.P055.015	VH	GQLVESGGGLVKPGGSLRLSCKASGFYW GPGAMSWVRQAPGKGLEWVGSISPKGGS AEYASKVYGRFTISRDNNDQTL YLQMNSL RAEDTAVYYCARDIGFFDTWGQGLVT VSS
SEQ ID NO: 38	19	C3bBb.P055.015	VL	DYQMTQSPSSLSASVGDRVTITCEAHSQIS NYLAWYQQKPGKAPKLLIFDAKYRAPEV PSRFGSGSGSPDFTLTISSLQPEDFATYYCQ QYNDFWLTFGQGTKVEIK
SEQ ID NO: 39	20	P1AF8499	VH	EVQLVESGGGLVQPGGSLRLSCAASGFSW EHYAMTWVRQAPGKGLEWVGSISPKGDH KYYNTKFIDRF TISRDN SKNTL YLQMNSL RAEDTAVYYCARDWDYFDEWGQGLVT VSS
SEQ ID NO: 40	20	P1AF8499	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 41	21	GQ-5_1	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRF TISRDN SKNTL YLQMNS LRAEDTAVYYCARDWDYFDEWGQGLV TVSS
SEQ ID NO: 42	21	GQ-5_1	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 43	22	GQ-11_1	VH	EVQLVESGGGLVQPGGSLRLSCAASGFSW EHYAMTWVRQAPGKGLEWVGSISPKGDH KYYNTKFIDRF TISRDN SKNTL YLQMNSL RAEDTAVYYCARDWDYFDEWGQGLVT VSS
SEQ ID NO: 44	22	GQ-11_1	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 45	23	PT5622.F19	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRF TISRDN EKNL YLQMNSL RAEDTAVYYCARDWEYFDNWGQGLVT VSS
SEQ ID NO: 46	23	PT5622.F19	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 47	24	PT5624.P06	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVIAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRF TISRDN EKNL YLQMNSL RAEDTAVYYCARDWEYFDNWGQGLVT VSS

SEQ ID NO: 48	24	PT5624.P06	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 49	25	PT5624.M09	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 50	25	PT5624.M09	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 51	26	PT5626.M10	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFTISRDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGTLVT VSS
SEQ ID NO: 52	26	PT5626.M10	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 53	27	PT5626.C10	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 54	27	PT5626.C10	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 55	28	PT5628.E16	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPRGNT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDYWGGQTLVT VSS
SEQ ID NO: 56	28	PT5628.E16	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 57	29	PT5630.D05	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 58	29	PT5630.D05	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 59	30	PT5630.A20	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 60	30	PT5630.A20	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 61	31	PT5632.A13	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGGQTL VTVSS

SEQ ID NO: 62	31	PT5632.A13	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 63	32	PT5634.N13	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDN SKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGT LVT VSS
SEQ ID NO: 64	32	PT5634.N13	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 65	33	PT5634.M24	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFTISRDEKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGT L TVSS
SEQ ID NO: 66	33	PT5634.M24	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 67	34	PT5636.P22	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDRWGQGT LVT VSS
SEQ ID NO: 68	34	PT5636.P22	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 69	35	PT5625.G07	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LV TVSS
SEQ ID NO: 70	35	PT5625.G07	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYC QYRNTPYTFGQGTKLEIK
SEQ ID NO: 71	36	PT5627.M20	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LV TVSS
SEQ ID NO: 72	36	PT5627.M20	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YREEPTYTFGQGTKLEIK
SEQ ID NO: 73	37	PT5627.M12	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LV TVSS
SEQ ID NO: 74	37	PT5627.M12	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 75	38	PT5629.F09	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LV TVSS

SEQ ID NO: 76	38	PT5629.F09	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 77	39	PT5629.H08	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 78	39	PT5629.H08	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 79	40	PT5631.D21	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 80	40	PT5631.D21	VL	AIQMTQSPSSLASVGDRTTTCQSSHWS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 81	41	PT5633.I03	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 82	41	PT5633.I03	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPYTFGQGTKLEIK
SEQ ID NO: 83	42	PT5635.C08	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 84	42	PT5635.C08	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGQGTKLEIK
SEQ ID NO: 85	43	PT5639.G15	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 86	43	PT5639.G15	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 87	44	PT5622.A20	VH	EVQLVESGGGLVQPGGSLRLSCAASGFR WDKYAMSWVRQAPGKGLEWVGEISPRG DSKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWEYFDN WGQGT LTVSS
SEQ ID NO: 88	44	PT5622.A20	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 89	45	PT5622.C12	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY EHYAMSWVRQAPGKGLEWVGSISPRGDH KYYNTKFIDRFTISRDN SKNTLYLQMNSL RAEDTAVYYCARDWDYFDTW GQGT LVSS

SEQ ID NO: 90	45	PT5622.C12	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 91	46	PT5622.G24	VH	GVQLVESGGGLVQPGGSLRLSCAASGFRY DIYAMSWVRQAPGKGLEWVGEISPEGNH KYYNTKFIDRFTISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDTWGQGTIVT VSS
SEQ ID NO: 92	46	PT5622.G24	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 93	47	PT5622.I20	VH	KVQLVESGGGLVQPGGSLRLSCAASGYT YDIAMSWVRQAPGKGLEWVGEISPDGN TKYYNTKFIDRFTISRDNENKNTLYQMNS LRAEDTAVYYCARDWEYFDHWGQGTIV TVSS
SEQ ID NO: 94	47	PT5622.I20	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 95	48	PT5622.J24	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YEHYAMSWVRQAPGKGLEWVGSISPKGQ HKYYNTKFIDRFTISRDNENKNTLYQMNS LRAEDTAVYYCARDWEYFDVWGQGTIV TVSS
SEQ ID NO: 96	48	PT5622.J24	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 97	49	PT5624.A21	VH	KVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPKGEH KYYNTKFIDRFTISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDGWGQGTIVT VSS
SEQ ID NO: 98	49	PT5624.A21	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 99	50	PT5624.B10	VH	KVQLVESGGGLVQPGGSLRLSCAASGFHY DIYAMSWVRQAPGKGLEWVGEISPDGRH KYYNTKFIDRFTISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDNWGQGTIVT VSS
SEQ ID NO: 100	50	PT5624.B10	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 101	51	PT5624.N05	VH	GVQLVESGGGLVQPGGSLRLSCAASGFKY EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFTISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDYWQGTIVT VSS
SEQ ID NO: 102	51	PT5624.N05	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 103	52	PT5624.P11	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNENKNTLYQMN SLRAEDTAVYYCARDWDYFDQWGQGTIV TVSS

SEQ ID NO: 104	52	PT5624.P11	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 105	53	PT5626.A12	VH	RVQLVESGGGLVQPGGSLRLSCAASGFK WDHYAMSWVRQAPGKGLEWVGSISPDG NHKYYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGGQTL VTVSS
SEQ ID NO: 106	53	PT5626.A12	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 107	54	PT5626.N08	VH	KVQLVESGGGLVQPGGSLRLSCAASGYK YDHYAMSWVRQAPGKGLEWVGEISPEGN SKYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGGQTLVT VSS
SEQ ID NO: 108	54	PT5626.N08	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 109	55	PT5626.N18	VH	KVQLVESGGGLVQPGGSLRLSCAASGFKY EVYAMSWVRQAPGKGLEWVGEISPKGDT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGGQTLVT VSS
SEQ ID NO: 110	55	PT5626.N18	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 111	56	PT5626.O09	VH	RVQLVESGGGLVQPGGSLRLSCAASGFK WEIYAMSWVRQAPGKGLEWVGDISPDGQ TKYYNTKFIDRFTISRDEKNTLYLQMNS LRAEDTAVYYCARDWEYFDHWGGQTLV TVSS
SEQ ID NO: 112	56	PT5626.O09	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 113	57	PT5628.B13	VH	QVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDNWGGQTL VTVSS
SEQ ID NO: 114	57	PT5628.B13	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 115	58	PT5628.C21	VH	RVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDDDKNTLYLQMN SLRAEDTAVYYCARDWDYFDSWGQGT LTVSS
SEQ ID NO: 116	58	PT5628.C21	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 117	59	PT5628.E12	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR WDIYAMSWVRQAPGKGLEWVGSISPDGN HKYYNTKFIDRFTISRDDSKNTLYLQMNS LRAEDTAVYYCARDWDYFDTWGGQTLV TVSS

SEQ ID NO: 118	59	PT5628.E12	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 119	60	PT5628.I07	VH	KVQLVESGGGLVQPGGSLRLSCAASGFRY DYYAMSWVRQAPGKGLEWVGSISPRGDH KYYNTKFIDRFISRDNNDKNTLYLQMNSL RAEDTAVYYCARDWDYFDYWGGQTLVT VSS
SEQ ID NO: 120	60	PT5628.I07	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 121	61	PT5628.P14	VH	KVQLVESGGGLVQPGGSLRLSCAASGFT WEHYAMSWVRQAPGKGLEWVGSISPDG QHKYYNTKFIDRFISRDDSKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGGQTL VTVSS
SEQ ID NO: 122	61	PT5628.P14	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 123	62	PT5630.G05	VH	QVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPDG RHKYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGGQTL VTVSS
SEQ ID NO: 124	62	PT5630.G05	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 125	63	PT5630.K04	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRH KYYNTKFIDRFISRDEKNTLYLQMNSL RAEDTAVYYCARDWEYFDEWGGQTLVT VSS
SEQ ID NO: 126	63	PT5630.K04	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 127	64	PT5630.M11	VH	RVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFISRDDSKNTLYLQMN SLRAEDTAVYYCARDWDYFDHWGGQTL VTVSS
SEQ ID NO: 128	64	PT5630.M11	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 129	65	PT5630.N06	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPKGDT KYYNTKFIDRFISRDDDKNTLYLQMNSL RAEDTAVYYCARDWDYFDYWGGQTLVT VSS
SEQ ID NO: 130	65	PT5630.N06	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 131	66	PT5630.O08	VH	KVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFISRDDSKNTLYLQMN SLRAEDTAVYYCARDWDYFDSWGGQTL VTVSS

SEQ ID NO: 132	66	PT5630.O08	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 133	67	PT5632.A10	VH	RVQLVESGGGLVQPGGSLRLSCAASGFHF DKYAMSWVRQAPGKGLEWVGSISPKGRT KYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWDYFDNWGQGT LTVSS
SEQ ID NO: 134	67	PT5632.A10	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 135	68	PT5632.A15	VH	RVQLVESGGGLVQPGGSLRLSCAASGFR WDYYAMSWVRQAPGKGLEWVGSISPDG QHKYYNTKFIDRFTISRDDDKNTLYLQMN SLRAEDTAVYYCARDWDYFDHWGQGT LTVSS
SEQ ID NO: 136	68	PT5632.A15	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 137	69	PT5632.B15	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGEISPDG QNKYYNTKFIDRFTISRDN DKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGT LTVSS
SEQ ID NO: 138	69	PT5632.B15	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 139	70	PT5632.D11	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPEG NHKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGT LTVSS
SEQ ID NO: 140	70	PT5632.D11	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 141	71	PT5632.J23	VH	GVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGEISPDG RHKYYNTKFIDRFTISRDD SKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGT LTVSS
SEQ ID NO: 142	71	PT5632.J23	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 143	72	PT5634.A17	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPDG RTKYYNTKFIDRFTISRDD EKNTLYLQMN SLRAEDTAVYYCARDWEYFDTWGQGT LTVSS
SEQ ID NO: 144	72	PT5634.A17	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 145	73	PT5634.A21	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF DIYAMSWVRQAPGKGLEWVGEISPDGQS KYYNTKFIDRFTISRDD SKNTLYLQMN SLRAEDTAVYYCARDWDYFDNWGQGT LTVSS

SEQ ID NO: 146	73	PT5634.A21	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 147	74	PT5634.K10	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGEISPKG DNKYYNTKFIDRFTISRDDKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 148	74	PT5634.K10	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 149	75	PT5634.M16	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGEISPKG DSKYYNTKFIDRFTISRDDKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 150	75	PT5634.M16	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 151	76	PT5634.N11	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG QDKYYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWEYFDTWGQGTL VTVSS
SEQ ID NO: 152	76	PT5634.N11	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 153	77	PT5634.P19	VH	KVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPRG NHKYYNTKFIDRFTISRDDDNTLYLQMN SLRAEDTAVYYCARDWDYFDHWGQGTL VTVSS
SEQ ID NO: 154	77	PT5634.P19	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 155	78	PT5636.A16	VH	KVQLVESGGGLVQPGGSLRLSCAASGFKY DIYAMSWVRQAPGKGLEWVGDISPKGET KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWDYFDAWGQGTLVT VSS
SEQ ID NO: 156	78	PT5636.A16	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 157	79	PT5636.D21	VH	EVQLVESGGGLVQPGGSLRLSCAASGYKF DKYAMSWVRQAPGKGLEWVGEISPRGD HKYYNTKFIDRFTISRDDDNTLYLQMNS LRAEDTAVYYCARDWEYFDSWGQGTLV TVSS
SEQ ID NO: 158	79	PT5636.D21	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 159	80	PT5636.M03	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WDIYAMSWVRQAPGKGLEWVGEISPDGR TKYYNTKFIDRFTISRDDSKNTLYLQMNS LRAEDTAVYYCARDWDYFDTWGQGTLV TVSS

SEQ ID NO: 160	80	PT5636.M03	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 161	81	PT5636.N13	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPKGN HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDHWGQGTLV TVSS
SEQ ID NO: 162	81	PT5636.N13	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 163	82	PT5636.P11	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQF DHYAMSWVRQAPGKGLEWVGSISPRGDH KYYNTKFIDRFTISRDN SKNTLYLQMNSL RAEDTAVYYCARDWDYFDQWGQGTLVT VSS
SEQ ID NO: 164	82	PT5636.P11	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 165	83	PT5636.P15	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDYYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWDYFDGWGQGTL VTVSS
SEQ ID NO: 166	83	PT5636.P15	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 167	84	PT5638.C06	VH	KVQLVESGGGLVQPGGSLRLSCAASGYT WEHYAMSWVRQAPGKGLEWVGSISPDG RHKYYNTKFIDRFTISRDD SKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGGQTL VTVSS
SEQ ID NO: 168	84	PT5638.C06	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 169	85	PT5638.C20	VH	KVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPDGD HKYYNTKFIDRFTISRDDS SKNTLYLQMNS LRAEDTAVYYCARDWDYFDHWGQGTLV TVSS
SEQ ID NO: 170	85	PT5638.C20	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 171	86	PT5638.E14	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMTWVRQAPGKGLEWVGEISPRG DSKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWDYFDHWGQGTL VTVSS
SEQ ID NO: 172	86	PT5638.E14	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 173	87	PT5638.J23	VH	EVQLVESGGGLVQPGGSLRLSCAASGWS YDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGGQTL VTVSS

SEQ ID NO: 174	87	PT5638.J23	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 175	88	PT5638.O14	VH	RVQLVESGGGLVQPGGSLRLSCAASGFR WDYYAMSWVRQAPGKGLEWVGSISPDG EHKYYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWDYFDTWGQGT LTVSS
SEQ ID NO: 176	88	PT5638.O14	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 177	89	PT5638.P12	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DYYAMSWVRQAPGKGLEWVGSISPKGDT KYYNTKFIDRFTISRDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDIWGQGT LVTSS
SEQ ID NO: 178	89	PT5638.P12	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDPWEVPS RFGSGSHEDYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 179	90	PT5623.E21	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDNKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LVTSS
SEQ ID NO: 180	90	PT5623.E21	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPERPS RFGSGSHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 181	91	PT5623.F17	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDNKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LVTSS
SEQ ID NO: 182	91	PT5623.F17	VL	AIQMTQSPSSLASVGDRTTTCQSYWLS NYLAWYQQKPGKAPKLLIFDGDPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQY RDEPYTFGQGTKLEIK
SEQ ID NO: 183	92	PT5623.G08	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDNKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LVTSS
SEQ ID NO: 184	92	PT5623.G08	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPEIPS RFGSGSHEEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 185	93	PT5623.H05	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDNKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LVTSS
SEQ ID NO: 186	93	PT5623.H05	VL	AIQMTQSPSSLASVGDRTTTCQSTLWLS NYLAWYQQKPGKAPKLLIFDGDLPEIPS RFGSGSHEEYTLTISSLQPEDFATYYCQQ YKETPYTFGQGTKLEIK
SEQ ID NO: 187	94	PT5623.O08	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDNKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGT LVTSS

SEQ ID NO: 188	94	PT5623.O08	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YRDTPTYTFGQGTKLEIK
SEQ ID NO: 189	95	PT5625.A05	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 190	95	PT5625.A05	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYERPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRETPYTFGQGTKLEIK
SEQ ID NO: 191	96	PT5625.B14	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 192	96	PT5625.B14	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFSGSGSEEEYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 193	97	PT5625.C15	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 194	97	PT5625.C15	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPYEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YKETPTYTFGQGTKLEIK
SEQ ID NO: 195	98	PT5625.G05	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 196	98	PT5625.G05	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPYEVPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YRDTPTYTFGQGTKLEIK
SEQ ID NO: 197	99	PT5625.L22	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 198	99	PT5625.L22	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQQ YRETPYTFGQGTKLEIK
SEQ ID NO: 199	100	PT5625.O14	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 200	100	PT5625.O14	VL	AIQMTQSPSSLASVGDRTTTCQSQLWLS NYLAWYQQKPGKAPKLLIFDGDIPYERPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSEPTYTFGQGTKLEIK
SEQ ID NO: 201	101	PT5627.I21	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS

SEQ ID NO: 202	101	PT5627.I21	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSHEDYTLTISSLQPEDFATYYCQQ YREDPYTFGQGTKLEIK
SEQ ID NO: 203	102	PT5629.F04	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 204	102	PT5629.F04	VL	AIQMTQSPSSLASVGDRTTTCQVSHWLS NYLAWYQQKPGKAPKLLIFDGDLPYEIPS RFGSGSHDEYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 205	103	PT5629.L22	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 206	103	PT5629.L22	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RqTPYTFGQGTKLEIK
SEQ ID NO: 207	104	PT5629.L24	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 208	104	PT5629.L24	VL	AIQMTQSPSSLASVGDRTTTCQSqFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSHDEYTLTISSLQPEDFATYYCQQ YESEPYTFGQGTKLEIK
SEQ ID NO: 209	105	PT5629.M15	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 210	105	PT5629.M15	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSWDEYTLTISSLQPEDFATYYCQQ YRETPTYTFGQGTKLEIK
SEQ ID NO: 211	106	PT5631.H06	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 212	106	PT5631.H06	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSHEDYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 213	107	PT5631.K12	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 214	107	PT5631.K12	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFGSGSHDEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 215	108	PT5631.N17	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS

