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DIRIGES CONTRE L'HEPATITE B
(54) Title: COMPOSITIONS AND METHODS RELATED TO HUMAN NEUTRALIZING ANTIBODIES TO HEPATITIS B

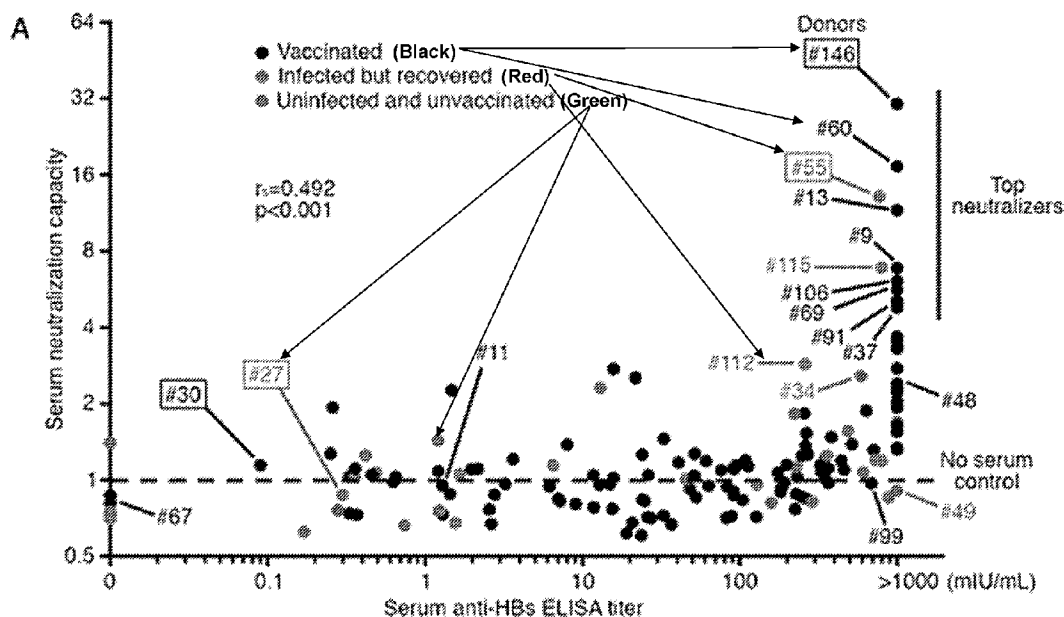


Fig. 1

(57) **Abrégé/Abstract:**

Provided are broadly neutralizing antibodies (bNAbs) and antigen binding fragments thereof that bind with specificity to epitopes expressed by Hepatitis B virus (HBV). The bNAbs target non-overlapping epitopes on the HBV S antigen (HBsAg). Pharmaceutical compositions that contain the bNAbs, or modified bNAbs, are provided. Combinations of the bNAbs are included, and are useful for prophylaxis and therapy of HBV infection, and for inhibiting development of HBV escape mutations in infected individuals. Expression vectors encoding the bNAbs and antigenic fragments of them are included, as are methods of making the bNAbs and antigenic fragments of them. HBV peptides for use as vaccines are provided, and include at least two non-overlapping epitopes from the HBsAg. Diagnostic reagents comprising the bNAbs or antigenic fragments thereof are provided, as are methods of detecting HBV and diagnosing HBV infection.

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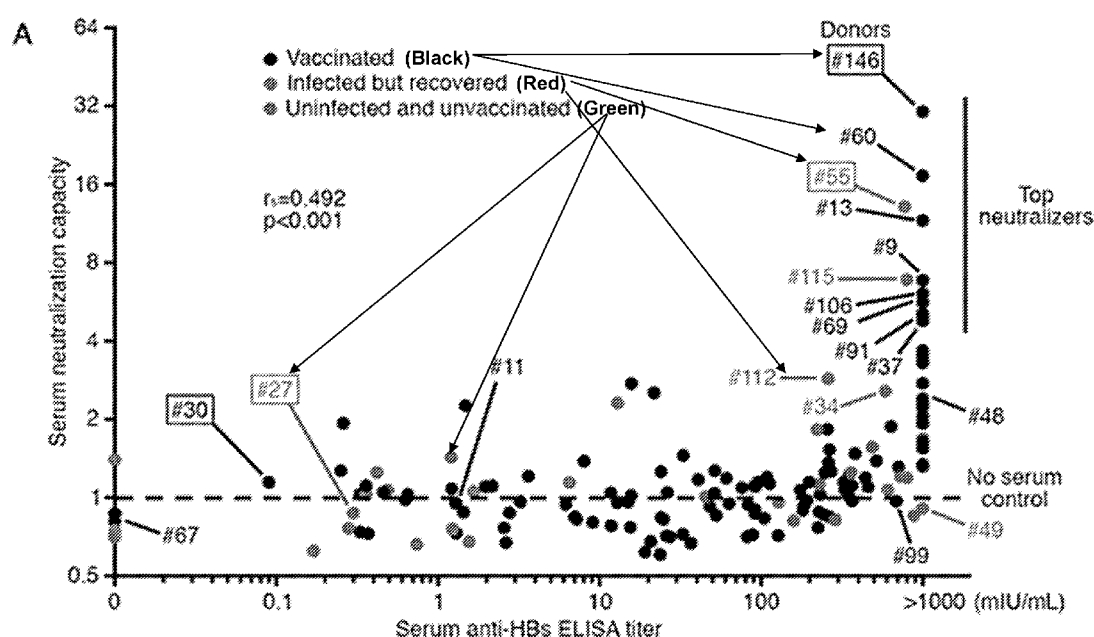


Fig. 1

(57) Abstract: Provided are broadly neutralizing antibodies (bNAbs) and antigen binding fragments thereof that bind with specificity to epitopes expressed by Hepatitis B virus (HBV). The bNAbs target non-overlapping epitopes on the HBV S antigen (HBsAg). Pharmaceutical compositions that contain the bNAbs, or modified bNAbs, are provided. Combinations of the bNAbs are included, and are useful for prophylaxis and therapy of HBV infection, and for inhibiting development of HBV escape mutations in infected individuals. Expression vectors encoding the bNAbs and antigenic fragments of them are included, as are methods of making the bNAbs and antigenic fragments of them. HBV peptides for use as vaccines are provided, and include at least two non-overlapping epitopes from the HBsAg. Diagnostic reagents comprising the bNAbs or antigenic fragments thereof are provided, as are methods of detecting HBV and diagnosing HBV infection.

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COMPOSITIONS AND METHODS RELATED TO HUMAN NEUTRALIZING ANTIBODIES TO HEPATITIS B

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional patent application no. 62/898,735, filed September 11, 2019, and to U.S. provisional patent application no. 62/982,276, filed February 27, 2020, the entire disclosures of each of which are incorporated herein by reference in their entireties.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] This invention was made with government support under grant no. UL1TR001866 awarded by The National Institutes of Health. The government has certain rights in the invention.

SEQUENCE LISTING

[0003] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on September 9, 2020, is named 076091_00092_SL.txt and is 307,317 bytes in size.