SEQ ID NO: 216	108	PT5631.N17	VL	AIQMTQSPSSLASVGDRTTTCQSTLWLS NYLAWYQQKPGKAPKLLIFDGDPWEIPS RFSGSGSWDEYTLTISSLQPEDFATYYCQQ YRYTPYTFGQGTKLEIK
SEQ ID NO: 217	109	PT5631.P07	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 218	109	PT5631.P07	VL	AIQMTQSPSSLASVGDRTTTCQSQYWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYKDTPTYTFGQGTKLEIK
SEQ ID NO: 219	110	PT5633.E09	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 220	110	PT5633.E09	VL	AIQMTQSPSSLASVGDRTTTCQAqHWLS NYLAWYQQKPGKAPKLLIFDGDPYERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YRETPYTFGQGTKLEIK
SEQ ID NO: 221	111	PT5633.G19	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 222	111	PT5633.G19	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YRSEPTYTFGQGTKLEIK
SEQ ID NO: 223	112	PT5635.F04	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 224	112	PT5635.F04	VL	AIQMTQSPSSLASVGDRTTTCQAHYWL SNYLAWYQQKPGKAPKLLIFDGDIPYEIPS RFSGSGSEDEYTLTISSLQPEDFATYYCQQ YRSTPTYTFGQGTKLEIK
SEQ ID NO: 225	113	PT5635.L21	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 226	113	PT5635.L21	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPYEIPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YRETPTYTFGQGTKLEIK
SEQ ID NO: 227	114	PT5635.O15	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 228	114	PT5635.O15	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YREEPTYTFGQGTKLEIK
SEQ ID NO: 229	115	PT5637.B23	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS

SEQ ID NO: 230	115	PT5637.B23	VL	AIQMTQSPSSLASVGDRTTTCQSQLWLS NYLAWYQQKPGKAPKLLIFDGDLPYEIPSR RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRETPYTFGQGTKLEIK
SEQ ID NO: 231	116	PT5637.C20	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 232	116	PT5637.C20	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR RFGSGSGHDEYTLTISSLQPEDFATYYCQQY REDPYTFGQGTKLEIK
SEQ ID NO: 233	117	PT5637.K09	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 234	117	PT5637.K09	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 235	118	PT5637.L15	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 236	118	PT5637.L15	VL	AIQMTQSPSSLASVGDRTTTCQSQYWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRSEPYTFGQGTKLEIK
SEQ ID NO: 237	119	PT5637.M03	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 238	119	PT5637.M03	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 239	120	PT5637.P15	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 240	120	PT5637.P15	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR RFGSGSGHDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 241	121	PT5639.B15	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS
SEQ ID NO: 242	121	PT5639.B15	VL	AIQMTQSPSSLASIGDRVTTCQSQYWLS NYLAWYQQKPGKAPKLLIFDGDIPWELPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 243	122	PT5639.P05	VH	GQLVESGGGLVQPGGSLRLSCAASGFTW DHYAMTWVRQAPGKGLEWVGSISPKGD HKYYNTKFIDRFTISRDN SKNTLYLQMNS LRAEDTAVYYCARDWDYFDEWGQGTLV TVSS

SEQ ID NO: 244	122	PT5639.P05	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDLPYETPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YRTPYTFGQGTKLEIK
SEQ ID NO: 245	123	PT5625.G07_22 .F19_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 246	123	PT5625.G07_22 .F19_2	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPYTFGQGTKLEIK
SEQ ID NO: 247	124	PT5625.G07_24 .M09_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 248	124	PT5625.G07_24 .M09_1	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPYTFGQGTKLEIK
SEQ ID NO: 249	125	PT5625.G07_24 .P06_2	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 250	125	PT5625.G07_24 .P06_2	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPYTFGQGTKLEIK
SEQ ID NO: 251	126	PT5625.G07_26 .C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 252	126	PT5625.G07_26 .C10_1	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPYTFGQGTKLEIK
SEQ ID NO: 253	127	PT5625.G07_26 .M10_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFTISRDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGTLVT VSS
SEQ ID NO: 254	127	PT5625.G07_26 .M10_2	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPYTFGQGTKLEIK
SEQ ID NO: 255	128	PT5625.G07_28 .E16_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPRGNT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDYWGQGTLVT VSS
SEQ ID NO: 256	128	PT5625.G07_28 .E16_1	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPYTFGQGTKLEIK
SEQ ID NO: 257	129	PT5625.G07_30 .A20_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS

SEQ ID NO: 258	129	PT5625.G07_30 .A20_1	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPTYFGQGTKLEIK
SEQ ID NO: 259	130	PT5625.G07_32 .A13_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGQGT LTVSS
SEQ ID NO: 260	130	PT5625.G07_32 .A13_2	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPTYFGQGTKLEIK
SEQ ID NO: 261	131	PT5625.G07_34 .M24_1	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGT LTVSS
SEQ ID NO: 262	131	PT5625.G07_34 .M24_1	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPTYFGQGTKLEIK
SEQ ID NO: 263	132	PT5625.G07_34 .N13_3	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGT LTVSS
SEQ ID NO: 264	132	PT5625.G07_34 .N13_3	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPTYFGQGTKLEIK
SEQ ID NO: 265	133	PT5625.G07_36 .P22_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDRWGQGT LTVSS
SEQ ID NO: 266	133	PT5625.G07_36 .P22_1	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEV SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNTPTYFGQGTKLEIK
SEQ ID NO: 267	134	PT5627.M20_2 4.M09_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGT LTVSS
SEQ ID NO: 268	134	PT5627.M20_2 4.M09_1	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQ YREEPTYFGQGTKLEIK
SEQ ID NO: 269	135	PT5627.M20_2 4.P06_1	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DHYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGT LTVSS
SEQ ID NO: 270	135	PT5627.M20_2 4.P06_1	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQ YREEPTYFGQGTKLEIK
SEQ ID NO: 271	136	PT5627.M20_2 6.C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGT LTVSS

SEQ ID NO: 272	136	PT5627.M20_2 6.C10_1	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYLTITSSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 273	137	PT5627.M20_2 6.M10_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFITSRDDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGTIVT VSS
SEQ ID NO: 274	137	PT5627.M20_2 6.M10_2	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYLTITSSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 275	138	PT5627.M20_2 8.E16_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPRGNT KYYNTKFIDRFITSRDNSKNTLYLQMNSL RAEDTAVYYCARDWEYFDYWGQGTIVT VSS
SEQ ID NO: 276	138	PT5627.M20_2 8.E16_2	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYLTITSSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 277	139	PT5627.M20_3 0.D05_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFITSRDNDKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTIVT VSS
SEQ ID NO: 278	139	PT5627.M20_3 0.D05_1	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYLTITSSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 279	140	PT5627.M20_3 2.A13_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFITSRDNSKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGQGTIVT VSS
SEQ ID NO: 280	140	PT5627.M20_3 2.A13_1	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYLTITSSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 281	141	PT5627.M20_3 4.M24_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFITSRDDEKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGTIVT VSS
SEQ ID NO: 282	141	PT5627.M20_3 4.M24_2	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYLTITSSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 283	142	PT5627.M20_3 4.N13_4	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFITSRDNSKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTIVT VSS
SEQ ID NO: 284	142	PT5627.M20_3 4.N13_4	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFGSGSGHDEYLTITSSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 285	143	PT5627.M20_3 6.P22_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFITSRDNEKNTLYLQMNSL RAEDTAVYYCARDWEYFDRWGQGTIVT VSS

SEQ ID NO: 286	143	PT5627.M20_3 6.P22_1	VL	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPYERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGTKLEIK
SEQ ID NO: 287	144	PT5627.M12_2 2.F19_1	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 288	144	PT5627.M12_2 2.F19_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 289	145	PT5627.M12_2 4.M09_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 290	145	PT5627.M12_2 4.M09_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 291	146	PT5627.M12_2 6.M10_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFTISRDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGTLVT VSS
SEQ ID NO: 292	146	PT5627.M12_2 6.M10_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 293	147	PT5627.M12_3 2.A13_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGGQTL VTVSS
SEQ ID NO: 294	147	PT5627.M12_3 2.A13_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 295	148	PT5627.M12_3 4.M24_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFTISRDEKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGGQTL VTVSS
SEQ ID NO: 296	148	PT5627.M12_3 4.M24_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 297	149	PT5627.M12_3 4.N13_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 298	149	PT5627.M12_3 4.N13_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPYTFGQGTKLEIK
SEQ ID NO: 299	150	PT5629.F09_26 .C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS

SEQ ID NO: 300	150	PT5629.F09_26.C10_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 301	151	PT5629.F09_28.E16_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGESIPRGNT KYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGT LTVSS
SEQ ID NO: 302	151	PT5629.F09_28.E16_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 303	152	PT5629.F09_30.A20_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGESIPRG DHKYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGT LTVSS
SEQ ID NO: 304	152	PT5629.F09_30.A20_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 305	153	PT5629.F09_30.D05_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGESIPDG RTKYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGT LTVSS
SEQ ID NO: 306	153	PT5629.F09_30.D05_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 307	154	PT5629.F09_32.A13_3	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGESIPKG DHKYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGQGT LTVSS
SEQ ID NO: 308	154	PT5629.F09_32.A13_3	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 309	155	PT5629.F09_36.P22_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF EHYAMSWVRQAPGKGLEWVGESIPKGDH KYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDRWGQGT LTVSS
SEQ ID NO: 310	155	PT5629.F09_36.P22_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 311	156	PT5629.H08_22.F19_4	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGESIPDGRT KYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGT LTVSS
SEQ ID NO: 312	156	PT5629.H08_22.F19_4	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 313	157	PT5629.H08_24.M09_4	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGESIPDG DTKYYNTKFIDRFISRDDKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGT LTVSS

SEQ ID NO: 314	157	PT5629.H08_24.M09_4	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 315	158	PT5629.H08_24.P06_2	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DHYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 316	158	PT5629.H08_24.P06_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 317	159	PT5629.H08_26.C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 318	159	PT5629.H08_26.C10_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 319	160	PT5629.H08_26.M10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGTLVT VSS
SEQ ID NO: 320	160	PT5629.H08_26.M10_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 321	161	PT5629.H08_28.E16_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPRGNT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDYWGQGTLVT VSS
SEQ ID NO: 322	161	PT5629.H08_28.E16_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 323	162	PT5629.H08_30.A20_2	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 324	162	PT5629.H08_30.A20_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 325	163	PT5629.H08_30.D05_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 326	163	PT5629.H08_30.D05_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 327	164	PT5629.H08_32.A13_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGQGTL VTVSS

SEQ ID NO: 328	164	PT5629.H08_32 .A13_1	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 329	165	PT5629.H08_34 .M24_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYNTKFIDRFTISRDEKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGTL VTVSS
SEQ ID NO: 330	165	PT5629.H08_34 .M24_2	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 331	166	PT5629.H08_34 .N13_2	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 332	166	PT5629.H08_34 .N13_2	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 333	167	PT5629.H08_36 .P22_4	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDRWGQGTLVT VSS
SEQ ID NO: 334	167	PT5629.H08_36 .P22_4	VL	AIQMTQSPSSLSASVGDRVTITCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSEDEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 335	168	PT5631.D21_22 .F19_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 336	168	PT5631.D21_22 .F19_2	VL	AIQMTQSPSSLSASVGDRVTITCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 337	169	PT5631.D21_24 .M09_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 338	169	PT5631.D21_24 .M09_1	VL	AIQMTQSPSSLSASVGDRVTITCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 339	170	PT5631.D21_24 .P06_4	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVIAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 340	170	PT5631.D21_24 .P06_4	VL	AIQMTQSPSSLSASVGDRVTITCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 341	171	PT5631.D21_26 .C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS

SEQ ID NO: 342	171	PT5631.D21_26 .C10_1	VL	AIQMTQSPSSL.SASVGDRVTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 343	172	PT5631.D21_26 .M10_4	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFISRDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGTTLVT VSS
SEQ ID NO: 344	172	PT5631.D21_26 .M10_4	VL	AIQMTQSPSSL.SASVGDRVTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 345	173	PT5631.D21_28 .E16_3	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPRGNT KYYNTKFIDRFISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDYWGQGTTLVT VSS
SEQ ID NO: 346	173	PT5631.D21_28 .E16_3	VL	AIQMTQSPSSL.SASVGDRVTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 347	174	PT5631.D21_30 .A20_4	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTTL VTVSS
SEQ ID NO: 348	174	PT5631.D21_30 .A20_4	VL	AIQMTQSPSSL.SASVGDRVTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 349	175	PT5631.D21_30 .D05_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTTL VTVSS
SEQ ID NO: 350	175	PT5631.D21_30 .D05_1	VL	AIQMTQSPSSL.SASVGDRVTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 351	176	PT5631.D21_32 .A13_4	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGQGTTL VTVSS
SEQ ID NO: 352	176	PT5631.D21_32 .A13_4	VL	AIQMTQSPSSL.SASVGDRVTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 353	177	PT5631.D21_34 .M24_4	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFISRDEKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGTTL VTVSS
SEQ ID NO: 354	177	PT5631.D21_34 .M24_4	VL	AIQMTQSPSSL.SASVGDRVTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 355	178	PT5631.D21_34 .N13_2	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTTLVT VSS

SEQ ID NO: 356	178	PT5631.D21_34.N13_2	VL	AIQMTQSPSSLASVGDRTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 357	179	PT5631.D21_36.P22_3	VH	RVQLVESGGGLVQPGGSLRLSCAASGKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDRWGQGLVT VSS
SEQ ID NO: 358	179	PT5631.D21_36.P22_3	VL	AIQMTQSPSSLASVGDRTTTCQSSHWLS NYLAWYQQKPGKAPKLLIFDGDLPWEVP SRFSGSGSEDEYTLTISSLQPEDFATYYCQ QYRYTPYTFGQGTKLEIK
SEQ ID NO: 359	180	PT5633.I03_22.F19_1	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRFISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDNWGQGLVT VSS
SEQ ID NO: 360	180	PT5633.I03_22.F19_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 361	181	PT5633.I03_24.M09_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYYNTKFIDRFISRDDSKNTLYQMN SLRAEDTAVYYCARDWEYFDNWGQGL VTVSS
SEQ ID NO: 362	181	PT5633.I03_24.M09_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 363	182	PT5633.I03_24.P06_4	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDNWGQGLVT VSS
SEQ ID NO: 364	182	PT5633.I03_24.P06_4	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 365	183	PT5633.I03_26.C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKLEWVGSISPKG DHKYYNTKFIDRFISRDNENKNTLYQMN SLRAEDTAVYYCARDWDYFDRWGQGL VTVSS
SEQ ID NO: 366	183	PT5633.I03_26.C10_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 367	184	PT5633.I03_26.M10_4	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKLEWVGSISPRGNH KYYNTKFIDRFISRDNENKNTLYQMNSL RAEDTAVYYCARDWDYFDHWGQGLVT VSS
SEQ ID NO: 368	184	PT5633.I03_26.M10_4	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFSGSGSHEDYTLTISSLQPEDFATYYCQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 369	185	PT5633.I03_28.E16_4	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKLEWVGEISPRGNT KYYNTKFIDRFISRDNENKNTLYQMNSL RAEDTAVYYCARDWEYFDYWGQGLVT VSS

SEQ ID NO: 370	185	PT5633.I03_28. E16_4	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 371	186	PT5633.I03_30. A20_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNNDKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 372	186	PT5633.I03_30. A20_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 373	187	PT5633.I03_30. D05_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFTISRDNNDKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 374	187	PT5633.I03_30. D05_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 375	188	PT5633.I03_32. A13_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGQGTL VTVSS
SEQ ID NO: 376	188	PT5633.I03_32. A13_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 377	189	PT5633.I03_34. M24_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFTISRDNDEKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGTL VTVSS
SEQ ID NO: 378	189	PT5633.I03_34. M24_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 379	190	PT5633.I03_34. N13_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 380	190	PT5633.I03_34. N13_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 381	191	PT5633.I03_36. P22_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDRWGQGTLVT VSS
SEQ ID NO: 382	191	PT5633.I03_36. P22_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEDYTLTISSLQPEDFATYYCQQ YRNTPTYTFGQGTKLEIK
SEQ ID NO: 383	192	PT5635.C08_22 .F19_1	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS

SEQ ID NO: 384	192	PT5635.C08_22.F19_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGGTKLEIK
SEQ ID NO: 385	193	PT5635.C08_24.M09_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYNTKFIDRFTISRDDSKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 386	193	PT5635.C08_24.M09_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGGTKLEIK
SEQ ID NO: 387	194	PT5635.C08_24.P06_1	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 388	194	PT5635.C08_24.P06_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGGTKLEIK
SEQ ID NO: 389	195	PT5635.C08_26.C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 390	195	PT5635.C08_26.C10_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGGTKLEIK
SEQ ID NO: 391	196	PT5635.C08_26.M10_2	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFTISRDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGTLVT VSS
SEQ ID NO: 392	196	PT5635.C08_26.M10_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGGTKLEIK
SEQ ID NO: 393	197	PT5635.C08_28.E16_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPRGNT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDYWGQGTLVT VSS
SEQ ID NO: 394	197	PT5635.C08_28.E16_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGGTKLEIK
SEQ ID NO: 395	198	PT5635.C08_30.A20_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 396	198	PT5635.C08_30.A20_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGGTKLEIK
SEQ ID NO: 397	199	PT5635.C08_30.D05_3	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS

SEQ ID NO: 398	199	PT5635.C08_30 .D05_3	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGQGTKLEIK
SEQ ID NO: 399	200	PT5635.C08_32 .A13_3	VH	RVQLVESGGGLVQPGGSLRLSCAASGYR WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWDYFDYWGQGTL VTVSS
SEQ ID NO: 400	200	PT5635.C08_32 .A13_3	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGQGTKLEIK
SEQ ID NO: 401	201	PT5635.C08_34 .M24_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGTL VTVSS
SEQ ID NO: 402	201	PT5635.C08_34 .M24_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGQGTKLEIK
SEQ ID NO: 403	202	PT5635.C08_34 .N13_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDN SKNTLYLQMNSL RAEDTAVYYCARDWEYFDN WGQGT LVT VSS
SEQ ID NO: 404	202	PT5635.C08_34 .N13_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGQGTKLEIK
SEQ ID NO: 405	203	PT5635.C08_36 .P22_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFTISRDN SKNTLYLQMNSL RAEDTAVYYCARDWEYFDRWGQGT LVT VSS
SEQ ID NO: 406	203	PT5635.C08_36 .P22_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEVPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRSTPYTFGGQGTKLEIK
SEQ ID NO: 407	204	PT5639.G15_22 .F19_2	VH	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRFTISRDN SKNTLYLQMNSL RAEDTAVYYCARDWEYFDN WGQGT LVT VSS
SEQ ID NO: 408	204	PT5639.G15_22 .F19_2	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGSHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGGQGTKLEIK
SEQ ID NO: 409	205	PT5639.G15_24 .P06_1	VH	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVIAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDN SKNTLYLQMNSL RAEDTAVYYCARDWEYFDN WGQGT LVT VSS
SEQ ID NO: 410	205	PT5639.G15_24 .P06_1	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGSHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGGQGTKLEIK
SEQ ID NO: 411	206	PT5639.G15_24 .M09_4	VH	KVQLVESGGGLVQPGGSLRLSCAASGFR WEHYAMSWVRQAPGKGLEWVGEISPDG DTKYYNTKFIDRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARDWEYFDN WGQGT LVT VSS

SEQ ID NO: 412	206	PT5639.G15_24 .M09_4	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 413	207	PT5639.G15_26 .M10_3	VH	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRFTISRDEKNTLYLQMNSL RAEDTAVYYCARDWDYFDHWGQGLVT VSS
SEQ ID NO: 414	207	PT5639.G15_26 .M10_3	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 415	208	PT5639.G15_28 .E16_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFTY DHYAMSWVRQAPGKGLEWVGEISPRGNT KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDYWGQGLVT VSS
SEQ ID NO: 416	208	PT5639.G15_28 .E16_1	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 417	209	PT5639.G15_30 .A20_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGLVT VSS
SEQ ID NO: 418	209	PT5639.G15_30 .A20_1	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 419	210	PT5639.G15_30 .D05_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGLVT VSS
SEQ ID NO: 420	210	PT5639.G15_30 .D05_1	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 421	211	PT5639.G15_34 .N13_4	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGLVT VSS
SEQ ID NO: 422	211	PT5639.G15_34 .N13_4	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 423	212	PT5639.G15_34 .M24_3	VH	EVQLVESGGGLVQPGGSLRLSCAASGFQ WDHYAMSWVRQAPGKGLEWVGEISPRG DTKYYNTKFIDRFTISRDEKNTLYLQMN SLRAEDTAVYYCARDWEYFDYWGQGLVT VSS
SEQ ID NO: 424	212	PT5639.G15_34 .M24_3	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 425	213	PT5639.G15_36 .P22_3	VH	RVQLVESGGGLVQPGGSLRLSCAASGFKF EHYAMSWVRQAPGKGLEWVGEISPKGDH KYYNTKFIDRFTISRDNKNTLYLQMNSL RAEDTAVYYCARDWEYFDRWGQGLVT VSS

SEQ ID NO: 426	213	PT5639.G15_36 .P22_3	VL	AIQMTQSPSSLASVGDRTTTCQSTHWLS AYLAWYQQKPGKAPKLLIFDGDIPYERPS RFGSGSGSHDEYTLTISSLQPEDFATYYCQQ YRNEPYTFGQGTKLEIK
SEQ ID NO: 427	214	PT5625.G07_30 .D05_1	VH	KVQLVESGGGLVQPGGSLRLSCAASGYR YDKYAMSWVRQAPGKGLEWVGEISPDG RTKYYNTKFIDRFTISRDNNDKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTL VTVSS
SEQ ID NO: 428	214	PT5625.G07_30 .D05_1	VL	AIQMTQSPSSLASVGDRTTTCQAQYWL SNYLAWYQQKPGKAPKLLIFDGDLPYEVF SRFSGSGSHDEYTLTISSLQPEDFATYYCQ QYRNPYTFGQGTKLEIK
SEQ ID NO: 429	215	PT5627.M12_2 6.C10_1	VH	RVQLVESGGGLVQPGGSLRLSCAASGFT WDHYAMSWVRQAPGKGLEWVGSISPKG DHKYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 430	215	PT5627.M12_2 6.C10_1	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPTYTFGQGTKLEIK
SEQ ID NO: 431	216	PT5627.M12_3 0.A20_2	VH	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFTISRDNNDKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSS
SEQ ID NO: 432	216	PT5627.M12_3 0.A20_2	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPWEIPS RFGSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPTYTFGQGTKLEIK
SEQ ID NO: 433	217	PT5629.F09_34 .N13_3	VH	KVQLVESGGGLVQPGGSLRLSCAASGFTY DAYAMSWVRQAPGKGLEWVGEISPRGES KYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTLVT VSS
SEQ ID NO: 434	217	PT5629.F09_34 .N13_3	VL	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIK
SEQ ID NO: 435	1	PIAG9426	HC	QVQLVESGGGLVQPGGSLRLSCAASGFKY DVIAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFTISRDNKNTLYLQMN SLRAEDTAVYYCARDWEYFDNWGQGTLVT VSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMASRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLAQDWLNG KEYKCKVSNKALGAPIEKTKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTTPVLDSDGS FFLYSKLTVDKSRWQQGNVFCSCVMHEA LHNA Y T Q K S L S L S P
SEQ ID NO: 436	1	PIAG9426	LC	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPYEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGQGTKLEIKRTVAAPSVEIFPPSD EQLKSGTASVVCLLNNFYYPREAKVQWKV DNALQSGNSQESVTEQDSKDSYLSSTL TLISKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC

SEQ ID NO: 437	2	P1AG9376	HC	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRF ^T ISRDN ^D DKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGT LTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVT ^S WNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICN VNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMASRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLT ^S LAQDWL NGKEYKCKVSNKALGAPIEKTISKAKGQP REPQVYTLPPSRDELTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYK ^T TPVLDSD GSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNA ^Y TQKSLSLSP
SEQ ID NO: 438	2	P1AG9376	LC	AIQMTQSPSSLSASVGDRT ^V ITTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDL ^P YERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGT ^K LEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFY ^P REAKVQWK VDNALQSGNSQESVTEQDSK ^D STYSLST LTL ^S SKADY ^E KHKVYACEVTHQGLSSPVT KSFNRGEC
SEQ ID NO: 439	3	P1AG9372	HC	EVQLVESGGGLVQPGGSLRLSCAASGFRF DIYAMSWVRQAPGKGLEWVGEISPDGRT KYYNTKFIDRF ^T ISRDN ^E DKNTLYLQMNSL RAEDTAVYYCARDWEYFDN ^W GQGT ^L VT VSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVT ^S WNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMASRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLT ^S LAQDWLNG KEYKCKVSNKALGAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYK ^T TPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNA ^Y TQKSLSLSP
SEQ ID NO: 440	3	P1AG9372	LC	AIQMTQSPSSLSASVGDRT ^V ITTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDL ^P YERPS RFGSGSGHDEYTLTISSLQPEDFATYYCQQ YREEPYTFGQGT ^K LEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFY ^P REAKVQWK VDNALQSGNSQESVTEQDSK ^D STYSLST LTL ^S SKADY ^E KHKVYACEVTHQGLSSPVT KSFNRGEC
SEQ ID NO: 441	4	P1AG9420	HC	RVQLVESGGGLVQPGGSLRLSCAASGFRY DHYAMSWVRQAPGKGLEWVGSISPRGNH KYYNTKFIDRF ^T ISRDE ^K DKNTLYLQMNSL RAEDTAVYYCARDWDYFDH ^W GQGT ^L VT VSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVT ^S WNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMASRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLT ^S LAQDWLNG KEYKCKVSNKALGAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYK ^T TPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNA ^Y TQKSLSLSP

SEQ ID NO: 442	4	PIAG9420	LC	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR FSGSGSHEEYTLTISSLQPEDFATYYCQQY RETPYTFGGGTKLEIKRTVAAPSVFIFPPSD EQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKDYSLSSSTL TLTKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC
SEQ ID NO: 443	5	PIAG9391	HC	QVQLVESGGGLVQPGGSLRLSCAASGFKY DYYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFITSRDNEKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMASRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLAQDWLNG KEYCKVSNKALGAPIEKTSKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTTPVLDSDGS FFLYSKLTVDKSRWQQGNVVFSCSVMHEA LHNAYTQKSLSLSP
SEQ ID NO: 444	5	PIAG9391	LC	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPTYTFGGGTKLEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDYSLSS TLTKADYEKHKVYACEVTHQGLSSPVT KSFNRGEC
SEQ ID NO: 445	6	PIAH1205	HC	KVQLVESGGGLVQPGGSLRLSCAASGFK WEHYAMSWVRQAPGKGLEWVGSISPRG DHKYYNTKFIDRFITSRDNDKNTLYLQMN SLRAEDTAVYYCARDWDYFDRWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICN VNHKPSNTKVDKKVEPKSCD
SEQ ID NO: 446	6	PIAH1205	LC	AIQMTQSPSSLASVGDRTTTCQSQFWLS NYLAWYQQKPGKAPKLLIFDGDLPIERPS RFSGSGSHDEYTLTISSLQPEDFATYYCQQ YREEPTYTFGGGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDYSLSSST LTLTKADYEKHKVYACEVTHQGLSSPVT KSFNRGEC
SEQ ID NO: 447	7	PIAH1199	HC	QVQLVESGGGLVQPGGSLRLSCAASGFKY DYYAMSWVRQAPGKGLEWVGEISPRGDS KYYNTKFIDRFITSRDNEKNTLYLQMNSL RAEDTAVYYCARDWEYFDNWGQGTLVT VSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCD
SEQ ID NO: 448	7	PIAH1199	LC	AIQMTQSPSSLASVGDRTTTCQASYWLS NYLAWYQQKPGKAPKLLIFDGDIPEIPSR RFSGSGSHEEYTLTISSLQPEDFATYYCQQ YRDTPTYTFGGGTKLEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDYSLSS TLTKADYEKHKVYACEVTHQGLSSPVT KSFNRGEC
SEQ ID NO: 449	1	PIAG9426	HCDR1	GFKYDYYAMS

SEQ ID NO: 450	1	P1AG9426	HCDR2	EISPRGDSKYYNTKFD
SEQ ID NO: 451	1	P1AG9426	HCDR3	DWEYFDN
SEQ ID NO: 452	1	P1AG9426	LCDR1	QASYWLSNYLA
SEQ ID NO: 453	1	P1AG9426	LCDR2	DGDIPY
SEQ ID NO: 454	1	P1AG9426	LCDR3	QQYRETPYT
SEQ ID NO: 455	2	P1AG9376	HCDR1	GFKWEHYAMS
SEQ ID NO: 456	2	P1AG9376	HCDR2	SISPRGDHKYYNTKFD
SEQ ID NO: 457	2	P1AG9376	HCDR3	DWDYFDR
SEQ ID NO: 458	2	P1AG9376	LCDR1	QSQFWLSNYLA
SEQ ID NO: 459	2	P1AG9376	LCDR2	DGDLPY
SEQ ID NO: 460	2	P1AG9376	LCDR3	QQYREEPYT
SEQ ID NO: 461	3	P1AG9372	HCDR1	GFRFDIYAMS
SEQ ID NO: 462	3	P1AG9372	HCDR2	EISPDGRTKYYNTKFD
SEQ ID NO: 463	3	P1AG9372	HCDR3	DWEYFDN
SEQ ID NO: 464	3	P1AG9372	LCDR1	QSQFWLSNYLA
SEQ ID NO: 465	3	P1AG9372	LCDR2	DGDLPY
SEQ ID NO: 466	3	P1AG9372	LCDR3	QQYREEPYT
SEQ ID NO: 467	4	P1AG9420	HCDR1	GFRYDHYAMS
SEQ ID NO: 468	4	P1AG9420	HCDR2	SISPRGNHKYYNTKFD
SEQ ID NO: 469	4	P1AG9420	HCDR3	DWDYFDH
SEQ ID NO: 470	4	P1AG9420	LCDR1	QASYWLSNYLA
SEQ ID NO: 471	4	P1AG9420	LCDR2	DGDIPY
SEQ ID NO: 472	4	P1AG9420	LCDR3	QQYRETPYT
SEQ ID NO: 473	5	P1AG9391	HCDR1	GFKYDVYAMS
SEQ ID NO: 474	5	P1AG9391	HCDR2	EISPRGDSKYYNTKFD
SEQ ID NO: 475	5	P1AG9391	HCDR3	DWEYFDN
SEQ ID NO: 476	5	P1AG9391	LCDR1	QASYWLSNYLA
SEQ ID NO: 477	5	P1AG9391	LCDR2	DGDIPW
SEQ ID NO: 478	5	P1AG9391	LCDR3	QQYRDTPYT
SEQ ID NO: 479	6	P1AH1205	HCDR1	GFKWEHYAMS
SEQ ID NO: 480	6	P1AH1205	HCDR2	SISPRGDHKYYNTKFD
SEQ ID NO: 481	6	P1AH1205	HCDR3	DWDYFDR
SEQ ID NO: 482	6	P1AH1205	LCDR1	QSQFWLSNYLA
SEQ ID NO: 483	6	P1AH1205	LCDR2	DGDLPY
SEQ ID NO: 484	6	P1AH1205	LCDR3	QQYREEPYT
SEQ ID NO: 485	7	P1AH1199	HCDR1	GFKYDVYAMS
SEQ ID NO: 486	7	P1AH1199	HCDR2	EISPRGDSKYYNTKFD
SEQ ID NO: 487	7	P1AH1199	HCDR3	DWEYFDN
SEQ ID NO: 488	7	P1AH1199	LCDR1	QASYWLSNYLA
SEQ ID NO: 489	7	P1AH1199	LCDR2	DGDIPW
SEQ ID NO: 490	7	P1AH1199	LCDR3	QQYRDTPYT
SEQ ID NO: 491		human FactorB wt (FB) with His Tag and Precision site		HHHHHHGSLEVLFGPGGTPWSLARPGG SCSLEGVEIKGGSFRLLQEQQALEYVCP FYPYPVQIRTCRSTGSWSTLKTQDQKTV KAECRAIHCPRPHDFENG EYWPRSPYYN SDEISFHCYDGYTLRGSANRTCQVNGRWS GQTAICDNGAGYCSNPGIPGTRKVG SQRLEDSVTYHCSRGLTLRGSQRRTCQEGGS WSGTEPSCQDSFMYDTPQEVAEAFSSLT ETIEGVDAEDGHGPGEQQKRKIVLDPSGS MNIYLVLDGSDSIGASNFTGAKKCLVNLIE KVASYGVKPRYGLVTYATYPKIWKVSE ADSSNADWVTKQLNEINYEDHKLKSGTN TKKALQAVYSMMSWPDVPPPEGWNRTR HVIILMTDGLHNMGGDPITVIDEIRDLLYI GKDRKNPREDYLDVYVFGVGPLVNQVNI

				NALASKKDNEQHVFVKVMDMENLEDVFY QMIDESQSLSLCGMVWEHRKGTDYHKQP WQAKISVIRPSKGHESCMGAVVSEYFVLT AAHCFTVDDKEHSIKVSVGGEKRDLEIEV VLFHPNYNINGKKEAGIPEFYDYDVALIKL KNKLKYGQTIRPICLPCTEGTTRALRLPPT TTCQQQKEELLPAQDIKALFVSEEEKKL RKEVYIKNGDKKGSCERDAQYAPGYDKV KDISEVVTPrFLCTGGVSPYADPNTCRGD SGGPLIVHKRSRFIQVGVISWGVVDVCKN QKRQKQVPAHARDFHINLFQVLPWLKEK LQDEDLGFL
SEQ ID NO: 492		human FB with D279G with His Tag and Precision site		HHHHHHGSLVLFQGPGGTPWSLARPQG SCSLEGVEIKGGSFRLLQEGQALEYVCP FYPYPVQTRTCRSTGWSLTKTQDQKT KAECRAIHCPRPDHFENGEYWPRSPYYN SDEISFHCYDGYTLRGSANRTCQVNGRWS GQTAICDNGAGYCSNP GPIGTRKVG SQR RLEDSVTYHCSRGLTLRGSQRRTCQEGGS WSGTEPSCQDSFMYDTPQEVAAFLSSLT ETIEGVDAEDGHGPGEQQKRKIVLDPSGS MNIYLVLDGSGSIGASNFTGAKKCLVNLIE KVASYGVKPRYGLVTYATYPKIWVKVSE ADSSNADWVTKQLNEINYEDHKLKSGTN TKKALQAVYSMMSWPDDVPPEGWNRTR HVIILMTDGLHNMGGDPITVIDEIRDLLYI GKDRKNPREDYLDVYVFGVGPLVNQVNI NALASKKDNEQHVFVKVMDMENLEDVFY QMIDESQSLSLCGMVWEHRKGTDYHKQP WQAKISVIRPSKGHESCMGAVVSEYFVLT AAHCFTVDDKEHSIKVSVGGEKRDLEIEV VLFHPNYNINGKKEAGIPEFYDYDVALIKL KNKLKYGQTIRPICLPCTEGTTRALRLPPT TTCQQQKEELLPAQDIKALFVSEEEKKL RKEVYIKNGDKKGSCERDAQYAPGYDKV KDISEVVTPrFLCTGGVSPYADPNTCRGD SGGPLIVHKRSRFIQVGVISWGVVDVCKN QKRQKQVPAHARDFHINLFQVLPWLKEK LQDEDLGFL
SEQ ID NO: 493		human FB with D279G, K350N and M458I with His Tag and Precision site		HHHHHHGSLVLFQGPGGTPWSLARPQG SCSLEGVEIKGGSFRLLQEGQALEYVCP FYPYPVQTRTCRSTGWSLTKTQDQKT KAECRAIHCPRPDHFENGEYWPRSPYYN SDEISFHCYDGYTLRGSANRTCQVNGRWS GQTAICDNGAGYCSNP GPIGTRKVG SQR RLEDSVTYHCSRGLTLRGSQRRTCQEGGS WSGTEPSCQDSFMYDTPQEVAAFLSSLT ETIEGVDAEDGHGPGEQQKRKIVLDPSGS MNIYLVLDGSGSIGASNFTGAKKCLVNLIE KVASYGVKPRYGLVTYATYPKIWVKVSE ADSSNADWVTKQLNEINYEDHKLNSGTN TKKALQAVYSMMSWPDDVPPEGWNRTR HVIILMTDGLHNMGGDPITVIDEIRDLLYI GKDRKNPREDYLDVYVFGVGPLVNQVNI NALASKKDNEQHVFVKVDIENLEDVFYQ MIDESQSLSLCGMVWEHRKGTDYHKQPW QAKISVIRPSKGHESCMGAVVSEYFVLT AHCFTVDDKEHSIKVSVGGEKRDLEIEV VLFHPNYNINGKKEAGIPEFYDYDVALIKL KNKLKYGQTIRPICLPCTEGTTRALRLPPT TTCQQQKEELLPAQDIKALFVSEEEKKL RKEVYIKNGDKKGSCERDAQYAPGYDKV KDISEVVTPrFLCTGGVSPYADPNTCRGDS GGPLIVHKRSRFIQVGVISWGVVDVCKNQ