BACKGROUND

[0004] Despite the existence of effective vaccines, hepatitis B virus (HBV) infection remains a major global health problem with an estimated 257 million people living with the infection. Whereas 95% of adults and 50-75% of children between the ages of 1 and 5 years spontaneously control HBV, only 10% of infants recover naturally. The remainder develop a chronic infection that can lead to liver cirrhosis and hepatocellular carcinoma. Although chronic infection can be suppressed with antiviral medications, there is no effective curative therapy (Dienstag, 2008; Revill et al., 2016; Thomas, 2019).

[0005] HBV is an enveloped double-stranded DNA virus of the *Hepadnaviridae* family. Its genome is the smallest genome among pathogenic human DNA viruses, with only four open reading frames. Infected liver cells produce both infectious HBV virions (Dane particles) and non-infectious subviral particles (Australia antigen) (Dane et al., 1970; Hu and Liu, 2017). The virion is a 42 nm-diameter particle containing the viral genome and HBV core antigen (HBcAg) encapsidated by a lipid membrane containing the hepatitis B surface

antigen (HBsAg) (Blumberg, 1964; Venkatakrishnan and Zlotnick, 2016). Subviral particles lack the viral genome.

[0006] HBV strains were originally grouped into four HBsAg serotypes (*adr*, *adw*, *ayw*, and *ayr*). Genetic analysis revealed several highly conserved domains and defined eight genotypes A-H, which are highly correlated with the 4 serotypes (Norder et al., 2004). The HBV surface protein, HBsAg, has 4 putative transmembrane domains and can be subdivided into PreS1-, PreS2- and S-regions. The S domain is a cysteine-rich protein consisting of 226 amino acids that contain all 4 of the transmembrane domains (Abou-Jaoude and Sureau, 2007). In addition, the S-protein can be glycosylated at asparagine residue 146 (Julithe et al., 2014).

[0007] Antibodies to HBsAg (anti-HBs) are associated with successful vaccination and recovery from acute infection, while antibodies to HBcAg (anti-HBc) are indicative of past or current HBV infection (Ganem, 1982). Indeed, the most significant difference between chronically infected and naturally recovered individuals is a robust antibody response to HBsAg (Ganem, 1982). Conversely, the inability to produce these antibodies during acute infection is associated with chronicity (Trepo et al., 2014). Whether these associations reflect an etiologic role for anti-HBs antibodies in protecting from or clearing established infection is not known. However, depletion of antibody-producing B lymphocytes in exposed humans by anti-CD20 therapies (e.g. rituximab) is associated with HBV reactivation, indicating that B cells and/or their antibody products play a significant role in controlling the infection (Loomba and Liang, 2017).

[0008] Several human antibodies against HBsAg have been obtained using a variety of methods including: phage display (Kim and Park, 2002; Li et al., 2017; Sankhyan et al., 2016; Wang et al., 2016); humanized mice (Eren et al., 1998); Epstein-Barr virus-induced B cell transformation (Heijntink et al., 2002; Heijntink et al., 1995; Sa'adu et al., 1992); hybridoma technology (Colucci et al., 1986); human B cell cultures (Cerino et al., 2015); and microwell array chips (Jin et al., 2009; Tajiri et al., 2010). However, the donors in these studies were not selected for serum neutralizing activity. Thus, there remains a need for improved approaches and compositions of combatting HBV infection. The present disclosure is pertinent to this need.

BRIEF SUMMARY

[0009] The disclosure provides in part a description of the human humoral immune response to HBsAg in immunized and spontaneously recovered individuals that had been

selected for high levels of serum neutralizing activity. The disclosure demonstrates that these individuals develop closely related bNAbs that target shared non-overlapping epitopes in HBsAg. The crystal structure of one of the antibodies with its peptide target reveals a loop that helps to explain why certain amino acid residues are frequently mutated in escape viruses and why combinations of bNAbs may be needed to control infection. *In vivo* experiments in humanized mice demonstrate that the bNAbs are protective and can be therapeutic when used in combination.

[0010] Any antibody described herein can comprise at least one modification of its constant region. The modification may be made for any one or more amino acids. The modification can have any of a number of desirable effects. In certain approaches, the modification increases in vivo half-life of the antibody, or alters the ability of the antibody to bind to Fc receptors, or alters the ability of the antibody to cross placenta or to cross a blood-brain barrier or to cross a blood-testes barrier, or inhibits aggregation of the antibodies, or a combination of said modifications, or wherein the antibody is attached to a label or a substrate. In embodiments, the modification improves the manufacturability of the antibody. In embodiments, any antibody or combination thereof described herein can be present in an immunological assay, such as an enzyme-linked immunosorbent assay (ELISA) assay, or an ELISA assay control. The ELISA assay can be any of a direct ELISA assay, an indirect ELISA assay, a sandwich ELISA assay, or a competition ELISA assay.

[0011] In another aspect the disclosure provides a method for prophylaxis or therapy of a hepatitis viral infection comprising administering to an individual in need thereof an effective amount of at least one antibody described herein, or an antigen binding fragment thereof. The antibody may comprise at least one modification of the constant region. In embodiments, the composition is administered to an individual who is infected with or is at risk of being infected with a hepatitis B virus. In one approach, at least two antibodies are administered, wherein optionally the two antibodies recognize distinct HBV epitopes. In an embodiment, administering at least two distinct antibodies suppresses formation of viruses that are resistant to the antibodies.

[0012] In another aspect the disclosure provides vaccine formulations. In an embodiment a vaccine formulation comprises an isolated or recombinant peptide or a polynucleotide encoding the peptide, wherein the peptide is derived from an epitope that is frequently targeted by HepB immune resistance, and which is located in a loop anchored by oppositely charged residues, as further described herein.

[0013] In another aspect the disclosure provides one or more recombinant expression vectors, and kits comprising the expression vectors. The expression vectors encode at least the heavy chain and the light chain CDRs of any of the antibodies of described herein. Cells comprising the recombinant expression vectors are included, as are methods of making antibodies by culturing cells that comprise expression vectors that express the antibodies, and separating antibodies from the cells. Cell culture media containing such cells and/or antibodies is also included.

BRIEF DESCRIPTION OF THE FIGURES

[0014] Figure 1. Antibody responses in HBV vaccinated and recovered

10 individuals. (A) Donor screen. Sera from 159 volunteers were evaluated for anti-HBs binding by ELISA (x-axis) and HBV serum neutralization capacity using HepG2-NTCP cells (y-axis). Serum neutralization capacity on the y-axis was calculated as the reciprocal of the relative percentage of infected HepG2-NTCP cells. The values for unexposed naïve donors are $\cong 1$. Neutralization tests were performed at 1:5 serum dilution in the final assay volume. Each dot represents an individual donor. Green indicates unvaccinated and unexposed, black indicates vaccinated, and red indicates spontaneously recovered. The dashed line indicates the no serum control. Top neutralizers (serum neutralization capacity higher than 4) are indicated (top right). Boxed are representative samples shown in Figure 2A. Spearman's rank correlation coefficient (r_s) and significance value (p). (B and C) Dose-dependent HBV neutralization by serum (B) or by purified IgG (C). Two assays were used to measure percent infection: ELISA to measure HBsAg protein in the medium (upper panels) and immunofluorescent staining for HBcAg in HepG2-NTCP cells (lower panels). Dashed line indicates virus-only control. (D) Schematic representation illustrating the three forms of the HBV surface protein: L-, M- and S-protein. These three forms of envelope protein all share the same S-region, with PreS1/PreS2 and PreS2 alone as the N-terminal extensions for L- and M-protein, respectively. (E) S-protein produced in Chinese hamster ovary (CHO) cells blocks serum neutralizing activity. Graphs show infection efficiency as a function of the amount of S-protein added. The concentration of polyclonal IgG antibodies (pAb) is indicated. Upper and lower panels are as in (B) and (C). A representative of at least two experiments is shown. See also Figure 8 and Table S1.