				KRQKQVPAHARDFHINLFQVLPWLKEKL QDEDLGFL
SEQ ID NO: 494		Complement Factor D		ILGGREAEAHARPYMASVQLNGAHLCCG VLVAEQWVLSAAHCLEDAADGKVQVLL GAHSLSQPEPSKRLYDVLRAVPHPSQPD TIDHDL LLLQLSEKATLGPAVRPLPWQRV DRDVAPGTLCDVAGWGVNHAGRRPDSL QHVLLPVLDRATCNRRTHHDGAITERLM CAESNRRDSCKGDSGGPLVCGGVLEGVV TSGSRVCGNRKKPGIYTRVASYAAWIDSV L
SEQ ID NO: 495		Complement C3 beta chain (C3b)		SPMYSITPNILRLESEETMVLEAHDAQGD VPVTVTVHDFPGKKLVLSSEKTVLTPATN HMGNVTF TIPANREFKSEKGRNKFVTVQA TFGTQVVEKVVLVSLQSGYLFIQTDKTIYT PGSTVL YRIFTVNHKLLPVGRTVMVNIE PEGIPVKQDSLSSQNQLGVLP.LSWDIPELV NMGQWKIRAYYENSPQQVFSTEFVKEY VLPSFEVIVEPTEKFYYIYNEKGLEVTITAR FLYGKKVEGTAFVIFGIQDGEQRISLPESL KRIPIEDGSGEVVLSRKVLLDGVQNPRAE DLVGKSLYVSA TVILHSGSDMVQAERSGI PIVTSPIYQIHFTKTPKYFKPGMPFDLMVFV TNPDGSPA YRVPVA VQGEDTVQSLTQGD GVAKLSINTHPSQKPLSITVRTKKQELSEA EQATRTMQALPYSTVGNSNNYLHLSVLR TELRPGETLVNFFLRMDRAHEAKIRYYT YLIMNKGRLKAGRQVREPGQDLVVLPLS ITTD FIPSFRLVAYYTLIGASGQREV VADS VWVDVKDSCVGS LVKSGQSED RQPVPG QQMTLKIEGDHGARVVLVA VDKGVFVLN KKNKLTQSKIWDVVEKADIGCTPGSGKD YAGVFS DAGL T TSSSGQQT AQRAELQCP QPAARRRRSVQLTEKRMDKV GKYPKELR KCCEDGMRENPMRFSCQRRTRFISLGEAC KKVFLDCCNYTELRRQHARASHLGLARS NLDEDIAEENIVSRSEFPESWLWNVEDLK EPPKNGISTKLMNIFLKDSITTWEILAVSM SDKKGICVADPFVTVMQDFFIDRLRPYS VVRNEQVEIRA VLYNYRQNQELKVRVEL LHNPAFCSLATTKRRHQQTVTIPKSSLSV PYVIVPLKTGLQEVEVKAAVYHHFISDGV RKSLKV VPEGIRMNKTVA VRTLDPERLGR EGVQKEDIPPADLSDQVPDTESETRILLQG TPVAQMTEDAVDAERLKHLIVTPSGCGEQ NMIGMTPTVIA VHYLDETEQWEKFGLEK RQGALELIKGYTQQLAFRQPSSAFAAFV KRAPSTWLTA YVVKVFS LAVNLIAIDSQV LCGAVKWLILEKQKPDGVFQEDAPVIHQE MIGGLRNNNEKDMALTAFVLISLQEAKDI CEEQVNSLPGSITKAGDFLEANYMNLQRS YTVAIAGYALAQMGRLKGPLL NKFLTTA KDKNRWEDPGKQLYNVEATSYALLALLQ LKDFDFVPPVVRWLN EQRYYG GYGSTQ ATFMVFQALAQYQKDAPDHQELNLDVSL QLPSRSSKITHRIHWESASLLRSEETKENE GFTVTAEGKGQGTLSVVTMYHAKAKDQL TCNKFDLKVTIKPAPETEKRPQDAKNTMI LEICTRYRGDQDATMSILDISMMTGFAPD TDDLKQLANGVDRIYSKYELDKAFSDRNT LIIYLDKVSHSEDDCLAFKVHQYFNVELIQ PGAVKVYAYYNLEESCTRFYHPEKEDGK LNKLCRDELRC AEENCFIQKSDDKV TLE ERLDKACEPGVDYVYKTRLVKVQLSNDF DEYIMAEIQTIKSGSDEVQVGQQRTFISPIK

				CREALKLEEKHYLMWGLSSDFWGEKPN LSYIIGKDTWVEHWPEEDECQDEENQKQC QDLGAFTESMVVFGCPN
SEQ ID NO: 496		human C3a		SVQLTEKRMDKVGKYPKELRKCCEDGMR ENPMRFSCQRRTRFISLGEACKKVFLDCC NYITELRRQHARASHLGLAR
SEQ ID NO: 497		Cynomolgus C3b		PMYSMITPNVLRLESEETVVLEAHDANGD VPVTVTVHDFPGKKLVLSSEKTVLTPATS HMGSVTIRIPANKEFKSEKGHNKFVTVQA TFGAQVVEKVVLVSLQSGYLFQTDKTIY TPGSTVLCRIFTVNHKLLPVGRTVVVNIEN PDGIPVKQDSLSSQNQFGILPLSWDIPELV NMGQWKIRAYYENSPQQVFSTEFVKEY VLPSEFVIVEPTEKFYYIYNQKGLEVTITA RFLYGKKVEGTAFVIFGIQDGEQRISLPES LKRIQIEDGSGDAVLSRKVLLDGVQNP RP EDLVGKSLYVSVTVILHSGSDMVQAERSG IPIVTSPIYQIHFTKPKYFKPGMPFDLMVF VTNPDGSPA YRVPVA VOGEDA VQSLTQG DGVAKLSINTHPSQKPLSITVRTKKRELSE AEQATRIMEAQPYSTVGNSNNYLHLSVP RAELRPGETLNVNLFLLRMDRTQEAKIRYY TYLIMNKGKLLKVGRQVREPGQDLVVL P LSITTDIPSFRLVAYYTLIGANGQREVVA DSVWVDVKDSCVGS LVKSGQSEDRQPL PGQQMTLKIEGDHGARVGLVAVDKGVFV LNKKNKLTQSKIWDVVEKADIGCTPGSGK DYAGVFS DAGLTFASSSGQQTAAQRAELQC PQPATRRRRSVQLAEKRMDKVGQYPKEL RKCEHGMRENPMRFSCQRRTRYITLDEA CKKAFLDCCNYITELRRQHARASHLGLAR SNLDEDIAEENIVSRSEFPESWLWKIEELK EAPKNGISTKLMNIFLKDSITTWEILAVSL S DKKGICVADPFEVTVMQDFFIDLRLPYSV VRNEQVEIRAVLYNYRQNEQELKVRVELL HNPAFCSLATAKRRHQQTVTIPPKSSL SVP YVIVPLKTGQQEVEVKAAVYHFFISDGV R KSLKVVP EGIRMNKTVAVRTLDPERLGQE GVQREDVPPADLSDQVPDTESETRILLQG TPVAQMTEDAIDAERLKH LIVTPSGCGEQ NMITMTPTVIAVHYLDETEQWEKFGPEKR QGALELIKKG YTQQLAFRQPSSAFAAFLN RAPSTWLTAYVVKVFLAVNLIAIDSQVL CGAVKWLILEKQKPDGVFQEDAPVIHQE MTGGFRNTNEKDMALTAFVLISLQEAKEI CEEQVNSLPGSITKAGDFLEANYMNLQRS YTVAIAAAYALAQMGRLKGPLL NKFLT TA KDKNRWEEPGQQLYNVEATSYALLALLQ LKDFDFVPPVVRWLNEQRYYGGGYGSTQ ATFMVFQALAQYQKDVDPDHKELNLDVSL QLPSRSSKIIHRIHWESASLLRSEETKENEG FTVTAEGKGQGTLSVVTMYHAKAKGQLT CNKFDLKVTIKPAPETEKRPQDAKNTMIL EICTRYRGDQDATMSILDISMMTGFPD T DDLKQLANGVDRYISKYELDKAFSDRNTL IYLDKVSHSEDDCIAFKVHQYFNVELIQP GAVKVYAYYNLAESCTRFYHPEKEDGKL NKL CRDELCRCAEENC FIKLDDKV TLEE RLDKACEPGVDYVYKTRLVKAQLSNDFD EYIMAIEQIIKSGSDEVQVGQQRTFISPIKC REALKLEERKHYLMWGLSSDFWGEKPNL SYIIGKDTWVEHWPEEDECQDEENQKQC QDLGTFITENMVVFGCPN
SEQ ID NO: 498		Cynomolgus Factor D (FD)		ILGGREAEAHARPYMASVQVNGEHL CGG VLVAEQWVLSAAHCLEDAADGKVQVLL

				GAHSLSQPEPSKRLYDVLRAVPHPSRDP TIDHDLQLLQSEKATLGPAVRPLPWQRV DRDVEPGTLCDVAGWGIVSHAGRRPDRL QHVLPLVLDRA TCNRRTHHDGAITQMMM CAESNRRDSCKGDSGGPLVCGGVLEGVV TSGSRVCGNRKKPGIYTRVASYAAWIDSL EVLFQGPESHIIIIII
SEQ ID NO: 499		Cynomolgus Factor B WT		HHHHHHGSLEVLFGPGGTPLSSAQPQGS CSLEGVEIKGGSFRLQEGQALEYVCPSGF YPYPVQTRTCRSTGWSWTLQTDRKTVK KAECRAIRCPRPQDFENG EYRPRSPYYNV SDEISFHCYDGYTLRGSANRTCQVNGRWS GQTAICDNGAGYCSNPGIPGTRKVGSRV RLEDSTVYHCSRGLTLRGSQRRTCQEGGS WSGTEPSCQDSFMYDTPQEVAEAFSSLT ETIEGVDAEDGHSPGEQQKRIILDPSGSM NIYLVL DGS SIGAGNFTGAKKCLVNLIEK VASYGVKPRYALVTYATYPRIWVKVSDQ ESSNADWVTKKLSEINYEDHKLKSGTNTK RALQAVYSMMSWPEDIPPEGWNRTRHVII LMTDGLHNMGGDPITVIDEIRDLLYIGKD RKNPREYLDVYVFGVGPLVDQVNINAL ASKKDNEQHVFVKVDMENLEDVFFQMID ESQSLSLCGMVWEHTTGTDYHKQPWQA KISVTRPSKGHESCMGAVVSEYFVLTAAH CFTVDDKEHSIKVSVGKKRDLEIEKVL FHP DYNISGKKEAGIPEFYDYDVALIKLKKKL NYDPTIRPICLPCTEGTTRALRLPPTTTCQQ QKEELLPAQDIKALFVSEEEKLTRKEVYI KNGDKKGCERDAQYAPGYDKVKDISEV VTPRFLCTGGVSPYADPNTCRGDSGGPLI VHKRSRFIQGVVISWGVVDVCKNQKRQK QVPAHARDFHVNLFQVLPWLKEKLQDED LGFL
SEQ ID NO: 500		Cynomolgus Factor B triple mutant (D279G_K350 N_M458I)		HHHHHHGSLEVLFGPGGTPLSSAQPQGS CSLEGVEIKGGSFRLQEGQALEYVCPSGF YPYPVQTRTCRSTGWSWTLQTDRKTVK KAECRAIRCPRPQDFENG EYRPRSPYYNV SDEISFHCYDGYTLRGSANRTCQVNGRWS GQTAICDNGAGYCSNPGIPGTRKVGSRV RLEDSTVYHCSRGLTLRGSQRRTCQEGGS WSGTEPSCQDSFMYDTPQEVAEAFSSLT ETIEGVDAEDGHSPGEQQKRIILDPSGSM NIYLVL DGS SIGAGNFTGAKKCLVNLIEK VASYGVKPRYALVTYATYPRIWVKVSDQ ESSNADWVTKKLSEINYEDHKLKSGTNTK RALQAVYSMMSWPEDIPPEGWNRTRHVII LMTDGLHNMGGDPITVIDEIRDLLYIGKD RKNPREYLDVYVFGVGPLVDQVNINAL ASKKDNEQHVFVKVDIENLEDVFFQMIDE SQSLSLCGMVWEHTTGTDYHKQPWQAKI SVTRPSKGHESCMGAVVSEYFVLTAAHCF TVDDKEHSIKVSVGKKRDLEIEKVL FHPD YNISGKKEAGIPEFYDYDVALIKLKKKLN YDPTIRPICLPCTEGTTRALRLPPTTTCQQQ KEELLPAQDIKALFVSEEEKLTRKEVYIK NGDKKGCERDAQYAPGYDKVKDISEVV TPRFLCTGGVSPYADPNTCRGDSGGPLIV HKRSRFIQGVVISWGVVDVCKNQKRQKQ VPAHARDFHVNLFQVLPWLKEKLQDEDL GFL
SEQ ID NO: 501		Human Factor B (wt, without signal peptide)		TPWSLARPQGSCSLEGVEIKGGSFRLQEG QALEYVCPSGFYYPYPVQTRTCRSTGWSW LKTQDQKTVRKAECRAIHCRPHDFENG

				YWPRSPYYNVSDSIFHCYDGYTLRGSAN RTCQVNGRWSGQTAICDNGAGYCSNPGIP IGTRKVG SQYRLSDSVTYHCSRGLTLRGS QRRTCQEGGSWSGTEPSCQDSFMYDTPQE VAEAFSSLTETIEGVDAEDGHGPGEQQK RKIVLDPSGSMNIYL VLDGSDSIGASNFTG AKKCLVN LIEKVASYGVKPRYGLVTYAT YPKIWVKVSEADSSNADWVTQLNEINY EDHKLKSGTNTKKALQAVYSMMSWPDD VPPEGWNRTRHVILMTDGLHNMGGDPIT VIDEIRDLLYIGKDRKNPREDYLDVYVFG VGPLVNQVNINALASKKDNEQHVFKVKD MENLEDVFYQMIDESQSLSLCGMVWEHR KGTDYHKQPWQAKISVIRPSKGHESCMG AVVSEYFVLTAAHCFVDDKEHSIKVSVG GEKRDLEIEVVL FHPNYNINGKKEAGIPEF YDYDVALIKLKNKLYGQTIRPICLPCTEG TTRALRLPPTTTCQQKEELLPAQDIKALF VSEEEKLTRKEVYIKNGDKKGSCERDAQ YAPGYDKVKDISEVVTPrFLCTGGVSPYA DPNTCRGDSGGPLIVHKRSRFIQVGVISWG VVDVCKNQKRQKQVPAHARDFHINLFQV LPWLKEKLQDEDLGFL
SEQ ID NO: 502		human constant light chain domain CL		RTVAAPSVFIFPPSDEQLKSGTASVVCLLN NFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSLTILSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 503		human constant heavy chain domain CH1		ASTKGPSVFPLAPSSKSTSGGTAAALGCLVK DYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVPSSSLGTQTYICNVNHKP SNTKVDKKVEPKSCD
SEQ ID NO: 504		Human Factor B (wt, with signal peptide)		MGSNLSPLCLMPFILGLSGGVTTTPWS LARPQGSCSLEGVEIKGGSFRLLQEGQALE YVCPSGFYPPVQTRTCRSTGSWSTLKTQ DQKTVRKAECRAIHCPRPDHFENGEYWP RSPYYNVSDSIFHCYDGYTLRGSANRTC QVNGRWSGQTAICDNGAGYCSNPGIPIGT RKVG SQYRLSDSVTYHCSRGLTLRGSQRR TCQEGGSWSGTEPSCQDSFMYDTPQEVAE AFLSSLTETIEGVDAEDGHGPGEQQKRKIV LDPSGSMNIYL VLDGSDSIGASNFTGAKK CLVN LIEKVASYGVKPRYGLVTYATYPKI WVKVSEADSSNADWVTQLNEINYEDHK LKSGTNTKKALQAVYSMMSWPDDVPPEG WNRTRHVILMTDGLHNMGGDPITVIDEIR DLLYIGKDRKNPREDYLDVYVFGVGPLV NQVNINALASKKDNEQHVFKVKDMENLE DVFYQMIDESQSLSLCGMVWEHRKGTDY HKQPWQAKISVIRPSKGHESCMGAVVSEY FVLTAAHCFVDDKEHSIKVSVGGEKRDLE IEVVL FHPNYNINGKKEAGIPEFYDYDVA LIKLNKLYGQTIRPICLPCTEGTTRALR LPPTTTCQQKEELLPAQDIKALFVSEEEK KLTRKEVYIKNGDKKGSCERDAQYAPGY DKVKDISEVVTPrFLCTGGVSPYADPNTC RGDSGGPLIVHKRSRFIQVGVISWGVVDV CKNQKRQKQVPAHARDFHINLFQVLPWL KEKLQDEDLGFL

EXAMPLES

The following examples are provided to aid the understanding of the present invention, the true scope of which is set forth in the appended claims. It is understood that modifications can be made in the procedures set forth without departing from the spirit of the invention.

Example 1:

Stabilization of human C3bBb complex

Wild-type C3bBb is a rapidly decaying complex unsuitable for antibody discovery purposes. In order to assess the influence of different mutations within the factor B (FB) subunit on the stability of C3bBb the following mutations were introduced in the FB protein: D279G, K350N and M458I. Unmutated FB is indicated in SEQ ID NO: 491, FB with a D279G mutation is indicated in SEQ ID NO: 492 and FB with D279G, K350N and M458I mutations is indicated in SEQ ID NO: 493. Numbering of the mutations is based on the amino acid sequence of human Factor B with signal peptide (SEQ ID NO: 504). Assembly and decay of the different described C3bBb variants was assessed by Bio Layer Interferometry (BLI) analysis on a sensor coated with C3b.

Stability detection with BLI:

a) C3bBb assembly in presence of Mg-ions

To analyze stability of the so formed C3bBb complexes having the different Bb subunits, C3b was biotinylated at cysteine 1010 by incubating plasma purified C3b (Complement Technology) overnight at 4°C in presence of 5 molar excess Maleimide-PEG3-biotin (Thermo Fisher Scientific) followed by purification on a Zeba spin column 40K (Thermo Fisher Scientific). This material was used to load streptavidin functionalized BLI sensors (SA sensors; Fortebio) in an Octet RED 384 device (Fortebio) at high density (5nm BLI signal). C3bBb was assembled by exposing the C3b loaded sensors to different recombinant factor B variants (i.e. unmutated SEQ ID NO: 491; D279G variant of SEQ ID NO: 492; D279G K350N M458I triple variant of SEQ ID NO: 493) in presence of 54 nM plasma purified factor D (Complement Technology) in HBS-T(Mg) buffer (150mM NaCl, 10mM HEPES, 1mM MgCl₂, 0.005% Tween20, pH 7.4) at 22°C. After allowing the convertase to reach equilibrium for 12 minutes, sensors were transferred to 200µl

HBS-T(Mg) buffer initiating dissociation of the assembled C3bBb. Convertase decay was followed for three hours.

After subtraction of the signal recorded from parallel reference sensors omitting the C3b loading step and subtraction of a control sensor omitting factor B and factor D, data of the dissociation phase was fitted to the double exponential $((A \cdot \exp((-1) \cdot B) \cdot x)) + (C \cdot \exp((-1) \cdot D) \cdot x))$ using XLfit (IDBS software), allowing for heterogeneity in the assembled convertase population. Half life ($= \ln(2)/B$) and relative importance of the main species are reported in **Table E1**.

b) C3bBb assembly in presence of Ni-ions

In another experiment, the structural Mg^{2+} ion coordinated in factor B VWA was substituted for Ni^{2+} in order to further stabilize the C3 convertase. The impact on C3bBb complex stability was explored using a setup that was identical to the precedent experiment, except that HBS-T(Ni) buffer (150mM NaCl, 10mM HEPES, 1mM $NiCl_2$, 0.005% Tween20, pH 7.4) was used instead of HBS-T(Mg).

Correction of the BLI trace was identical to the experiment in presence of magnesium. Different from the Mg^{2+} containing C3bBb complexes, only one species was detected during dissociation and a single exponential decay $(A \cdot \exp((-1) \cdot B) \cdot x))$ was used for analysis. The influence of the addition of Ni^{2+} ions during assembly of C3bBb using the different Bb proteins, i.e. wild type Bb, single mutated Bb D279G and triple mutated Bb D279G, K350N and M458I for the formation of the C3bBb complex are shown in **Table E1**.

Table E1: $t_{1/2}$ of C3bBb complex formed using different Bb proteins as measured by BLI

Bb comprised in C3bBb complex	t 1/2	prevalence of main species
wt FB, Mg^{2+}	4 min 46 s	93%
FB (D279G), Mg^{2+}	1 h 03 min	97%
FB (D279G, K350N and M458I), Mg^{2+}	1 h 59 min	93%
wt FB, Ni^{2+}	0h 29 min	100%
FB (D279G), Ni^{2+}	3 h 18 min	100%
FB (D279G, K350N and M458I), Ni^{2+}	11 h 18 min	100%

While wild type C3bBb complex formed in the presence of magnesium ions had a half-life of less than five minutes, stabilization by mutations within the Bb subunit of FB and further stabilizing C3bBb by formation in presence of Ni^{2+} ions results in a half life of up to 11 hours and 15 minutes (equaling 675 minutes, which equals a more than 135-fold increase in C3bBb half-life).

Assembly and purification of stabilized C3bBb complex for antibody discovery

C3b was biotinylated at cysteine 1010 by incubating plasma purified C3b (Complement Technology) 2 h at room temperature in presence of 0.4 mM EZ-Link HPDP-Biotin (Thermo Fisher Scientific) followed by purification on a NAP-10 Column (Thermo Fisher Scientific). The biotinylated C3b was mixed in a molar ratio of 1:1 with hu Factor B (i.e. unmutated SEQ ID NO: 491; D279G variant of SEQ ID NO: 492; D279G K350N M458I triple variant of SEQ ID NO: 493) additional added NiSO_4 to a final concentration of 5 mM. After 10 minutes of pre incubation at room temperature FactorD (Complement Technology) added in a molar ratio of 1 (C3b) : 1 (Factor B) : 0.02 (Factor D) and incubated for another 10 min at room temperature in the reaction buffer (20 mM Hepes, 150 mM NaCl, 5 mM NiSO_4 pH 7.4). The purification by size exclusion chromatography Superdex200 (Cytavia) follows immediately at room temperature in storage buffer (20 mM Hepes, 150 mM NaCl, 1 mM NiSO_4 pH 7.4).

Example 2:

Antibody screening using stabilized C3bBb complex

Antibodies specifically binding to the stabilized C3bBb complex were screened as follows:

Panning

For naïve selection, phage library panning was performed in 4 rounds, wherein the first round was performed with 800 nM of biotinylated C3bBb triple mutant-HPDP (wherein the C3bBb was formed in the presence of nickel ions using FB of SEQ ID NO: 493) pre-immobilized on Dynabeads M-280 Streptavidin (Thermofisher catalog number 11206D). Panning rounds 2–4 were performed with 150 nM of biotinylated target in solution, followed by capture of Fab-on-phage/target complexes on SpeedBead Magnetic Neutravidin Coated Particles (Cytiva, catalog number 78152104010350, round 2 and 4) or Dynabeads M-280 Streptavidin (round 3). In brief, in the first panning round the phage/target/bead complex were washed

2x with HBS-NT + NiSO₄ (0,01M HEPES pH7.4; 0,15M NaCl; Cytiva catalog BR-1006-70 supplemented with 0.1% Tween-20 and 1mM NiSO₄) and 1x with HBS-N + NiSO₄ (0,01M HEPES pH7.4; 0,15M NaCl; Cytiva catalog BR-1006-70 supplemented with 1mM NiSO₄). In panning rounds 2, 3 and 4 the phage/target/bead complex was washed 5x with HBS-NT + NiSO₄ and 2x with 1x HBS-N + NiSO₄. Captured phage clones bearing target-specific Fabs were eluted from the M-280 beads using 100mM DTT, used for infection of log-phase TG1 E. coli cells, and rescued using M13 K07 helper phage, according to standard protocols.

Screening

For screening of selection outputs, a polyclonal plasmid miniprep of the respective selection round was prepared from the infected TG1 E. coli cells. Plasmids were reformatted to produce soluble Fab in E. coli supernatants with a T7 tag at the C-terminus of the Fab CH1 domain. The ligated polyclonal plasmids encoding T7-tagged Fabs were transformed into TG1 E. coli cells (Zymo Research catalog number T3017), and single colonies were picked into microtiter plates. Soluble Fabs were expressed in microtiter plates and supernatants were clarified by centrifugation.

Binding of the antibodies to C3bBb was analyzed by different ELISA assays to analyze binding towards C3bBb formed from Factor B with three mutations D279G, K350N and M458I (herein referred to as “C3bBb triple mutant Elisa”) as well as controls assessing binding to different related components of the complement system, i.e. C3, C3a, C3b and Factor B, Ba, Bb. Briefly, the following protocols were used:

C3bBb triple mutant Elisa

Buffer:

50 mM Hepes pH 7,4 containing 150 mM NaCl, 0,5% BSA and 0,1% Tween20 was used as diluent for the ELISA. PBS containing 0,1% Tween20 was used as a washing buffer.

Method:

20 µl of a mixture of 500 ng/ml human C3bBb - Human Factor B Triple mutant (D279G_M350N_M458I)-Cys-HPDP-Biotin, 1:3000 Mouse anti Human kappa HRP (Southern Biotek 9230-05) and 1:2000 Mouse IgG anti T7 Tag HRP (Novagen 69048-3) was added to a Microcoat Streptavidine coated 384 well

Microplate (Microcoat 11974998001). 25 µl sample was added to the plate and incubated at room temperature for 1 hour. After incubation plates were washed with 90 µl/well washing buffer using a Biotek EL406 Washer and 30 µl TMB (3,3',5,5'-3,3,5,5-Tetramethylbenzidine, Roche 11835033001) was added. After a 5 Minute incubation at room temperature the optical density (OD) was measured at 370 nm using an EnVision Multimode Plate Reader (Perkin Elmer).

C3, C3a, C3b Counterscreening Elisa

Buffer:

50 mM Hepes pH 7,4 with 150 mM NaCl was used as coating buffer. 2% BSA in 50 mM Hepes pH 7,4 containing 150 mM NaCl, 0,5% BSA and 0,1% Tween20 was used as blocking buffer. 50 mM Hepes pH 7,4 containing 150 mM NaCl, 0,5% BSA and 0,1% Tween20 was used as diluent for the ELISA. PBS containing 0,1% Tween20 was used as a washing buffer.

Method:

A clear 384 well Nunc MaxiSorp Plate (Nunc, 464718) was coated with 25 µl of a mixture of 5 nM human C3 (Complement technology, A113), 5 nM human C3a (Complement technology, A118) and 2,5 nM human C3b (Complement technology, A114) in coating buffer and incubated at room temperature for 1 hour. After a single wash with 90 µl/well washing buffer on a EL406 Biotek washer, 90 µl blocking buffer was added and incubated for 30 Minutes at room temperature. After washing plates 3 times with 90 µl/well washing buffer on a EL406 Biotek washer 25 µl Sample was added to the plate and incubated at room temperature for 1 hour. After washing the plates as described above 25 µl Detection Mix (1:3000 Mouse anti Human kappa HRP (Southern Biotek 9230-05) and 1:2000 Mouse IgG anti T7 Tag HRP (Novagen 69048-3) was added. After a 1 hour incubation at room temperature plates were washed 6 times with 90 µl/well washing buffer using a Biotek EL406 Washer and 30 µl TMB (3,3',5,5'-3,3,5,5-Tetramethylbenzidine, Roche 11835033001) was added. After a 5 Minute incubation at room temperature the optical density (OD) was measured at 370 nm using a EnVision Multimode Plate Reader (Perkin Elmer).

Factor B, Ba, Bb Counterscreening Elisa

Buffer:

50 mM Hepes pH 7,4 with 150 mM NaCl was used as coating buffer. 2% BSA in 50 mM Hepes pH 7,4 containing 150 mM NaCl, 0,5% BSA and 0,1% Tween20 was used as blocking buffer. 50 mM Hepes pH 7,4 containing 150 mM NaCl, 0,5% BSA and 0,1% Tween20 was used as diluent for the ELISA. PBS containing 0,1% Tween20 was used as a washing buffer.

Method:

A clear 384 well Nunc MaxiSorp Plate (Nunc, 464718) was coated with 25 µl of a mixture of 10 nM human Factor B (Complement technology, A135), 5 nM human Ba (Complement technology, A154) and 10 nM human Bb (Complement technology, A155) in coating buffer and incubated at room temperature for 1 hour. After a single wash with 90 µl/well washing buffer on a EL406 Biotek washer, 90 µl blocking buffer was added and incubated for 30 Minutes at room temperature. After washing plates 3 times with 90 µl/well washing buffer on a EL406 Biotek washer 25 µl Sample was added to the plate and incubated at room temperature for 1 hour. After washing the plates as described above 25 µl Detection Mix (1:3000 Mouse anti Human kappa HRP (Southern Biotek 9230-05) and 1:2000 Mouse IgG anti T7 Tag HRP (Novagen 69048-3) was added in the sample area. After a 1 hour incubation at room temperature plates were washed 6 times with 90 µl/well washing buffer using a Biotek EL406 Washer and 30 µl TMB (3,3',5,5'-3,3,5,5-Tetramethylbenzidine, Roche 11835033001) was added. After a 5 Minute incubation at room temperature the optical density (OD) was measured at 370 nm using a EnVision Multimode Plate Reader (Perkin Elmer).

Example 3:

Identification and antigen binding of C3bBb antibodies

A variety of antibody molecules that showed activity in binding to C3bBb were identified from panning and screening as described in Example 2 and optionally, further engineering of the so-derived antibody molecules was conducted.

All antibodies were initially expressed as Fab fragments comprising a constant light chain domain of SEQ ID NO:502 and a constant heavy chain domain of SEQ ID NO:503. **Table E2** includes an overview over VH and VL amino acid sequences.

Table E2: amino acid sequences of antibodies identified in Example 2.

#	identifier	VH amino acid sequence (SEQ ID NO:)	VL amino acid sequence (SEQ ID NO:)
1	P1AG9426	1	2
2	P1AG9376	3	4
3	P1AG9372	5	6
4	P1AG9420	7	8
5	P1AG9391	9	10
6	P1AH1205	11	12
7	P1AH1199	13	14
8	C3bBb.P045.072	15	16
9	C3bBb.P045.236	17	18
10	C3bBb.P045.225	19	20
11	C3bBb.P048.152	21	22
12	C3bBb.P048.061	23	24
13	C3bBb.P048.127	25	26
14	C3bBb.P048.241	27	28
15	C3bBb.P048.230	29	30
16	C3bBb.P048.204	31	32
17	C3bBb.P048.333	33	34
18	C3bBb.P053.095	35	36
19	C3bBb.P055.015	37	38
20	P1AF8499	39	40
21	GQ-5_1	41	42
22	GQ-11_1	43	44
23	PT5622.F19	45	46
24	PT5624.P06	47	48
25	PT5624.M09	49	50
26	PT5626.M10	51	52
27	PT5626.C10	53	54
28	PT5628.E16	55	56
29	PT5630.D05	57	58
30	PT5630.A20	59	60
31	PT5632.A13	61	62
32	PT5634.N13	63	64
33	PT5634.M24	65	66
34	PT5636.P22	67	68
35	PT5625.G07	69	70
36	PT5627.M20	71	72
37	PT5627.M12	73	74
38	PT5629.F09	75	76

39	PT5629.H08	77	78
40	PT5631.D21	79	80
41	PT5633.I03	81	82
42	PT5635.C08	83	84
43	PT5639.G15	85	86
44	PT5622.A20	87	88
45	PT5622.C12	89	90
46	PT5622.G24	91	92
47	PT5622.I20	93	94
48	PT5622.J24	95	96
49	PT5624.A21	97	98
50	PT5624.B10	99	100
51	PT5624.N05	101	102
52	PT5624.P11	103	104
53	PT5626.A12	105	106
54	PT5626.N08	107	108
55	PT5626.N18	109	110
56	PT5626.O09	111	112
57	PT5628.B13	113	114
58	PT5628.C21	115	116
59	PT5628.E12	117	118
60	PT5628.I07	119	120
61	PT5628.P14	121	122
62	PT5630.G05	123	124
63	PT5630.K04	125	126
64	PT5630.M11	127	128
65	PT5630.N06	129	130
66	PT5630.O08	131	132
67	PT5632.A10	133	134
68	PT5632.A15	135	136
69	PT5632.B15	137	138
70	PT5632.D11	139	140
71	PT5632.J23	141	142
72	PT5634.A17	143	144
73	PT5634.A21	145	146
74	PT5634.K10	147	148
75	PT5634.M16	149	150
76	PT5634.N11	151	152
77	PT5634.P19	153	154
78	PT5636.A16	155	156
79	PT5636.D21	157	158
80	PT5636.M03	159	160
81	PT5636.N13	161	162
82	PT5636.P11	163	164
83	PT5636.P15	165	166

84	PT5638.C06	167	168
85	PT5638.C20	169	170
86	PT5638.E14	171	172
87	PT5638.J23	173	174
88	PT5638.O14	175	176
89	PT5638.P12	177	178
90	PT5623.E21	179	180
91	PT5623.F17	181	182
92	PT5623.G08	183	184
93	PT5623.H05	185	186
94	PT5623.O08	187	188
95	PT5625.A05	189	190
96	PT5625.B14	191	192
97	PT5625.C15	193	194
98	PT5625.G05	195	196
99	PT5625.L22	197	198
100	PT5625.O14	199	200
101	PT5627.I21	201	202
102	PT5629.F04	203	204
103	PT5629.L22	205	206
104	PT5629.L24	207	208
105	PT5629.M15	209	210
106	PT5631.H06	211	212
107	PT5631.K12	213	214
108	PT5631.N17	215	216
109	PT5631.P07	217	218
110	PT5633.E09	219	220
111	PT5633.G19	221	222
112	PT5635.F04	223	224
113	PT5635.L21	225	226
114	PT5635.O15	227	228
115	PT5637.B23	229	230
116	PT5637.C20	231	232
117	PT5637.K09	233	234
118	PT5637.L15	235	236
119	PT5637.M03	237	238
120	PT5637.P15	239	240
121	PT5639.B15	241	242
122	PT5639.P05	243	244
123	PT5625.G07_22.F19_2	245	246
124	PT5625.G07_24.M09_1	247	248
125	PT5625.G07_24.P06_2	249	250
126	PT5625.G07_26.C10_1	251	252
127	PT5625.G07_26.M10_2	253	254
128	PT5625.G07_28.E16_1	255	256

129	PT5625.G07_30.A20_1	257	258
130	PT5625.G07_32.A13_2	259	260
131	PT5625.G07_34.M24_1	261	262
132	PT5625.G07_34.N13_3	263	264
133	PT5625.G07_36.P22_1	265	266
134	PT5627.M20_24.M09_1	267	268
135	PT5627.M20_24.P06_1	269	270
136	PT5627.M20_26.C10_1	271	272
137	PT5627.M20_26.M10_2	273	274
138	PT5627.M20_28.E16_2	275	276
139	PT5627.M20_30.D05_1	277	278
140	PT5627.M20_32.A13_1	279	280
141	PT5627.M20_34.M24_2	281	282
142	PT5627.M20_34.N13_4	283	284
143	PT5627.M20_36.P22_1	285	286
144	PT5627.M12_22.F19_1	287	288
145	PT5627.M12_24.M09_1	289	290
146	PT5627.M12_26.M10_2	291	292
147	PT5627.M12_32.A13_2	293	294
148	PT5627.M12_34.M24_2	295	296
149	PT5627.M12_34.N13_1	297	298
150	PT5629.F09_26.C10_1	299	300
151	PT5629.F09_28.E16_1	301	302
152	PT5629.F09_30.A20_1	303	304
153	PT5629.F09_30.D05_1	305	306
154	PT5629.F09_32.A13_3	307	308
155	PT5629.F09_36.P22_2	309	310
156	PT5629.H08_22.F19_4	311	312
157	PT5629.H08_24.M09_4	313	314
158	PT5629.H08_24.P06_2	315	316
159	PT5629.H08_26.C10_1	317	318
160	PT5629.H08_26.M10_1	319	320
161	PT5629.H08_28.E16_2	321	322
162	PT5629.H08_30.A20_2	323	324
163	PT5629.H08_30.D05_1	325	326
164	PT5629.H08_32.A13_1	327	328
165	PT5629.H08_34.M24_2	329	330
166	PT5629.H08_34.N13_2	331	332
167	PT5629.H08_36.P22_4	333	334
168	PT5631.D21_22.F19_2	335	336
169	PT5631.D21_24.M09_1	337	338
170	PT5631.D21_24.P06_4	339	340
171	PT5631.D21_26.C10_1	341	342
172	PT5631.D21_26.M10_4	343	344
173	PT5631.D21_28.E16_3	345	346

174	PT5631.D21_30.A20_4	347	348
175	PT5631.D21_30.D05_1	349	350
176	PT5631.D21_32.A13_4	351	352
177	PT5631.D21_34.M24_4	353	354
178	PT5631.D21_34.N13_2	355	356
179	PT5631.D21_36.P22_3	357	358
180	PT5633.I03_22.F19_1	359	360
181	PT5633.I03_24.M09_1	361	362
182	PT5633.I03_24.P06_4	363	364
183	PT5633.I03_26.C10_1	365	366
184	PT5633.I03_26.M10_4	367	368
185	PT5633.I03_28.E16_4	369	370
186	PT5633.I03_30.A20_1	371	372
187	PT5633.I03_30.D05_1	373	374
188	PT5633.I03_32.A13_1	375	376
189	PT5633.I03_34.M24_2	377	378
190	PT5633.I03_34.N13_1	379	380
191	PT5633.I03_36.P22_2	381	382
192	PT5635.C08_22.F19_1	383	384
193	PT5635.C08_24.M09_1	385	386
194	PT5635.C08_24.P06_1	387	388
195	PT5635.C08_26.C10_1	389	390
196	PT5635.C08_26.M10_2	391	392
197	PT5635.C08_28.E16_1	393	394
198	PT5635.C08_30.A20_1	395	396
199	PT5635.C08_30.D05_3	397	398
200	PT5635.C08_32.A13_3	399	400
201	PT5635.C08_34.M24_2	401	402
202	PT5635.C08_34.N13_1	403	404
203	PT5635.C08_36.P22_1	405	406
204	PT5639.G15_22.F19_2	407	408
205	PT5639.G15_24.P06_1	409	410
206	PT5639.G15_24.M09_4	411	412
207	PT5639.G15_26.M10_3	413	414
208	PT5639.G15_28.E16_1	415	416
209	PT5639.G15_30.A20_1	417	418
210	PT5639.G15_30.D05_1	419	420
211	PT5639.G15_34.N13_4	421	422
212	PT5639.G15_34.M24_3	423	424
213	PT5639.G15_36.P22_3	425	426
214	PT5625.G07_30.D05_1	427	428
215	PT5627.M12_26.C10_1	429	430
216	PT5627.M12_30.A20_2	431	432
217	PT5629.F09_34.N13_3	433	434

From the antibodies identified during screening, candidate P1AF8499 (#20 in **Table E2**, comprising VH SEQ ID NO: 39 and VL SEQ ID NO: 40) was selected based on its selectivity, convertase inhibition and impact on convertase stability profile for further optimization.