[0015] Figure 2. S-protein-specific antibodies. (A) Frequency of S-protein-specific memory B cells. Representative flow cytometry plots displaying the percentage of all IgG⁺ memory B cells that bind to both allophycocyanin- and phycoerythrin-tagged S-protein (S-

protein-APC and S-protein-PE). Flow cytometry plots from other individuals are shown in Figure 9A. Experiments were repeated two times. (B) Dot plot showing the correlation between the frequency of S-protein-binding IgG⁺ memory B cells and the serum neutralizing activity. Spearman's rank correlation coefficient (r_s) and significance value (p). (C) Each pie chart represents the antibodies from an individual donor, and the total number of sequenced antibodies with paired heavy and light chains is indicated in the center. Antibodies with the same combination of IGH and IGL variable gene sequences and closely related CDR3s in each individual are shown. The slices with the same color indicate shared antibodies with the same or similar combination of IGH and IGL variable genes between individuals (Figure 9B). Grey slices indicate antibodies with closely related sequences that are unique to a single donor. In white are singlets. (D) V(D)J alignments for representative IGHV3-30/IGLV3-21, IGHV3-33/IGLV3-21 and IGHV3-23/IGLV3-21 antibodies from donors #60/#146 (H006 and H008), #146/#13 (H014 and H012), and #13/#60/#146 (H021, H003 and H004) respectively. Boxed grey residues are shared between antibodies. See also Figure 9 and Table S2. Figure discloses SEQ ID NOS 1438-1451, respectively, in order of appearance.

[0016] Figure 3. Broad cross-reactivity. (A) Binding to S-protein (*adr* serotype). 50% effective concentration (EC₅₀ in ng/ml) required for binding of the indicated human monoclonal antibodies to the S-protein. Libivirumab (Eren et al., 2000; Eren et al., 1998) and anti-HIV antibody 10-1074 (Mouquet et al., 2012) were used as positive and negative controls, respectively. All antibodies were tested. (B) Comparative binding of the mature and unmutated common ancestor (UCA) of antibodies H006, H019, and H020 to S-protein by ELISA. (C) Anti-HBs antibody binding to 5 different serotypes of HBsAg. Similar to panel (A), EC₅₀ values are color-coded: red, ≤50 ng/ml; orange, 50 to 100 ng/ml; yellow, 100 to 200 ng/ml; and white, > 200 ng/ml. The abbreviation b.d. indicates below detection. All antibodies were tested. All experiments were performed at least two times. See also Figure 10.

[0017] Figure 4. HBsAg epitopes. (A) Competition ELISA defines 3 groups of antibodies. Results of competition ELISA shown as percent of binding by biotinylated antibodies and illustrated by colors: black, 0-25%; dark grey, 26-50%; light grey, 51-75%; white, >76%. Weak binders (H002, H012, H013, H014, H018) were excluded. Representative of two experiments. (B) Results of ELISA on alanine scanning mutants of S-protein. Only the amino acids vital for antibody binding are shown. Binding to mutants relative to wild-type S-protein: black, 0-25%; dark grey, 26-50%; light grey, 51-75%; white, >75%. Additional details are provided in Figure 11. (C) Results of ELISA on human escape

mutations of S-protein. Wild-type S-protein and empty vector serve as a positive and negative controls, respectively. Binding to mutants relative to wild-type S-protein: black, 0-25%; dark grey, 26-50%; light grey, 51-75%; white, >75%. Amino acid mutations in bold represent frequently observed mutations in humans (Ma and Wang, 2012). The antibodies tested in (B and C) were selected from Group-I, -II, -III based on their neutralizing activity (Figure 5A-5C). All experiments were performed at least two times. See also Figure 11.

[0018] Figure 5. *In vitro* neutralization by the monoclonal antibodies. (A and B)

In vitro neutralization assays using HepG2-NTCP cells. Percent infection in the presence of the indicated concentrations of bNAbs measured by ELISA of HBsAg in medium (A) and anti-HBcAg immunofluorescence (B). Anti-HIV antibody 10-1074 (Mouquet et al., 2012) and libivirumab (Eren et al., 2000; Eren et al., 1998) were used as negative and positive controls respectively. The corresponding IC₅₀s are shown in the left and middle column of panel (C). All experiments were repeated a minimum of two times. (C) bNAb 50% maximal inhibitory concentration (IC₅₀) calculated based on HBsAg ELISA (left column) and HBcAg immunofluorescence (middle column) for the *in vitro* neutralization assays using HepG2-NTCP cells, or HBeAg ELISA (right column) for *in vitro* neutralization using primary human hepatocytes. The abbreviation b.d. and n.d. indicate below detection and not done respectively. (D) *In vitro* neutralization using primary human hepatocytes. The levels of HBeAg in medium were measured by ELISA. The calculated IC₅₀ values are shown in the right column of panel (C). Experiments were repeated three times. (E) *In vitro* neutralization assay using HepG2-NTCP cells. IgG antibodies were compared to their corresponding Fab fragments. Concentrations of Fab fragments were adjusted to correspond to IgG. Experiment was performed two times. See also Figure 12.

[0019] Figure 6. Crystal structure of H015 bound to its recognition motif. A

single crystal was used to obtain a high resolution (1.78 Å) structure. (A) Synthetic peptides (SEQ ID NOS 1452-1455, respectively, in order of appearance) spanning the antigenic loop region were subjected to ELISA for antibody binding. Among the tested antibodies, only H015 binds peptides-11 and -12. Experiments were performed three times and details are in Figure 13A. (B and C) The peptide binds to CDR1 (R31), CDR2 (W52 and F53) and CDR3 (E99, P101, L103, and L104) of H015 heavy chain (green) and CDR3 (P95) of the light chain (cyan) (B). The interacting residues (C) on the heavy chain (green) are R31 (main chain), W52, F53 (main chain), E99, P101 (main chain), L103 (main chain), L104 (hydrophobic). One contact with the light chain (cyan) is with P95. (D) Electron density map of the bound peptide as seen in the 2Fo-Fc map contoured at 1 RMSD indicating high occupancy (92%).