5 To this end two phage libraries were created containing diversification of the parental candidate antibody either in the heavy chain CDRs, or in the light chain CDRs. The libraries were panned and screened against the target as described in **Example 2**.

10 Candidates with improved properties compared to the parental molecule were selected and heavy and light chains of individual molecules were combined into single molecules in a combinatorial manner. Improved versions of the parental antibody candidate are antibodies #1-#7 as well as antibodies #23 to #217 as indicated in **Table E2** further below.

15 Binding of the antibodies to human C3bBb was analyzed by different ELISA assays, as described in **Example 2** to analyze binding towards human C3bBb formed from Factor B with three mutations D279G, K350N and M458I (herein referred to as “C3bBb triple mutant ELISA”) as well as controls assessing binding to different related components of the complement system, i.e. C3, C3a, C3b and Factor B, Ba, Bb. Results of the different ELISA assays for the antibodies as defined in **Table E2**

20 are shown in **Table E3**.

Table E3: Antigen binding of C3bBb complex of antibodies identified in Table E2 using C3bBb triple mutant ELISA

#	identifier	C3bBb (D279G/350N/M458I)	C3bBb (D279G)	C3/C3a/C3b	CFB/Ba/Bb	negative control
8	C3bBb.P045.072	2,904	0,023	-0,005	-0,010	-0,026
9	C3bBb.P045.236	1,815	-0,003	0,005	0,000	-0,024
10	C3bBb.P045.225	2,615	0,017	0,027	-0,021	-0,003
11	C3bBb.P048.152	0,405	-0,035	-0,007	-0,005	-0,025
12	C3bBb.P048.061	1,899	0,004	0,001	0,006	0,015

13	C3bBb.P048.127	0,187	2,423	-0,006	0,002	-0,010
14	C3bBb.P048.241	2,384	2,573	0,170	0,037	0,051
15	C3bBb.P048.230	2,692	2,670	0,210	0,021	0,018
16	C3bBb.P048.204	1,341	1,943	0,126	0,015	-0,014
17	C3bBb.P048.333	2,786	2,758	0,274	0,034	0,008
18	C3bBb.P053.095	-0,006	0,353	-0,001	0,003	0,008
19	C3bBb.P055.015	-0,010	0,860	-0,014	0,004	-0,014
23	PT5622.F19	2,7865	2,8105	-0,002	-0,0145	-0,0955
24	PT5624.P06	2,93375	2,76175	0,0175	0,05575	-0,02825
25	PT5624.M09	2,88075	2,72575	-0,0035	-0,01025	-0,07625
26	PT5626.M10	2,7295	2,4185	-0,00175	-0,0075	-0,05975
27	PT5626.C10	2,4645	2,1365	-0,01175	-0,0235	-0,07275
28	PT5628.E16	2,3335	2,4705	0,013	-0,0215	-0,087
29	PT5630.D05	2,41075	2,42475	-0,006	-0,01625	-0,10825
30	PT5630.A20	2,14975	2,28075	0,013	-0,01925	-0,07925
31	PT5632.A13	2,34725	2,41225	0,012	-0,02675	-0,079
32	PT5634.N13	2,58075	2,25775	0,025	0,02175	-0,06425
33	PT5634.M24	2,08675	1,68075	0,027	0,02075	-0,04625
34	PT5636.P22	2,7385	2,2665	0,049	0,0165	0,0055
35	PT5625.G07	2,26575	1,43375	-0,006	-0,01225	-0,0875
36	PT5627.M20	2,09725	1,48025	0,00975	0,01525	-0,01875
37	PT5627.M12	1,96125	1,16125	0,00875	-0,00175	-0,05675
38	PT5629.F09	2,172	1,536	-0,003	-0,015	-0,07725
39	PT5629.H08	1,893	0,93	0,003	-0,003	-0,06825
40	PT5631.D21	1,597	0,671	-0,018	-0,032	-0,087
41	PT5633.I03	0,9495	0,2615	0,008	-0,0175	-0,09175
42	PT5635.C08	1,646	0,676	-0,004	-0,017	-0,07625
43	PT5639.G15	1,25525	0,43425	-0,014	-0,02575	-0,05875
44	PT5622.A20	2,4135	2,2785	-0,014	-0,0365	-0,0745
45	PT5622.C12	2,5055	2,5475	-0,007	-0,0235	-0,1035
46	PT5622.G24	2,7145	2,3815	0,007	0,0025	-0,0715
47	PT5622.I20	2,6745	2,5155	0,005	0,0095	-0,0945
48	PT5622.J24	2,6815	2,5955	0,031	0,0085	0,0195
49	PT5624.A21	2,36775	2,72575	-0,0105	-0,02625	-0,06325
50	PT5624.B10	2,68475	2,79175	-0,0095	-0,02525	-0,09025
51	PT5624.N05	2,59275	2,51675	0,0105	0,07275	-0,06425

52	PT5624.P11	2,67675	2,78175	0,0235	0,02175	-0,00625
53	PT5626.A12	2,5245	2,3225	0,03925	-0,0205	-0,04575
54	PT5626.N08	2,9095	2,6135	0,01525	0,0095	-0,04375
55	PT5626.N18	2,7745	2,8355	0,01125	0,0015	-0,04475
56	PT5626.O09	2,6955	2,4135	0,00025	0,0065	-0,04975
57	PT5628.B13	2,3475	2,0165	0,038	-0,0255	-0,087
58	PT5628.C21	2,5615	2,8435	-0,007	-0,0285	-0,09
59	PT5628.E12	2,4015	2,3075	0,008	-0,0185	-0,093
60	PT5628.I07	2,3375	2,5365	0,014	-0,0115	-0,084
61	PT5628.P14	2,4965	2,3855	0,033	0,0185	-0,024
62	PT5630.G05	2,34275	2,11075	-0,009	-0,01225	-0,10725
63	PT5630.K04	1,96875	1,56875	-0,006	-0,01325	-0,10625
64	PT5630.M11	2,53775	2,35075	0,009	0,00575	-0,09325
65	PT5630.N06	2,33875	1,97975	0,012	0,00875	-0,08625
66	PT5630.O08	2,55475	2,22675	0,003	0,00475	-0,08125
67	PT5632.A10	2,11325	1,10025	0,009	-0,03875	-0,081
68	PT5632.A15	2,44325	2,20125	0,008	-0,04475	-0,081
69	PT5632.B15	2,41625	2,42125	-0,049	-0,04375	-0,09
70	PT5632.D11	2,47725	2,01625	0,01	-0,02275	-0,081
71	PT5632.J23	2,17625	2,17325	0,047	-0,01075	-0,067
72	PT5634.A17	2,38575	1,77875	-0,014	-0,03525	-0,06325
73	PT5634.A21	2,38175	2,40675	-0,001	-0,02225	-0,07825
74	PT5634.K10	2,55575	2,82475	-0,009	-0,02825	-0,10725
75	PT5634.M16	2,32575	2,51775	0,001	-0,00225	-0,09525
76	PT5634.N11	2,46075	2,31875	0,017	0,00575	-0,07625
77	PT5634.P19	2,16375	1,91875	0,051	0,05675	0,00975
78	PT5636.A16	2,4105	2,2515	-0,006	-0,0325	-0,0645
79	PT5636.D21	2,0895	1,5595	-0,002	-0,0195	-0,0705
80	PT5636.M03	2,3435	2,0835	0	-0,0195	-0,0665
81	PT5636.N13	2,5165	2,3515	0,038	0,0165	-0,0215
82	PT5636.P11	2,0955	1,1785	0,034	0,0315	-0,0105
83	PT5636.P15	2,3905	2,0715	0,04	0,0275	0,0115
84	PT5638.C06	1,8775	1,5045	0,021	-0,0275	-0,10825
85	PT5638.C20	1,8975	1,6935	-0,006	-0,0305	-0,10425
86	PT5638.E14	2,0825	1,6525	0,008	-0,0225	-0,10325
87	PT5638.J23	1,5375	0,7815	0,055	0,0885	-0,07825

88	PT5638.O14	2,1635	1,3795	0,108	0,0135	-0,06925
89	PT5638.P12	2,1835	1,3065	0,098	0,0375	-0,02925
90	PT5623.E21	2,1255	0,9965	-0,0105	-0,0165	-0,09625
91	PT5623.F17	2,1345	1,1215	-0,0075	-0,0205	-0,08725
92	PT5623.G08	2,0515	1,2285	0,0165	-0,0125	-0,09225
93	PT5623.H05	1,7455	0,8205	0,0005	-0,0135	-0,09125
94	PT5623.O08	2,0355	0,6395	-0,0025	0,0155	-0,07525
95	PT5625.A05	2,06975	1,07475	-0,011	-0,02125	-0,0585
96	PT5625.B14	1,60275	0,60975	-0,008	-0,01525	-0,0835
97	PT5625.C15	1,85375	0,84275	-0,014	-0,02225	-0,0905
98	PT5625.G05	1,84375	0,88175	0,007	-0,01425	-0,0855
99	PT5625.L22	1,38775	0,45375	0,003	-0,00125	-0,0685
100	PT5625.O14	1,89675	0,71975	0,016	0,02175	-0,0575
101	PT5627.I21	1,11525	0,42125	0,00475	-0,00375	-0,05775
102	PT5629.F04	2,073	1,086	-0,007	0,027	-0,06525
103	PT5629.L22	1,925	0,996	0,004	-0,007	-0,06325
104	PT5629.L24	1,929	0,724	0,001	-0,004	-0,04625
105	PT5629.M15	2,284	1,287	0,005	0,002	-0,07025
106	PT5631.H06	1,235	0,368	0	-0,014	-0,081
107	PT5631.K12	1,905	1,014	-0,005	-0,017	-0,091
108	PT5631.N17	1,825	0,872	0,015	0,013	-0,046
109	PT5631.P07	1,858	0,598	0,004	-0,001	-0,007
110	PT5633.E09	0,6525	0,2785	-0,013	-0,0345	-0,09775
111	PT5633.G19	0,9495	0,2375	0,016	-0,0135	-0,08475
112	PT5635.F04	1,671	0,649	-0,013	-0,022	-0,07625
113	PT5635.L21	1,896	1,355	0,01	-0,001	-0,05725
114	PT5635.O15	1,647	0,674	0	0,014	-0,05125
115	PT5637.B23	2,044	1,284	0,018	-0,047	-0,1105
116	PT5637.C20	1,972	1,224	-0,011	-0,034	-0,1155
117	PT5637.K09	1,716	0,708	-0,001	-0,023	-0,1165
118	PT5637.L15	1,975	1,252	0,025	-0,012	-0,0965
119	PT5637.M03	2,026	1,181	0,022	-0,028	-0,1155
120	PT5637.P15	2,142	1,292	0,037	0,019	-0,0185
121	PT5639.B15	1,68625	0,80525	-0,018	-0,02675	-0,06275
122	PT5639.P05	0,94025	0,34925	0,004	0,00825	-0,01175

Seven candidate antibodies were generated and further characterized with respect to their potential for therapeutic application, five antibodies were generated as a full length IgG1 (Mab) and two antibodies were generated as Fab fragments (see **Table E4**).

5 All Mabs and Fabs were produced in a serum-free medium, with the ExpiCHO Expression System (Thermo Fisher Scientific). For cultivation of the ExpiCHO cells the corresponding High-Titer Protocol was used. The Molar Plasmid Ratio was target dependent 1:1 or 1:3 Light Chain to Heavy Chain.

10 The purification of antibodies performed by Kappa Select (Cytavia) followed by size exclusion chromatography Superdex200 (Cytavia) in 20 mM Histidine, 140 mM NaCl pH 6.0. The purification of Fab's started by Kappa Select (Cytavia) followed by a CaptureSelect CH1-XL (Thermo Fisher Scientific) Step and finalized by Superdex200 (Cytavia) in 20 mM Histidine, 140 mM NaCl pH 6.0.

15 **Table E4:** amino acid sequences of clinical candidate antibodies identified in **Example 2**.

#	identifier	VH amino acid sequence	VL amino acid sequence	HC amino acid sequence	LC amino acid sequence
1	P1AG9426 (Mab)	1	2	435	436
2	P1AG9376 (Mab)	3	4	437	438
3	P1AG9372 (Mab)	5	6	439	440
4	P1AG9420 (Mab)	7	8	441	442
5	P1AG9391 (Mab)	9	10	443	444
6	P1AH1205 (Fab)	11	12	445	446
7	P1AH1199 (Fab)	13	14	447	448

Example 4:
Trimeric complex formed by C3bBb and a Fab fragment of the invention
analyzed by cryo electron microscopy

20 A trimeric complex of parental antibody P1AF8499 (#20) with the C3bBb complex was analyzed by electron microscopy. Briefly, the following protocol was adhered to:

Cryo-EM grid preparation. Purified recombinant complex of human C3bBb triple mutant + Fab P1AF8499 in 20 mM HEPES, 150 mM NaCl, 1 mM NiSO₄, pH 7.4 were frozen in liquid nitrogen (0.15 mg/ml, 0.7 μ M). After thawing, 3 μ l were applied to freshly glow-discharged Quantifoil R1.2/1.3 400-mesh copper grids (Plano). Grids were blotted (Whatman filter paper, Grade 1) for 4 s at 20 °C under 95% chamber humidity and plunge frozen in liquid ethane using a EM GP2 plunge freezer (Leica).

Cryo-EM data acquisition. Two datasets were collected on an FEI Titan Krios (Thermo Fisher Scientific, Waltham, MA, USA) at C-CINA, University of Basel, operating at 300 keV and equipped with a Gatan Quantum-LS imaging energy filter (GIF, 20 eV energy-loss window; Gatan Inc, Pleasanton, CA, USA). Altogether, 7550 movies of 40 frames were acquired with a K2 Summit direct electron detector (Gatan Inc) in the counted mode at a physical pixel size of 0.82 Å and a total electron dose of 56 e⁻/Å² with the SerialEM software [LK1]. Initial quality check of captured images was performed by the FOCUS programme [LK3] that employed the MotionCor2 programme [LK2] for correction of frame movements and their dose-weighting, and the CTFFIND4 programme [LK4] for the estimation of CTF parameters. Images displaying a resolution lower than 7 Å or average drifts higher than 2 Å per frame were excluded from the analysis.

Cryo-EM data processing. Image stacks were processed using cryoSPARC v3.3 (Structura Biotechnology). Frame motion was corrected and contrast-transfer function (CTF) parameters were fit from movies using the 25-4 Å band of the spectrum. Images with CTF fits to 4.5 Å or better were selected for particle picking using a spherical blob picker with maximum and characteristic diameters of 100 and 200 Å, respectively. Three rounds of 2D classification with 150 classes and a box size of 384 pixels were performed to sort C3bBb- P1AF8499 protein particles from debris and other false positives. The remaining particles were subjected to ab initio reconstruction and homogenous refinement to obtain a preliminary 3D reconstruction, which was used to create low-pass filtered templates for another round of particle picking. The picking and classification procedure was repeated to obtain a particle selection of 497884 particles. Reference volumes for 3D heterogeneous refinement were obtained by ab initio reconstruction into 4 classes, and particles were further classified using 2500 batch size and 4 full iterations. One class with the best structural features containing 172991 particles was selected for non-uniform refinement. For model building and figure preparation, sharpened maps

were used. Maps were filtered according to the local resolution using the implementation of blocres within cryoSPARC.

Model building. The structure of C3bBb (PDB 2WIN) was deconstructed into four separate models (TED-CUB, B2-MG, C345C and cleaved factor B). These models were fitted as rigid bodies into the cryo-EM map. After modelling P1AF8499 and performing manual adjustments mostly pertaining to P1AF8499 CDRs, a single round of real space refinement using the phenix.real_space_refinement tool with tight secondary structure restraints (TC1) was used to correct global structural differences between the initial model and the map. The model was further manually adjusted in Coot (TC2) through iterative rounds of model building and real space refinement. Phenix.mtriage was used to compute model vs map FSC curves that are consistent with our resolution estimate from the half-map FSC measurement.