(E) The recognition motif, KPSDGN (SEQ ID NO: 1), adopts a sharp hairpin conformation due to the salt-bridge between K141 and D144 and is facilitated by kinks at P142 and G145. Glycine 145 (G145, circled) is the residue that escapes the immune system when mutated to an arginine. See also Figure 13.

5 **[0020] Figure 7. Anti-HBs bNAbs are protective and therapeutic *in vivo*.** (A and E) Diagram of the prophylaxis and treatment protocols, respectively. (B) Prophylaxis with isotype control antibody 10-1074 (Mouquet et al., 2012). (C and D) Prophylaxis with H020 and H007 respectively. The dashed line in (B-D) indicates the detection limit. (F) Treatment of viremic huFNRG mice with control antibody 10-1074. (G and H) Treatment of viremic
10 huFNRG mice with H020 alone or H007 alone, respectively. HBV DNA levels in serum were monitored on a weekly basis. Two independent experiments comprising a total of 5 to 8 mice were combined and displayed. (I) Mutations in the S-protein sequence from the indicated mice (red arrows) in (G), (H) and (J). S-protein sequence chromatograms are shown in Figure 14. (J-L) Treatment of viremic huFNRG mice with combination of anti-HBs bNAb H006 +
15 H007 (J), or H017 + H019 (K), or H016 + H017 + H019 (L), respectively. Sequencing showed that none of the mice in (K) and (J) carried viruses with escape mutations in the S-protein. See also Figure 14.

[0021] Figure 8. Characterization of Antibody Immune Response Against HBV, Related to Figure 1. (A) Schematic representation of different stages of HBV infection.
20 Vaccinated or infected naturally recovered individuals were recruited for this study. (B) Sera (1:50 dilution in the final assay volume) from 159 volunteers were screened, see also Figure 1A. (C-E) Comparison of anti-HBs ELISA titers (upper panel) and their serum neutralization capacity (lower panel) between different groups of individuals. Vaccinated or recovered individuals show statistically higher anti-HBs titers (upper panel, C) and more potent
25 neutralizing activity (lower panel, C) than the uninfected unvaccinated individuals. Younger individuals (≤ 45 years old) showed slightly higher antibody immune response against HBsAg (D). No difference was found between genders (E).

[0022] Figure 9. Antibody Cloning and Sequence Analysis of Anti-HBs, Related to Figure 2. (A) Frequency of S-protein-specific memory B cells in peripheral blood
30 mononuclear cells of all twelve donors. Details are similar to Figure 2A. (B) Pie charts show the distribution of anti-HBs antibodies. Figure legends are similar to Figure 2C. VH and VL genes for each slice are shown and the 20 chosen anti-HBs antibodies are labeled. (C) Phylogenetic tree of all cloned anti-HBs antibodies based on IGH Fab region. IGH Fab

regions from 244 memory B cells sorted with HBsAg were aligned followed by tree construction.

[0023] Figure 10. Autoreactivity of 20 anti-HBs antibodies, Related to Figure 3.

(A) Autoreactivity of monoclonal antibodies. Positive control antibody efficiently stained the nucleus of HEp-2 cells. Twenty anti-HBs antibodies, as well as anti-HBs antibody libivirumab and anti-HIV antibody 10-1074, were also tested. (B) Polyreactivity profiles of 20 anti-HBs antibodies. ELISA measures antibody binding to the following antigens: double-stranded DNA (dsDNA), insulin, keyhole limpet hemocyanin (KLH), lipopolysaccharides (LPS), and single-stranded DNA (ssDNA). Red and green lines represent positive control antibody ED38 and negative control antibody mGO53 respectively, while dashed lines show cut-off values for positive reactivity (Gitlin et al., 2016).

[0024] Figure 11. Alanine Scanning and Peptide Screening, Related to Figure 4.

(A) Results of ELISA on alanine scanning mutants of HBsAg. Binding to mutants was normalized to wild-type S-protein: black, 0-25%; dark grey, 26-50%; light grey, 51-75%; white, >76%. Experiments were performed three times. Underlined cysteines, alanines, and amino acids known to be critical for S-protein production were not mutated (Salisie and Bureau, 2009). Figure discloses SEQ ID NO: 1456. (B) Schematic diagram of alanine scanning results. Figure discloses the primary amino acid sequence as SEQ ID NO: 1456 and the sequence containing alanine mutations as SEQ ID NO: 1457.

[0025] Figure 12. *In Vitro* Neutralization Assay of anti-HBs bNAbs Unmutated Common Ancestor Antibodies or Combinations, Related to Figure 5. (A-B) *In vitro*

neutralization assay of anti-HBs bNAbs and their corresponding unmutated common ancestor (UCA) antibodies. The relative infection rates were calculated based on either HBsAg protein level in culture medium (A) or HBcAg staining intracellularly (B). (C) *In vitro* neutralization assay of anti-HBs bNAbs recognizing different epitopes and the same total amount of antibody combination at 1:1 or 1:1:1 ratio.

[0026] Figure 13. Detailed Information of Crystal Structure of H015 and Its Linear Epitope, Related to Figure 6. (A) Synthesized peptides (SEQ ID NOS 1458-1476,

respectively, in order of appearance) for antigenic loop region were subjected to ELISA for antibody binding. Among the tested antibodies, only H015 binds peptide-11 and -12. (B) Data collection and refinement statistics for H015 Fab are summarized. Statistics for the highest-resolution shell are shown in parentheses. Refinement program PHENIX 1.16. (C) The green/red density is the unbiased omit map. Red is negative density equated to noise. (D) Table of contacts within the peptide and between Fab fragment and peptide.

[0027] Figure 14. HBV DNA levels and S-protein Sequences in Antibody-Treated huFNRG Mice, Related to Figure 7.

(A) HBV DNA levels in representative individual huFNRG mice treated by control antibody 10-1074, anti-HBs bNAbs H020, anti-HBs bNAbs H007, combination of anti-HBs bNAbs (H006 + H007), (H017 + H019), and (H016 + H017 + H019). HBV DNA levels in mouse sera were monitored on a weekly basis. The mice without arrows bear no escape mutations at the last time point. (B) Part of the S-protein sequences from the indicated mice (arrows and numbers) are shown below as chromatograms, with mutations marked by arrowheads. (B) discloses the S-protein amino acid and nucleotide sequences as SEQ ID NOS 1477 and 1478, respectively. The sequences represented by the subsequent chromatograms that disclose amino acid residues and nucleotides are SEQ ID NOS 1479, 1480, 1480, 1480-1482, 1479, 1478, 1480, 1480, 1478, 1480, and 1483-1488, respectively, in order of columns. (C-D) HBsAg levels in mouse sera before and after antibody infusion. Mice were treated by anti-HBs combination H017 + H019 (C) (see Figure 7K) and H016 + H017 + H019 (D) (see Figure 7L). Each line represents a mouse with concentrations of serum HBsAg level expressed in NCU/ml (national clinical units per milliliter).

DETAILED DESCRIPTION OF THE DISCLOSURE

[0028] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

[0029] Every numerical range given throughout this specification includes its upper and lower values, as well as every narrower numerical range that falls within it, as if such narrower numerical ranges were all expressly written herein.