Results are shown in **Figure 1**. The left image shows the trimeric complex formed between P1AF8499 Fab fragment and C3bBb. The epitope bound by P1AF8499 comprises amino acids from both components, C3b and Bb (**Figure 1, right image**). Hence, crossreactivity with individual subunits of C3bBb should be minimal or even excluded. The following epitope bound by P1AF8499 Fab fragment was identified by defining interaction of amino acid residues within 5 Å of P1AF8499:

Table E5: epitope bound by parental antibody P1AF8499 Fab fragment

Subunit of C3bBb	SEQ NO: of subunit	ID of amino acid residues within subunit
C3b	495	Arg444, Lys534, Gly539, Ser540, Val524, Lys544, Gly546, Gln547, Ser548, Arg551, Gln557, Gln558, Thr560, Lys562, Glu564, Glu758, Pro759, Lys761, Asn762, Ile764, Leu768, Asn770, Asp797
Bb subunit of human FB	501	Tyr465, Lys473, Ile474, Ser475, Ile477, Gly482, His483, Lys513, Val514, Ser515, Lys520, Arg521, Asp522, Glu610, Lys613

Example 5:**Antigen binding to human and cynomolgus C3bBb complex as analyzed by SPR**

5 Antigen binding of the antibodies of Example 3 to C3bBb from different species was assessed by SPR, using the following setup:

 A Biacore T200 system was primed with 1x HBS-P+ buffer (10 mM HEPES, 150 mM NaCl and 0.05% v/v Surfactant P20), prepared from a 10x stock (Cytiva BR100671). A CAP chip (part of the Biotin CAPture KIT - Cytiva 28920233) was docked to the system and equilibrated overnight.

10 **Human C3bBb binding characteristics**

 In the following, the measurement on human C3bBb complex is described. The running buffer was changed to HBS-P+ supplemented with 5 mM NiSO₄, to obtain stabilization of the C3bBb complex, which was built up on the chip surface from scratch in every cycle. Flow cells (FCs) 1 and 2 were used as active FCs. The sample compartment temperature was set to 12 °C, while the analysis temperature was defined to 25°C and 37°C, respectively, dependent on the assay step. Each analysis cycle started with an injection of the undiluted CAP reagent (part of the Biotin CAPture KIT - Cytiva 28920233) for 300 s at 5 µl/min passing over both FCs. Biotinylated-C3b was injected to FC 1 and 2 at 9 nM and 10 µl/min for 30 s (IgG analysis) and 60 s (Fab analysis), respectively. The injection was done separately on each FC to obtain comparable levels on both FCs. D-biotin (Invitrogen B20656) was injected at 50 µM and 10 µl/min for 60 s to both FCs, to block the remaining biotin binding sites. The FB triple mutant was injected to FC 2 at 100 nM and 5 µl/min for 300s to build the intermediate C3bB on FC2. Subsequently, FD was injected to FC 2 at 100 nM and 5 µl/min for 300s to build the C3bBb complex. After a stabilization period of 60 s, the sample injection for a single cycle kinetic was started. The sample was injected for 60 s at 30 µl/min to both FCs with five increasing concentrations of a 3-fold dilution series. The final dissociation time was set to 1200 s at 30 µl/min, due to the highly stable interaction. To regenerate the surface for the next cycle, the standard CAP chip regeneration, 8 M Gua-NaOH, was injected for 120s to both FCs. Finally, running buffer was injected for 60 s at 30 µl/min to both FCs with a final stabilization period of 60 s.

 For the analysis, a double referencing, with subtraction of the reference flow cell (FC1) signals and the bracketing reference blank cycles with buffer injection

only, was executed. The curves were fitted in the BIAevaluation Software using a 1:1 fit model for Fabs and the heterogeneous ligand model for IgGs to separate affin and avid binding, respectively.

Results of the interaction to human C3bBb are shown in **Table E6**.

5 **Table E6:** human C3bBb binding of clinical candidate antibodies of Example 3.

#	identifier	KD 37 °C	KD 25 °C
1	P1AG9426 (Mab)	14 pM	< 1 pM
2	P1AG9376 (Mab)	< 1 pM	< 1 pM
3	P1AG9372 (Mab)	11.6 pM	< 1 pM
4	P1AG9420 (Mab)	11 pM	< 1 pM
5	P1AG9391 (Mab)	1.6 pM	< 1 pM
6	P1AH1205 (Fab)	95 pM	16 pM
7	P1AH1199 (Fab)	200 pM	30 pM

Cynomolgus C3bBb binding characteristics

10 In order to measure the kinetic to cynomolgus C3bBb, the setup described above was adopted. To built cynomolgus C3bBb, the respective cynomolgus components were used: biotinylated cyno C3b (SEQ ID NO: 497), cyno FB (triple mutant, SEQ ID NO: 500) and cyno FD (SEQ ID NO: 498). Concentrations and injection times of the three components were changed as following: Injection of biotinylated cyno C3b at 60 nM and 10 µl/min for 180 s (IgG analysis) and 300 s (Fab analysis), respectively; Injection of cyno FB triple mutant at 400 nM and 5µl/min for 400 s; Injection of cyno FD at 600 nM and 5 µl/min for 400 s. Each
15 concentration of the analytes was injected for 75 s and the dissociation time was shortened to 300 s. All remaining parameters remained as described for the measurement on the human C3bBb complex.

Results are shown in **Table E7**.

20 **Table E7:** cynomolgus C3bBb binding of clinical candidate antibodies in Example 3.

#	identifier	KD 37 °C	KD 25 °C
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1	P1AG9426 (Mab)	197 nM	206 nM
2	P1AG9376 (Mab)	26 nM	50 nM
3	P1AG9372 (Mab)	260 nM	207 nM
4	P1AG9420 (Mab)	277 nM	117 nM
5	P1AG9391 (Mab)	150 nM	130 nM
6	P1AH1205 (Fab)	126 nM	65 nM
7	P1AH1199 (Fab)	460 nM	245 nM

Example 6:**Assessment of crossreactivity towards other components of the alternative pathway as analyzed by SPR**

5 In order to show that the binders are specific for the C3bBb complex the binding against individual components as well as precursor and breakdown products of the complex was tested in Biacore (also confirmed in ELISA and BLI). Proteins tested were: C3b (component of the complex), C3 (precursor of C3b), C3d, iC3b, C3a (breakdown products of C3b), as well as Bb (component of the complex), FB (precursor of Bb) and Ba (breakdown product of FB).

10 The off-target SPR assay was set up as described below.

A Biacore T200 system was equipped with a CM5 chip and primed with 1x HBS-N (10 mM HEPES, 150 mM NaCl), prepared from a 10x stock solution (Cytiva BR100670). An anti-human Fab antibody (Thermo Fisher Scientific 7103082100) was immobilized to all flow cells (FC1-4) in an amine coupling with default settings and a capture antibody injection time of 420 s at 10 µl/min and 30 µg/ml in 10 mM Acetate pH 5.

20 For the following analysis, the system was primed with HBS-P + 1 mM NiSO₄. After at least three initial conditioning cycles with capturing and regeneration, three antibodies were captured each cycle on FC 2, 3 and 4, respectively, at 10 µg/ml for 20 s. The off-target was injected at 200 nM for 60 s and the dissociation was followed for 60 s at a flow rate of 10 µl/min. Each cycle finished with a regeneration using 10 mM Glycine pH 2.1 for 70 s at 30 µl/min and a final stabilization time of 120 s. For each antibody, the different off-target injection cycles were bracketed by buffer injection cycles for double referencing purposes.

25 In order to analyze the potential off-target binding, the default binding and stability report points were analyzed. The RUs at the two report points were extracted

after double referencing the curves (active flow cell subtracted by blank flow cell FC1 and the respective blank cycles). The RU values were normalized to binding [%] and stability [%], respectively, using the following equation:

5 binding [%] or stability [%] =(double ref. binding or stability [RU] /capture level [RU])*(capture molecule [MW]/analyte [MW])*100

Results are shown in **Table E8**, which reports response levels directly after binding and after reaching stability (calculated as theoretical Rmax in %).

Table E8: Crossreactivity of indicated antibodies of Example 3 to components of the alternative pathway

binding	P1AG9376	P1AG9372	P1AG9426	P1AG9391	P1AH1205	P1AH1199
#	2	3	1	5	6	7
C3b	0.06	0.06	0.32	0.49	0	0.39
C3	0.14	0.72	2.01	2.61	0.01	2.39
C3d	0	0	0	0	0	0.53
iC3b	0	0.04	0.34	0.44	0	0.36
C3a	0	5.67	6.13	14.53	1.33	18.94
Bb	0	0	0	0	0	0.29
FB	0	0.11	0.16	0.20	0	0.53
Ba	0	0	0	0	0	0.72
stability	P1AG9376	P1AG9372	P1AG9426	P1AG9391	P1AH1205	P1AH1199
#	2	3	1	5	6	7
C3b	0.04	0.01	0.08	0.15	0.01	0.18
C3	0.02	0.24	1.07	1.72	0.01	1.65
C3d	0	0	0	0	0	0.48
iC3b	0	0.02	0.21	0.26	0.00	0.25
C3a	0	1.45	0.53	3.87	0.65	7.40
Bb	0	0	0	0	0	0.27
FB	0	0.06	0.07	0.14	0	0.46
Ba	0	0	0	0	0	0.50

Example 7:**Further characteristics of antibodies of the invention**

5 **Thermal stability** of antibodies of Example 3 was assessed by exposing the antibody to increasing temperature in a controlled gradient and structural unfolding (T_m by intrinsic fluorescence) and/or aggregation propensity (T_{agg} by SLS) are determined.

Apparent hydrophobicity was evaluated by determining the retention time on a hydrophobic HPLC column in comparison with known high and low hydrophobicity standard molecules.

10 **FcRn affinity** was assessed as follows: Interaction with immobilized FcRn was measured via SPR as no specific interaction is expected: biotinylated scFcRn was immobilized to a Series S Sensor Chip SA (500-600 RU). The antibodies were injected at 10 μ l/min for 60 s at 5 nM. The dissociation was followed for 90 s. The run was performed at 25°C in PBS-P pH 6 and the surface was regenerated using
15 PBS-P pH 8 for 60s at 30 μ l/min. The sensorgrams of the double referenced signals were compared to FcRn binding competent (Herceptin, wt FC part) and incompetent (Faricimab, Triple A FC part) controls. The positive control was diluted in a two fold dilution series down to 3.125 % of 5 nM. The results were double referenced (control flow cell and buffer cycle) using the Biacore T200 Evaluation Software 3.0. The
20 binding response (RU) of the positive control at different concentrations was used to create a standard curve. The remaining binding % (derived from the binding RUs) of all candidates at 100 % concentration (5 nM) were calculated. All candidates indicated very low (< 1 or 5 %) FcRn surface interaction compared to the positive control. The negative control (Faricimab 3A) showed similar signals as P1AH1205
25 and P1AH1199.

Heparin affinity chromatography was done on specific HPLC affinity columns. The corresponding retention times are compared to established thresholds based on known molecules with good and bad PK.

30 **Quality of antibody integrity** was measured monitoring high molecular weight species with retention times shorter than the main species. This was done by using a size exclusion HPLC setup with UV A280 nm detection. Obtained peaks were integrated using a custom baseline and calculating the area under the curve. Relative areas to the total curve integral are displayed. Conditions for this chromatography were selected based on molecule size and the manufacturer's

recommendation for protein analysis. Fragmentation of molecules is assessed using reduced and untreated capillary gel electrophoresis with intrinsic protein fluorescence detection. The low molecular weight species with shorter migration times than the main species are monitored and peak areas under the curve are integrated. Relative areas to the total curve integral are displayed. Functional integrity of the molecules is assessed with a binding assay specific for the target of the molecule (as described in example 5). Relative active concentrations were determined in cases of thermally stressed material. Putative asparagine and aspartic acid degradation hotspots are experimentally confirmed or excluded by tryptic Peptide Mapping MS analysis. Integration of the peak area of extracted ion chromatograms (XIC) was performed for wildtype and modified peptides. The ratio of modified peptides XIC areas relative to the wildtype XIC areas were taken into account when evaluating a potential modification site in the predicted complementarity determining regions.

Viscosity was assessed at different concentrations of the molecules of interest in a salt free generic buffer system. This is done by co incubating the molecule of interest at different concentrations with beads and detection by dynamic light scattering. The maximum feasible concentration is defined by a viscosity limit relevant for the target product profile and determined by fitting the available data to an appropriate model and applying the relevant threshold.

Table E9: Further characteristics of indicated antibodies

	P1AG9376	P1AG9372	P1AG9426	P1AG9391	P1AH1205	P1AH1199
#	2	3	1	5	6	7
Thermal stability (DLS T _{agg} / DLS T _m)	56	62	63	59	68	67
Apparent hydrophobicity (HIC)	0	0.1	0.2	0.1	-0.4	-0.2
FcRn affinity on biacore	No interaction	No interaction	No interaction	No interaction	No interaction	No interaction
Heparin affinity chromatography	0.87	0.28	0.23	0.26	0.81	0.12
Titer in CHO pools	3.4 g/l	1.6 g/l	6.0 g/l	3.3 g/l	3.0 g/l	2.6 g/l
Quality	> 70%	> 70%	> 70%	> 70%	> 70%	> 70%

max feasible conz below viscosity limit (mg/ml)	29.9	96.5	81.8	85.7	220.2	223.2
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Example 8:

Integrity of antibodies of the invention under thermal stress

Stability of antibodies of Example 3 under different stress conditions was assessed as follows: molecules were stored in solution in polypropylene vials with screw caps under conditions mimicking both physiological (phosphate buffered saline pH 7.4) and shelf life indicating conditions (Histidine/HCl, sodium chloride buffer pH 6.0). The molecule solutions were stored for prolonged periods of time at relevant temperatures (physiological: 37 °C and elevated stressed conditions: 40 °C). Subsequent analysis focuses on changes observed in the stored samples compared to an untreated control.

The changes were analyzed with the methods for integrity determination in Example 7.

Table E10: Residual activity of antibodies treated under stress conditions [%]

#	identifier	40 °C HisNaCl 37 °C PBS 2 weeks	40 °C HisNaCl 37 °C PBS 4 weeks
3	P1AG9372 (Mab)	98	97
2	P1AG9376 (Mab)	100	-
5	P1AG9391 (Mab)	99	97
1	P1AG9426 (Mab)	99	98
6	P1AH1205 (Fab)	99	98
7	P1AH1199 (Fab)	96	97

Example 9:

Potency of antibodies of the invention (Wieslab assay and hemolysis assay)

Wieslab assay: Potency of antibodies of Example 3 was assessed by the Wieslab Complement system Alternative pathway (AP) kit. This kit is an enzyme immunoassay for the determination of functional alternative complement pathway in human serum.

It combines principles of a hemolytic assay for complement activation with the use of specific antibodies to detect the generated neoantigen, which is proportional to the functional activity of the complement pathway. In brief, 2-fold dilution series of the antibody candidates and control compounds Pegcetacoplan (APL-2, a C3-inhibitor, Eur J Clin Invest. 2015 April ; 45(4): 423–440. doi:10.1111/eci.12419) and Iptacopan (LNP023, an FB-inhibitor, Proc Natl Acad Sci USA. 2019 Apr 16;116(16):7926-7931. doi: 10.1073/pnas.1820892116. Epub 2019 Mar 29) were provided in Histidine-buffer and then pre-incubated on ice for 15 min with human serum. The actual serum concentration at this point was 90%. This mixture was diluted 1:18 in a diluent with a specific blocker (so that only AP will be activated) and incubated for another 15 min at RT. Solution was added to a 96-well plate specifically coated with activators of the AP and incubated for 60 min at 37°C. Wells were washed and C5b-9 detected following the protocol. After 30 min the absorbance was measured at 405 nm and the amount of complement activation calculated using Xlfit.

Table E11: IC50 of indicated antibodies in Wieslab AP functional assay

#	identifier	IC50 (nM)	95conf_i
3	P1AG9372 (Mab)	36.7	8.8
2	P1AG9376 (Mab)	35.7	9.7
5	P1AG9391 (Mab)	39.1	9.2
4	P1AG9420 (Mab)	51.8	11.2
1	P1AG9426 (Mab)	46.4	7.4
6	P1AH1205 (Fab)	71.6	13.0
7	P1AH1199 (Fab)	115.4	24.3

Hemolysis assay: In another experiment, the potency of the antibodies was assessed via an alternative pathway hemolysis assay. In brief, 2-fold dilution series of the antibody candidates and control compounds APL-2 (C3-inhibitor) and LNP023 (FB-inhibitor) were provided in Histidine-buffer. Samples were prepared at 4°C or kept on ice so that the complement cascade would not start. Washed Rabbit Erythrocytes (RBC) were added to a V-shaped 96-well plate together with the dilution series of antibodies in a buffer appropriate for the alternative pathway. Normal human serum was added at a final assay concentration of 6.7% Complement activation was started by incubating the plates at 37°C. Every 10 min the plates were shaken for 1 min with 800 rpm to prevent the total sedimentation of the RBCs. Hemolysis reaction was stopped after 60 min with the addition of ice-cold NaCl-

solution containing 10mM EDTA. Plates were centrifuged for 3 min at 1250xg at 4°C to pellet the non-lysed RBCs. Supernatant was carefully transferred and the absorbance was measured at 405 nm. Percentage of hemolysis was calculated: (OD test sample - OD BG or blank) / (OD full lysis - OD BG or blank) x 100. IC50 values were calculated using Xlfit,

Table E12: IC50 of indicated antibodies in hemolysis assay

#	identifier	IC50 (nM)	95conf_i
3	P1AG9372 (Mab)	11.2	1.8
2	P1AG9376 (Mab)	10.4	2.9
5	P1AG9391 (Mab)	13.0	2.0
4	P1AG9420 (Mab)	16.3	3.5
1	P1AG9426 (Mab)	12.8	1.8
6	P1AH1205 (Fab)	23.8	1.1
7	P1AH1199 (Fab)	48.1	2.8

In another experiment, the potency of the antibodies was assessed via a BLI based C3b deposition assay.

BLI based C3b deposition assay: The activated carbonyl group created upon C3 cleavage by the C3 convertase reacts and forms covalent adducts with nucleophiles in close proximity to the enzyme. We utilized this property to measure convertase activity by quantifying the C3b mass deposited on a BLI sensor loaded with C3bBb and exposed to C3.