[0030] This disclosure includes every nucleotide sequence described herein, and in the tables and figures, and all sequences that are complementary to them, RNA equivalents of DNA sequences, all amino acid sequences described herein, and all polynucleotide sequences encoding the amino acid sequences. Every antibody sequence and functional fragments of them are included. Polynucleotide and amino acid sequences having from 80-99% similarity, inclusive, and including ranges of numbers there between, with the sequences provided here are included in the invention. All of the amino acid sequences described herein can include amino acid substitutions, such as conservative substitutions, that do not adversely affect the function of the protein or polypeptide that comprises the amino acid sequences. It will be recognized that when reference herein is made to an “antibody” it does not necessarily mean

a single antibody molecule. For example, “administering an antibody” includes administering a plurality of the same antibodies. Likewise, a composition comprising an “antibody” can comprise a plurality of the same antibodies.

[0031] For amino acid and polynucleotide sequences of this disclosure, contiguous
5 segments of the sequences are included, and can range from 2 amino acids, up to full-length protein sequences. Polynucleotide sequences encoding such segments are also included.

[0032] The disclosure includes DNA and RNA sequences encoding the antibodies and antigen fragments thereof, and any virus peptides described herein for use in prophylactic and therapeutic approaches as protein or DNA and/or RNA vaccines, which may be
10 formulated and/or delivered according to known approaches, given the benefit of this disclosure. The disclosure includes a cDNA sequences encoding the antibodies, antigen binding fragments thereof, and any viral proteins or peptides described herein. Expression vectors that contain cDNAs are also included, and encode said antibodies, antigen binding fragments thereof, and viral proteins and peptides.

[0033] All sequences from the figures, text, and tables of this application or patent
15 include every amino acid sequence associated with every Donor ID, and all possible combinations of the amino acid sequences given for all complementarity determining regions (CDRs), e.g., all combinations of heavy chain CDR1, CDR2, CDR3 sequences, and all combinations of light chain CDR1, CDR2, and CDR3 sequences, including heavy chain
20 sequences, and light chain sequences that are either lambda or kappa light chain sequences. The disclosure includes all combinations of antibodies described herein. One or more antibodies may also be excluded from any combination of antibodies.

[0034] The disclosure includes antibodies described herein, which are present in an *in vitro* complex with one or more hepatitis B proteins.

[0035] In embodiments, the disclosure provides an isolated or recombinant antibody
25 that binds with specificity to a hepatitis B virus epitope, and wherein the antibody optionally comprises a modification of its amino acid sequence, including but not limited to a modification of its constant region.

[0036] In embodiments, one or more antibodies described herein bind with specificity
30 to an epitope present in the HBsAg protein or the S-protein in the unmutated, or mutated form.

[0037] In embodiments, the antibodies described herein bind to a hepatitis B protein that comprises one or more HepB escape mutations. In embodiments, the antibodies bind to a hepatitis B virus protein that comprises a mutation that is a substitution of a large positively

charged residue for a small neutral residue. In embodiments, the mutation is present in the so-called “a” determinant area, which is known in the art. In embodiments, the epitope is present in the major hydrophilic region of the HBsAg protein. In embodiments, the epitope to which the antibodies bind is present in the S-protein, including but not necessarily limited to the predicted or actual extracellular domain of the S-protein.

[0038] In embodiments, the epitope to which the described antibodies bind is common to HBsAg L-protein, M-protein, or S-protein. In embodiments, the antibodies bind to an epitope present in the L-protein version of HBsAg, which comprises the amino acid sequence that is accessible via Accession number: AAL66340.1 as that amino acid sequence exists in the database as of the filing date of this application or patent. In an embodiment, this amino acid sequence is:

MGGWSSKPRQGMGTNLSVPNPLGFFPDHQLDPAFGANSNNPDWDFNPNKDHWPENQVG
AGAFGPGFTPPHGGLLGWSPQAQGILTTVPVAPPPASTNRQSGRQPTPISPPLRDSHPQAMQ
WNSTTFHQALLDPRVRGLYFPAGGSSSGTVNPVPTTASPISSIFSRTGDPAPNMESTTSGFLGP
LLVLQAGFFLLTRILTIPQSLDSWWTSLNFLGGAPTCPGQNSQSPTSNHSPTSCPPICPGYRWM
CLRRFIIFLIFILLCLIFLLVLLDYQGMLPVCPLLPGTSTTSTGPCKTCTSPAQGTSMFPSCCCTKP
SDGNCTCIPISSWAFARFLWEWASVRFSWLSLLVPFVQWFVGLSPTVWLSVIWMMWYWG
PCLYNILSPFLPLLPIFFCLWVYI (SEQ ID NO: 2).

[0039] In embodiments, the disclosure includes use of only two proteins, or at least two proteins. In an embodiment, the S proteins may be used as bait to sort B cells purified from Chinese hamster ovary (CHO) cells, or any other suitable cell type, including but not limited to human cell cultures. In embodiments, the S protein comprises or consists of the amino acid sequence available under Uniprot ID_P30019, the amino acid sequence of which is incorporated herein as it exists in the database at the filing date of this application or patent.

In an embodiment, the S protein comprises the sequence:

MENTASGFLGPLLVLQAGFFLLTRILTIPQSLDSWWTSLNFLGGAPTCPGQNSQSPTSNHSPTS
CPPICPGYRWMCLRRFIIFLIFILLCLIFLLVLLDYHGMLPVCPLLPGTSTTSTGPCKTCTIPAQG
TSMFPSCCCTKPSDGNCTCIPISSWAFARFLWEWASVRFSWLSLLVPFVQWFVGLSPTVWLS
VIWMMWYWGPSLYNILSPFLPLLPIFFCLWVYI (SEQ ID NO: 3).

[0040] In non-limiting embodiments, the S polynucleotide sequence used for alanine scanning comprises:

ATGGAGAACATCACATCAGGATTCTAGGACCCCTGCTCGTGTTACAGGCGGGGTTTTTCTTG
 TTGACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGACTTCTCTCAATTTTCTA
 GGGGGATCTCCCGTGTGTCTTGGCCAAAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACC
 TCCTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATATTCCTC
 5 TTCATCCTGCTGCTATGCCTCATCTTCTTATTGGTTCTTCTGGATTATCAAGGTATGTTGCCC
 GTTTGTCCTCTAATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACCTGCACGACT
 CCTGCTCAAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAAACCTACGGATGGAAATTGC
 ACCTGTATTCCCATCCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCCTCAGTC
 CGTTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTTCAGTGGTTCGTAGGGCTTTCCCCCACT
 10 GTTTGGCTTTTCAGCTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAGCATCGTGAG
 TCCCTTTATACCGCTGTTACCAATTTTCTTTTGTCTCTGGGTATACATTTAA (SEQ ID NO:
 4).