To this end, biotinylated C3b was loaded with low density on a streptavidin functionalized SAX BLI sensor (Sartorius) in an Octet red 384 device, reaching a signal of 1 nm. The convertase was assembled by exposing it to 270 nM plasma purified factor B and 27nM plasma purified factor D in HBS-T buffer (150mM NaCl, 10mM HEPES, 1mM MgCl₂, 0.005% Tween20, pH 7.4) at 30°C for 5 min, at which time a dynamic equilibrium between convertase assembly and dissociation was reached. Active sensors were then exposed to C3 (500 nM) in presence of test items at different concentrations and control sensors to test item alone, for 15 min, at which time convertase was considered completely dissociated. After a further 5 min exposition to buffer to allow the release of non-covalently associated material, deposited C3b was calculated from the signal difference between active and control sensor and used as index for activity and IC50 calculation.

Table E13: IC50 of indicated antibodies in BLI assay

#	identifier	IC50 (nM)	95conf_i
3	P1AG9372 (Mab)	1.5	0.11
2	P1AG9376 (Mab)	2.2	0.30
5	P1AG9391 (Mab)	1.6	0.11
4	P1AG9420 (Mab)	1.4	0.23
1	P1AG9426 (Mab)	1.6	0.20
6	P1AH1205 (Fab)	4.5	0.27
7	P1AH1199 (Fab)	6.9	0.38

Example 10:
Potency of antibodies of the invention compared to prior art clinical candidates targeting the alternative pathway

5 In a control experiment, the potency of prior art clinical candidates targeting
the alternative pathways was compared using the assays described in the previous
examples. As controls, APL-2 peptide, which binds to C3 (Eur J Clin Invest. 2015
April ; 45(4): 423–440. doi:10.1111/eci.12419), and LNP023, which inhibits FB,
(Proc Natl Acad Sci USA. 2019 Apr 16;116(16):7926-7931. doi:
10.1073/pnas.1820892116. Epub 2019 Mar 29) were used.

Table E14: IC50 of indicated comparative compounds

identifier	Wieslab assay		Hemolysis assay		BLI assay	
	IC50 (nM)	95conf_i	IC50 (nM)	95conf_i	IC50 (nM)	95conf_i
APL-2	274.2	10.9	274.2	10.9	200	37.6
LNP023	161.4	15.2	161.4	15.2	14	1.17

Example 11:
Cross-reactivity of antibodies of the invention with different monkey species

15 Cross-reactivity of antibodies of the invention towards C3bBb from different
monkey species, i.e. Macaca Fascicularis (Cynomolgus) and Chlorocebus sabaeus
(African Green Monkey), was assessed using the potency assays (hemolysis assay)
which varied slightly to the one described in the previous examples depending on
the species.

In brief, 2-fold dilution series of the antibody candidates and control compounds APL-2 (C3-inhibitor) and LNP023 (FB-inhibitor) were provided in Histidine-buffer. Samples were prepared at 4°C or kept on ice so that the complement cascade would not start. Washed Rabbit Erythrocytes (RBC) were added to a V-shaped 96-well plate together with the dilution series of antibodies in a buffer appropriate for the alternative pathway.

For Cynomolgus normal human serum was added at a final assay concentration of 5% (serum pool of 2 individuals). The complement activation started with the incubation of the plates at 37°C. Every 10 min the plates were shaken for 1 min with 800 rpm to prevent the total sedimentation of the RBCs. Hemolysis reaction was stopped after 20 min with the addition of ice-cold NaCl-solution containing 10mM EDTA. Plates were centrifuged for 3 min at 1000 xg at 4°C to pellet the non-lysed RBCs. Supernatant was carefully transferred and the absorbance was measured at 405 nm. Percentage of hemolysis was calculated: (OD test sample - OD BG or blank) / (OD full lysis - OD BG or blank) x 100. IC50 values were calculated using Xlfit.

For African Green Monkey (AGM) normal human serum was added at a final assay concentration varying between 4.2% and 6.7% depending on the individual animal. These concentrations were determined in a previous experiment as well with the incubation time and temperature to have the appropriate level of hemolysis. The biggest difference to the ‘regular’ hemolysis assay was that the plates were incubated at RT and the activation was stopped after 20 min and the plates were further processed as described above.

Table E15: Cross-reactivity of indicated compounds in hemolysis assay

identifier	#	Macaca Fascicularis		Chlorocebus sabaeus	
		IC50 (nM)	95conf_i	IC50 (nM)	95conf_i
P1AG9372 (Mab)	3	1115	176.2	111.8	30.4
P1AG9376 (Mab)	2	802	1108.9	27.6	6.4
P1AG9391 (Mab)	5	981	445.5	74.8	27.3
P1AG9420 (Mab)	4	>578		>578	

P1AG9426 (Mab)	1	>2000	584.3	139.9	42.2
P1AH1205 (Fab)	6	3059	600.8	445.9	149.2
P1AH1199 (Fab)	7	>6000	2246.5	1306.5	248.4
APL-2		316	30.3	147.4	16.3
LNP023		73.2	7.1	113.0	11.3

Example 12:

Impact of antibodies of the invention on convertase dissociation

Impact of different anti-C3bBb antibodies (inhibitors) on half-life of tripartite complex comprising C3bBb inhibitors and C3bBb

5 Impact of C3bBb inhibitors (Inh) on the convertase stability was investigated by analyzing the decay of C3bBb:Inh tripartite complex assembled on a Bio Layer interferometry sensor.

10 To this end, biotinylated C3b was loaded at low density on a streptavidin functionalized SAX BLI sensor on an Octet red384 device (Sartorius), reaching a signal of 1.5 nm. The convertase was assembled by exposing the sensor to 270 nM plasma buffer (150mM NaCl, 10mM HEPES, 1mM MgCl₂, 0.005% Tween20. pH 7.4)) at 30°C for 5 min, at which time a dynamic equilibrium between convertase assembly and dissociation was reached. The convertase loaded sensors were then exposed to 500 nM test items in continued presence of FB and FD for 10 min
15 allowing the inhibitor to reach binding equilibrium with the convertase.

 Signal decay of the C3bBb:Inh tripartite complex was followed on the control sensor and fitted to an exponential function using XL fit (IDBS software) to calculate the tripartite complex half-life. Data were compared to a parallel assay performed in absence of inhibitor, revealing that some of the explored C3bBb
20 specific binders strongly stabilized the convertase, a probable effect of C3b –Bb interface binding, whereas other inhibitors did not stabilize the convertase.

Table E16a:

#	identifier	Concen- tration (nM)	Initial deposition	C3b deposition inhibition	C3bBb t1/2 (s)	C3bBb:Inh t1/2 (s)	Increase (%)
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			rate inhibition (%)	(%)			
8	P045.072 (Fab)	500	87	Not determined	207	2453	1085
10	P045.225 (Fab)	500	82	Not determined	207	1105	434
9	P045.236 (Fab)	500	58	Not determined	207	484	134
20	P046.185 (Fab)	500	88	Not determined	207	229	11
13	P046.127 (Fab)	500	100	Not determined	207	4120	1890
19	P055.015 (Fab)	500	90	Not determined	204	628	207

5 In another experiment, the impact of selected inhibitors on the convertase half-life was quantitatively examined in conditions ensuring that the convertase was saturated with tested compounds. Design similar to the previous experiment was implemented, except that C3b loading was limited to 1 nm BLI signal. Compounds were tested over a 316-fold dilution range, equilibration with the convertase extended to 15 min and exposure to C3 (paralleling convertase decay on the control sensor) limited to 15 min.

10 At the highest concentration tested, 31.6nM, 63.2nM, 320nM and 5µM for respectively Mabs, and Fabs, convertase activity was essentially fully suppressed suggesting that, in the experimental condition, convertase occupancy was close to 100% . Furthermore analysis of the BLI signal shift associated to Mab and Fab binding confirmed that saturation was achieved. Therefore the reported half-life refers to the tripartite complex and not a bound/unbound convertase mixture.

Table E16b:

#	Identifier	Concentration (nM)	Initial deposition rate inhibition (%)	C3b deposition inhibition (%)	C3bBb t1/2 (s)	C3bBb:I nh t1/2 (s)	t1/2 increase (%)
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3	P1AG9372 (Mab)	31.6	100	97	229	318	39
2	P1AG9376 (Mab)	31.6	99	99	197	299	52
5	P1AG9391 (Mab)	31.6	100	99	231	313	35
4	P1AG9420 (Mab)	31.6	99	96	188	215	14
1	P1AG9426 (Mab)	31.6	100	99	257	326	27
6	P1AH1205 (Fab)	63.2	97	96	184	207	14
7	P1AH1199 (Fab)	63.2	94	93	204	219	7.3

Example 13:

Antibodies of the invention are selective inhibitors of the alternative pathway and do not inhibit the classical pathway and lectin pathway

5 In order to confirm that the antibodies of the invention are selective inhibitors of the alternative pathway, a classical pathway hemolysis assay was performed as follows

10 In brief, 2-fold dilution series of the antibody candidates and control compounds APL-2 (C3-inhibitor) and LNP023 (FB-inhibitor) were provided in Histidine-buffer. Everything was prepared at RT except for the serum which was kept on ice so that the complement cascade would not start. Washed Ab-sensitized sheep erythrocytes (EA) were added to a V-shaped 96-well plate together with the dilution series of antibodies in a buffer appropriate for the classical pathway. Normal human serum was added at a final assay concentration of 2% and mixed gently with the other components. Complement activation was started by incubating the plates at 37°C shaking continuously at 600 rpm to prevent the total sedimentation of the EAs. Hemolysis reaction was stopped after 30 min with the addition of ice-cold NaCl-solution containing 10mM EDTA. Plates were centrifuged for 2 min at 1000 xg at 4°C to pellet the non-lysed EAs. Supernatant was carefully transferred and the absorbance was measured at 405 nm. Percentage of hemolysis was calculated: (OD test sample - OD BG or EDTA ctrl) / (OD full lysis - OD BG or EDTA ctrl) x 100. IC50 values were calculated using Xlfit.

15

20

Table E17: IC50 of indicated molecules assessed by classical pathway hemolysis assay

#	identifier	IC50 (nM)	95conf i
3	P1AG9372 (Mab)	> 2000	
2	P1AG9376 (Mab)	> 2000	
5	P1AG9391 (Mab)	> 2000	
4	P1AG9420 (Mab)	> 578	
1	P1AG9426 (Mab)	> 2000	
6	P1AH1205 (Fab)	> 6000	
7	P1AH1199 (Fab)	> 6000	
	APL-2	1022	170.7
	LNP023	> 20.000	

As expected, LNP023, a Factor B-inhibitor does not inhibit the classical pathway. It is specific for the alternative pathway only.

5 **Example 14:**
Binding to wild-type human C3bBb

Specific binding of antibody P1AG9426 (#1) of the invention of the wild-type human C3bBb complex was analyzed via SPR analysis.

Wild-type human C3bBb SPR assay

10 A Biacore T200 system was equipped with a CM5 chip and primed with 1x HBS-N (10 mM HEPES, 150 mM NaCl), prepared from a 10x stock solution (Cytiva BR100670). An anti-human Fab antibody (Thermo Fisher Scientific 7103082100) was immobilized to all flow cells (FC1-4) in an amine coupling with default settings and a capture antibody injection time of 420 s at 10 µl/min and 30 µg/ml in 10 mM
15 Acetate pH 5.

 The following method was run in HBS-P + 1 mM NiSO₄. If not stated differently, the samples were diluted in the running buffer. The antibody was captured for 60 s at 10 µl/min (diluted in HBS-N). Afterwards the prebuilt C3bBb wt complex was injected for 120 s at 10 µl/min with 600 s dissociation. The complex
20 was prebuilt by incubating 300 nM human C3b, 310 nM human wt Factor B and 40 nM human Factor D for 5 min at RT. The surface was regenerated by injecting 10 mM Glycine pH 2.1 for 60 s at 30 µl/min. The data were analyzed by double-

referencing the signals on FC2 to FC1 and a buffer cycle, injecting running buffer instead of C3bBb wt complex.

Example 15:
C5 convertase inhibition

5 **Hemolysis assay:** The standard hemolysis assay was modified in order to assess the inhibitory potential of the antibodies specifically at the level of the alternative pathway C5-convertase. Samples were prepared at 4°C or kept on ice so that the complement cascade would not start. Washed Rabbit Erythrocytes (RBC) were added to a V-shaped 96-well plate in a low salt (60 mM NaCl) buffer appropriate for the alternative pathway, but containing also 200 nM C5-inhibitor (Crovalimab) to prevent MAC formation. Cells were pre-heated for 10 min at 37°C followed by the addition of ice-cold normal human serum at a final assay concentration of 6.7% and incubated for additional 10 minutes with constant shaking enabling the formation of C3- and C5-convertases, but no C5 cleavage. The formation of further convertases was stopped by adding a buffer containing 40 mM EDTA, cells were spin down, and the pellet was resuspended in 2 consecutive steps: first with a buffer containing final 1.25% guinea pig serum (as a source of the complement proteins C5-9 needed for MAC formation), EDTA and the antibodies (see Table E18 for concentrations), followed by a buffer containing Mg-EGTA. Under these conditions, there is no de novo convertase formation and the inhibition of hemolysis is a direct consequence of the inhibition of C5-convertases formed earlier. Hemolysis was measured after incubating the cells for 1h at 37°C with constant shaking.

Table E18: C5 convertase inhibition of indicated antibodies

#	identifier	Concentration (nM)	Level of inhibition [%]
3	P1AG9372 (Mab)	21	68
2	P1AG9376 (Mab)	58	70
5	P1AG9391 (Mab)	52	73
4	P1AG9420 (Mab)	165	63
1	P1AG9426 (Mab)	276	63
6	P1AH1205 (Fab)	520	74
20	P1AF8499	1000	70
153	PT5629.F09_30.A20_1	839	73
	LNP023	20000	70

PATENT CLAIMS

1. An antibody that binds to human C3bBb.
- 5 2. An antibody that binds to human C3bBb, wherein the antibody:
 - binds to wild-type human C3bBb; and/or
 - binds to recombinant human C3bBb, which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:491;
 - binds to recombinant human C3bBb, which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:492; and/or
 - 10 - binds to recombinant human C3bBb, which comprises the Bb subunit of factor B (FB) according to SEQ ID NO:493; and/or
 - binds to recombinant human C3bBb, which comprises the Bb subunit of a recombinant Factor B (FB) protein, which comprises a D279G mutation and optionally mutations K350N and/or a M458I;
 - 15 - inhibits the alternative pathway; and/or
 - is an agonist or antagonist of C3bBb activity; and/or
 - specifically binds to cynomolgus C3bBb and human C3bBb,
 - specifically binds to African green monkey C3bBb and human C3bBb,
 - 20 - binds with an affinity of ≤ 300 pM at 37 °C as measured by SPR, and/or
 - does not stabilize C3 convertase.
3. An antibody that binds to human C3bBb that binds to an epitope of human C3bBb that includes amino acid residues of the C3b subunit and amino acid residues of the Bb subunit of human FB.
- 25 4. An antibody that binds to human C3bBb that binds to an epitope comprising the following amino acid residues on C3bBb as detected by cryogenic electron microscopy:
 - 30 - C3b subunit: Arg444, Lys534, Gly539, Ser540, Val524, Lys544, Gly546, Gln547, Ser548, Arg551, Gln557, Gln558, Thr560, Lys562, Glu564, Glu758, Pro759, Lys761, Asn762, Ile764, Leu768, Asn770, Asp797, and

- Bb subunit: Tyr465, Lys473, Ile474, Ser475, Ile477, Gly482, His483, Lys513, Val514, Ser515, Lys520, Arg521, Asp522, Glu610, Lys613.

5. An antibody that binds to the same or an overlapping epitope as an antibody having a VH domain of SEQ ID NO: 39 and a VL domain of SEQ ID NO: 40 (P1AF8499).
6. An antibody that binds to human C3bBb, wherein the antibody comprises the heavy and light chain CDRs of an antibody selected from Table D1.
7. The antibody of one of the preceding claims, comprising
 - i) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:449; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:450; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:451, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:452; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:453; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:454 (corresponding to antibody #1, P1AG9426);
 - ii) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:455; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:456; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:457, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:458; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:459; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:460 (corresponding to antibody #2, P1AG9376);
 - iii) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:461; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:462; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:463, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:464; (e) CDR-L2 comprising the amino acid sequence of SEQ ID

- NO:465; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:466 (corresponding to antibody #3, P1AG9372);
- iv) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:467; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:468; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:469, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:470; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:471; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:472 (corresponding to antibody #4, P1AG9420);
- v) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:473; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:474; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:475, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:476; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:477; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:478 (corresponding to antibody #5, P1AG9391);
- vi) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:479; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:480; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:481, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:482; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:483; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:484 (corresponding to antibody #6, P1AH1205); or
- vii) a heavy chain variable domain (VH) (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:485; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:486; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:487, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:488; (e) CDR-L2 comprising the amino acid sequence of SEQ ID

NO:489; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:490 (corresponding to antibody #7, P1AH1199).

8. The antibody of any one of the preceding claims, wherein the antibody
5 comprises a VH domain with a VH3 framework and a VL domain with a V kappa1 framework.
9. The antibody of any of the preceding claims, comprising a sequence selected from the group consisting of
 - 10 i) a VH domain comprising SEQ ID NO:1 and a VL domain comprising SEQ ID NO:2 (corresponding to antibody #1, P1AG9426);
 - ii) a VH domain comprising SEQ ID NO:3 and a VL domain comprising SEQ ID NO:4 (corresponding to antibody #2, P1AG9376);
 - 15 iii) a VH domain comprising SEQ ID NO:5 and a VL domain comprising SEQ ID NO:6 (corresponding to antibody #3, P1AG9372);
 - iv) a VH domain comprising SEQ ID NO:7 and a VL domain comprising SEQ ID NO:8 (corresponding to antibody #4, P1AG9420);
 - v) a VH domain comprising SEQ ID NO:9 and a VL domain comprising SEQ ID NO:10 (corresponding to antibody #5, P1AG9391);
 - 20 vi) a VH domain comprising SEQ ID NO:11 and a VL domain comprising SEQ ID NO:12 (corresponding to antibody #6, P1AH1205); or
 - vii) a VH domain comprising SEQ ID NO:13 and a VL domain comprising SEQ ID NO:14 (corresponding to antibody #7, P1AH1199).
- 25 10. An isolated nucleic acid encoding the antibody of any of claims 1 to 8.
11. A host cell comprising the nucleic acid of claim 9.
12. A method of producing an antibody that binds to human C3bBb comprising
30 culturing the host cell of claim 10 under conditions suitable for the expression of the antibody.

13. A pharmaceutical composition comprising the antibody of any of claims 1 to 8 and a pharmaceutically acceptable carrier.
14. The antibody of any one of claims 1 to 8 or the pharmaceutical composition
5 of claim 12 for use as a medicament.
15. Use of the antibody of any one of claims 1 to 8 or the pharmaceutical composition of any of claim 12 in the manufacture of a medicament for treatment of an ocular disease.