[0041] The amino acid sequence encoded by the DNA sequence immediately above
 is:

15 MENITSGFLGPLLVLQAGFFLLTRILTIPQSLDSWWTSLNFLGGSPVCLGQNSQSPTSNHSPTSC
 PPICPGYRWMCLRRFIIFLLFILLCLIFLLVLLDYQGMLPVCPLIPGSTTTSTGPCKTCTTPAQGN
 SMFPSCCCTKPTDGNCTCIPISSWAFACYLWEWASVRFWSLLVPFVQWFVGLSPTVWLS
 AIWMMWYWGPSLYSIVSPFIPLLPIFFCLWVYI (SEQ ID NO: 5).

[0042] In embodiments, antibodies of this disclosure bind to an epitope present in any
 20 of the foregoing amino sequences, including linear and confirmation epitopes that may be
 formed by proteins comprising or consisting of said sequences.

[0043] In an embodiment, the isolated or recombinant antibody or antigen binding
 fragment thereof binds with specificity to an epitope comprised by a structurally defined
 peptide loop, as further described herein. In embodiments, the loop is as generally depicted in
 25 Figure 6, which comprises a partial structure of HepB surface protein, and demonstrates the
 existence of a loop that includes the most frequently targeted residue found in human escapes
 G145. Without intending to be bound by any particular theory, it is considered that this
 structure explains why this mutant can escape, and also why additional commonly found
 escape mutants exist. Further, the structure and the antibody peptide complex represents a
 30 new and previously undiscovered target for drug discovery. Thus, in embodiments, the
 disclosure provides for screening drug candidates that can interfere with formation of this
 structure, and thus which may also interfere with the viability of the virus. Those skilled in

the art will recognize from the present disclosure how to design an assay to determine whether or not drug candidates could interfere with the complex, and how antibodies described in herein may be used in such an assay.

[0044] In embodiments, antibodies described herein bind with specificity to an amino acid sequence comprised by any peptide sequence described herein. In embodiments, the peptide comprises the sequence KPSDG (SEQ ID NO: 6), or mutants thereof. In embodiments, antibodies described herein bind with specificity to an epitope in an amino acid sequence that comprises the sequence PSSSSTKPSDGNSTS (SEQ ID NO: 7), or mutants thereof. Additional and non-limiting examples of peptides of this disclosure include those shown on Figure 6, e.g., peptide-11 and peptide-12.

[0045] In embodiments, the disclosure comprises compositions and methods that involve use of more than one distinct antibody or antigen binding fragment thereof. In embodiments, the methods of this disclosure comprise administering a combination of antibodies or antigen binding fragment thereof which bind distinct hepatitis B epitopes. In embodiments, distinct antibodies recognize epitopes present in two dominant non-overlapping antigenic sites on the HBsAg, or epitopes present on the S-protein. In embodiments, the disclosure provides for use of a combination of the Group-I and Group-II antibodies described herein. Thus, the disclosure comprises co-administration or sequential administration of a combination of antibodies. In an embodiment, administration of a combination of distinct antibodies suppresses formation of viruses that are resistant to the effects of any one of the antibodies alone. In embodiments, the disclosure includes administering a combination comprising at least one Group I antibody and at least one Group II antibody, wherein at least one of the antibodies is G145R mutation resistant. In non-limiting embodiments, antibodies that are provided by the present disclosure, and which can be administered to an individual in need thereof, comprise at least one of H006, H007, H0017, H0019, or H020. Further, H005, H008 and H009 are similar to H006, and therefore may be used as alternatives to H006.

[0046] All combinations of H and L chains described herein are included, including all kappa and lambda light chains. In embodiments, a single antibody of this disclosure may comprise an H+L chain from one antibody, and an H+L chain from another antibody. In embodiments, the antibodies comprise modifications that are not coded for in any B cells obtained from an individual, and/or the antibodies are not produced by immune cells in an individual from which a biological sample from the individual is used at least in part to identify and/or generate and/or characterize the antibodies of this disclosure. In embodiments,

antibodies provided by this disclosure can be made recombinantly, and can be expressed with a constant region of choice, which may be different from a constant region that was coded for in any sample from which the amino acid sequences of the antibodies were deduced.

[0047] As discussed above, in embodiments, the disclosure includes a combination of antibodies or antigen binding fragments thereof, or a composition comprising or consisting of said antibodies or antigen binding fragments thereof. In embodiments, a combination of antibodies of this disclosure are effective in preventing viral escape by mutation. In this regard, the disclosure includes data demonstrating that not all antibody combinations are effective in preventing escape by mutation, such as the combination of H006 and H007, which are ineffective. Thus, in embodiments, a combinations of antibodies or antigen binding fragments collectively target more than one commonly occurring escape mutation, examples of which escape mutations are known in the art and are described herein. Accordingly, combinations of antibodies and antigen binding fragments thereof of this disclosure may target non-overlapping groups of common escape mutations. In embodiments, the disclosure thus includes a proviso that excludes any combination of antibodies that collectively only target separate epitopes but have overlapping sensitivity to commonly occurring escape mutations.

[0048] In embodiments, at least one antibody or antigen binding fragment thereof included in this disclosure, and in the combinations and methods of this disclosure, has greater virus neutralizing activity than a control neutralizing activity value, such as the neutralizing capability of libivirumab. In embodiments, at least one antibody or antigen binding fragment of this disclosure exhibits a viral neutralizing activity with an IC_{50} values that is less than 128 ng/ml, or less than 35 ng/ml, or less than 5 ng/ml, and including all integers and ranges of integers between 128 and 5 ng/ml. Such neutralizing activity can be determined using known approaches, such as by ELISA or immunofluorescence assays, and as further described in Example 5 of this disclosure. In embodiments, an antibody or antigen binding fragment thereof that is encompassed by this disclosure includes but is not limited to antibodies or antigen binding fragments selected from the H016, H017 and H019 antibodies, as defined by their CDRs. In an embodiment, the disclosure includes combinations of these antibodies, and can include antigen binding fragments thereof. In embodiments, the combination of antibodies comprises the H017 and H019 antibodies, and/or antigen binding fragments thereof. In an embodiment, the combination optionally further comprises the H016 antibody or an antigen binding fragment thereof. In embodiments, a combination of the disclosure comprises a combination that consists of only the H017 and H019 antibodies or

antigen binding fragments thereof. In embodiments, a combination of the disclosure comprises a combination that consists of only the H016, H017, and H019 antibodies or antigen binding fragments thereof. Methods of administration of the described antibody combinations, and all other antibodies and antigen binding fragments thereof described herein, sequentially and concurrently are included within the scope of this disclosure. Thus, the disclosure includes administering to an individual in need concurrently or sequentially a combination of antibodies or antigen binding fragments thereof, which in certain embodiments comprise or consist of H017 and H019, or H016, H017, and H019 and antigen binding fragments thereof. Additional antibodies and antibody combinations, including antigen binding fragments thereof, include but are not limited to antibodies and antigen binding fragments thereof that comprise the heavy and light chain CDRs of H004, H005, and H009, and H020.

[0049] With respect to the H016, H017, and H019 antibodies, as can be seen from Table S2, the H016 antibody comprises a heavy chain CDR1 with the amino acid sequence GFTFPSHT (SEQ ID NO: 8), a heavy chain CDR2 with the amino acid sequence ISTTSEAI (SEQ ID NO: 9), and a heavy chain CDR3 with the amino acid sequence ARVGLALTISGYWYFDL (SEQ ID NO: 10). The H016 antibody comprises a kappa light chain CDR1 with the amino acid sequence QSISSN (SEQ ID NO: 11), a kappa light chain with the CDR2 amino acid sequence RAS, and a kappa light chain with the CDR3 amino acid sequence QQYDHWPLT (SEQ ID NO: 12).

[0050] As can be seen from Table S2, the H017 antibody comprises a heavy chain CDR1 with the amino acid sequence GFTFSNYW (SEQ ID NO: 13), a heavy chain CDR2 with the amino acid sequence ISTDGSST (SEQ ID NO: 14), and a heavy chain CDR3 with the amino acid sequence ARGSTYYFGSGSVDY (SEQ ID NO: 15). The H017 antibody comprises a lambda light chain with the CDR1 sequence SSDIGVYNY (SEQ ID NO: 16), a lambda light chain with the CDR2 sequence DVT, and a lambda light chain with the CDR3 sequence SSYRGSSTPYV (SEQ ID NO: 17).

[0051] As can be seen from Table S2, the H019 antibody comprises a heavy chain CDR1 with the amino acid sequence GGSITTGDYY (SEQ ID NO: 18), a heavy chain CDR2 with the amino acid sequence IYYSGST (SEQ ID NO: 19), and a heavy chain CDR3 with the amino acid sequence AIYMDEAWAFE (SEQ ID NO: 20). The H019 antibody comprises a lambda light chain CDR1 with the amino acid sequence QSIGNY (SEQ ID NO: 21), a lambda light chain with the CDR2 amino acid sequence AVS, and a lambda light chain with the CDR3 amino acid sequence QQSYTISLFT (SEQ ID NO: 22).

[0052] In certain embodiments, the antibodies contain one or more modifications, such as non-naturally occurring mutations. As non-limiting examples, in certain approaches the Fc region of the antibodies can be changed, and may be of any isotype, including but not limited to any IgG type, or an IgA type, etc. Antibodies of this disclosure can be modified to improve certain biological properties of the antibody, e.g., to improve stability, to modify effector functions, to improve or prevent interaction with cell-mediated immunity and transfer across tissues (placenta, blood-brain barrier, blood-testes barrier), and for improved recycling, half-life and other effects, such as manufacturability and delivery.

[0053] In embodiments, an antibody of this disclosure can be modified by using techniques known in the art, such as those described in Buchanan, et al., Engineering a therapeutic IgG molecule to address cysteinylolation, aggregation and enhance thermal stability and expression mAbs 5:2, 255–262; March/April 2013, and in Zalevsky J. et al., (2010) Nature Biotechnology, Vol. 28, No.2, p157-159, and Ko, S-Y, et al., (2014) Nature, Vol. 514, p642-647, and Horton, H. et al., Cancer Res 2008; 68: (19), October 1, 2008, from which the descriptions are incorporated herein by reference. In certain embodiments an antibody modification increases in vivo half-life of the antibody (e.g. LS mutations), or alters the ability of the antibody to bind to Fc receptors (e.g. GRLR mutations), or alters the ability to cross the placenta or to cross the blood-brain barrier or to cross the blood-testes barrier. Thus, in certain embodiments an antibody modification comprises a change of G to R, L to R, M to L, or N to S, or any combination thereof.

[0054] In embodiments bi-specific antibodies are provided by modifying and/or combining segments of antibodies as described herein, such as by combining heavy and light chain pairs from distinct antibodies into a single antibody. Suitable methods of making bispecific antibodies are known in the art, such as in Kontermann, E. et al., Bispecific antibodies, Drug Discovery Today, Volume 20, Issue 7, July 2015, Pages 838-847, the description of which is incorporated herein by reference.

[0055] In embodiments, any antibody described herein comprises a modified heavy chain, a modified light chain, a modified constant region, or a combination thereof, thus rendering them distinct from antibodies produced by humans. In embodiments, the modification is made in a hypervariable region, and/or in a framework region (FR).

[0056] In embodiments, mutations to an antibody described herein, including but not limited to the antibodies described, comprise modifications relative to the antibodies originally produced in humans. Such modifications include but are not necessarily limited to the heavy chain to increase the antibody half-life.

[0057] In embodiments, antibodies of this disclosure have variable regions that are described herein, and may comprise or consist of any of these sequences, and may include sequences that have from 80-99% similarity, inclusive, and including ranges of numbers there between, with the sequences expressly disclosed herein, provided antibodies that have
5 differing sequences retain the same or similar binding affinity as an antibody with an unmodified sequence. In embodiments, the sequences are at least 95%, 96%, 97%, 98% or 99% similar to an expressly disclosed sequence herein.

[0058] Antibodies comprising the sequences described in Table S2 have been isolated and characterized for at least binding affinity, and as otherwise described herein, such as for
10 virus neutralizing activity. Thus, in embodiments the disclosure provides neutralizing antibodies. The term “neutralizing antibody” refers to an antibody or a plurality of antibodies that inhibits, reduces or completely prevents viral infection. Whether any particular antibody is a neutralizing antibody can be determined by in vitro assays described in the examples below, and as is otherwise known in the art. The term “broadly neutralizing” antibody refers
15 to an antibody that can neutralize more than one strain or serotype of a virus.

[0059] Antibodies of this disclosure can be provided as intact immunoglobulins, or as antigen binding fragments of immunoglobulins, including but not necessarily limited to antigen-binding (Fab) fragments, Fab' fragments, (Fab')₂ fragments, Fd (N-terminal part of the heavy chain) fragments, Fv fragments (the two variable domains), dAb fragments, single
20 domain fragments or single monomeric variable antibody domains, isolated CDR regions, single-chain variable fragment (scFv), and other antibody fragments that retain virus-binding capability and preferably virus neutralizing activity as further described below. In embodiments, the variable regions, including but not necessarily limited to the described CDRs, may be used as a component of a Bi-specific T-cell engager (BiTE), bispecific killer
25 cell engager (BiKE), or a chimeric antigen receptor (CAR), such as for producing chimeric antigen receptor T cells (e.g. CAR T cells). In embodiments, the disclosure includes tri-valent antibodies, which can bind with specificity to three different epitopes.

[0060] Antibodies and antigens of this disclosure can be provided in pharmaceutical formulations. It is considered that administering a DNA or RNA polynucleotide encoding any
30 protein described herein (including peptides and polypeptides), such as antibodies and antigens described herein, is also a method of delivering such proteins to an individual, provided the protein is expressed in the individual. Methods of delivering DNA and RNAs encoding proteins are known in the art and can be adapted to deliver the protein, particularly the described antigens, given the benefit of the present disclosure. Similarly, the antibodies of

this disclosure can be administered as DNA molecules encoding for such antibodies using any suitable expression vector(s), or as RNA molecules encoding the antibodies.

[0061] Pharmaceutical formulations containing antibodies or viral antigens or polynucleotides encoding them can be prepared by mixing them with pharmaceutically acceptable carriers. Pharmaceutically acceptable carriers include solvents, dispersion media, isotonic agents and the like. The carrier can be liquid, semi-solid, e.g. pastes, or solid carriers. Examples of carriers include water, saline solutions or other buffers (such as phosphate, citrate buffers), oil, alcohol, proteins (such as serum albumin, gelatin), carbohydrates (such as monosaccharides, disaccharides, and other carbohydrates including glucose, sucrose, trehalose, mannose, mannitol, sorbitol or dextrans), gel, lipids, liposomes, resins, porous matrices, binders, fillers, coatings, stabilizers, preservatives, liposomes, antioxidants, chelating agents such as EDTA; salt forming counter-ions such as sodium; non-ionic surfactants such as TWEEN, PLURONICS or polyethylene glycol (PEG), or combinations thereof. In embodiments, a pharmaceutical/vaccine formulation exhibits an improved activity relative to a control, such as antibodies that are delivered without adding additional agents, or a particular added agent improves the activity of the antibodies.

[0062] The formulation can contain more than one antibody type or antigen, and thus mixtures of antibodies, and mixtures of antigens, and combinations thereof as described herein can be included. These components can be combined with a carrier in any suitable manner, e.g., by admixture, solution, suspension, emulsification, encapsulation, absorption and the like, and can be made in formulations such as tablets, capsules, powder (including lyophilized powder), syrup, suspensions that are suitable for injections, ingestions, infusion, or the like. Sustained-release preparations can also be prepared.

[0063] The antibodies and vaccine components of this disclosure are employed for the treatment and/or prevention of hepatitis B virus infection in a subject, as well as for inhibition and/or prevention of their transmission from one individual to another.

[0064] The term "treatment" of viral infection refers to effective inhibition of the viral infection so as to delay the onset, slow down the progression, reduce viral load, and/or ameliorate the symptoms caused by the infection.

[0065] The term "prevention" of viral infection means the onset of the infection is delayed, and/or the incidence or likelihood of contracting the infection is reduced or eliminated.

[0066] In embodiments, to treat and/or prevent viral infection, a therapeutic amount of an antibody or antigen vaccine disclosed herein is administered to a subject in need

thereof. The term "therapeutically effective amount" means the dose required to effect an inhibition of infection so as to treat and/or prevent the infection.

[0067] The dosage of an antibody or antigen vaccine depends on the disease state and other clinical factors, such as weight and condition of the subject, the subject's response to the therapy, the type of formulations and the route of administration. The precise dosage to be therapeutically effective and non-detrimental can be determined by those skilled in the art. As a general rule, a suitable dose of an antibody for the administration to adult humans parenterally is in the range of about 0.1 to 20 mg/kg of patient body weight per day, once a week, or even once a month, with the typical initial range used being in the range of about 2 to 10 mg/kg. Since the antibodies will eventually be cleared from the bloodstream, re-administration may be required. Alternatively, implantation or injection of the antibodies provided in a controlled release matrix can be employed.

[0068] The antibodies can be administered to the subject by standard routes, including oral, transdermal, and parenteral (e.g., intravenous, intraperitoneal, intradermal, subcutaneous or intramuscular). In addition, the antibodies and/or the antigen vaccines can be introduced into the body, by injection or by surgical implantation or attachment such that a significant amount of an antibody or the vaccine is able to enter blood stream in a controlled release fashion. In certain embodiments antibodies described herein are incorporated into one or more prophylactic compositions or devices to, for instance, neutralize a virus before it enters cells of the recipient's body. For example, in certain embodiments a composition and/or device comprises a polymeric matrix that may be formed as a gel, and comprises at least one of hydrophilic polymers, hydrophobic polymers, poly(acrylic acids) (PAA), poly(lactic acids) (PLA), carageenans, polystyrene sulfonate, polyamides, polyethylene oxides, cellulose, poly(vinylpyrrolidone) (PVP), poly(vinyl alcohol) (PVA), chitosan, poly(ethylacrylate), methylmethacrylate, chlorotrimethyl ammonium methylmethacrylate, hydroxyapatite, pectin, porcine gastric mucin, poly(sebacic acid) (PSA), hydroxypropyl methylcellulose (HPMC), cellulose acetate phthalate (CAP), magnesium stearate (MS), polyethylene glycol, gum-based polymers and variants thereof, poly (D,L)-lactide (PDLL), polyvinyl acetate and povidone, carboxypolymethylene, and derivatives thereof. In certain aspects the disclosure comprises including antibodies in micro- or nano-particles formed from any suitable biocompatible material, including but not necessarily limited to poly(lactic-co-glycolic acid) (PLGA). Liposomal and microsomal compositions are also included. In certain aspects a gel of this disclosure comprises a carbomer, methylparaben, propylparaben, propylene glycol, sodium carboxymethylcellulose, sorbic acid, dimethicone, a sorbitol solution, or a combination

thereof. In embodiments a gel of this disclosure comprises one or a combination of benzoic acid, BHA, mineral oil, peglicol 5 oleate, pegoxol 7 stearate, and purified water, and can include any combination of these compositions.

[0069] Antibodies of this disclosure can be produced by utilizing techniques available to those skilled in the art. For example, one or distinct DNA molecules encoding one or both of the H and L chains of the antibodies can be constructed based on the coding sequence using standard molecular cloning techniques. The resulting DNAs can be placed into a variety of suitable expression vectors known in the art, which are then transfected into host cells, which are preferably human cells cultured *in vitro*, but may include E. coli or yeast cells, simian COS cells, Chinese Hamster Ovary (CHO) cells, and human embryonic kidney 293 cells, etc. Antibodies can be produced from a single, or separate expression vectors, including but not limited to separate vectors for heavy and light chains, and may include separate vectors for kappa and lambda light chains as appropriate.

[0070] In embodiments, the antibodies may be isolated from cells. In embodiments, the antibodies are recombinant antibodies. "Recombinant" antibodies mean the antibodies are produced by expression within cells from one or more expression vectors.

[0071] In certain approaches the disclosure includes neutralizing antibodies as discussed above, and methods of stimulating the production of such antibodies.

[0072] In certain approaches the disclosure includes vaccinating an individual using a composition described herein, and determining the presence, absence, and/or an amount of neutralizing antibodies produced in response to the vaccination. Thus, methods of determining and monitoring efficacy of a vaccination at least in terms of neutralizing antibody production are included. In an embodiment, subsequent to determining an absence of neutralizing antibodies, and/or an amount of neutralizing antibodies below a suitable reference value, the invention includes administering a composition disclosed herein to the individual. Subsequent administrations and measurements can be made to track the treatment efficacy and make further adjustments to treatment accordingly.

[0073] Antibodies and proteins of this disclosure can be detectably labeled and/or attached to a substrate. Any substrate and detectable label conventionally used in immunological assays and/or devices is included. In embodiments the substrate comprises biotin, or a similar agent that binds specifically with another binding partner to facilitate immobilization and/or detection and/or quantification of antibodies and/or viral proteins.

[0074] In embodiments any type of enzyme-linked immunosorbent (ELISA) assay can be used, and can be performed using polypeptides and/or antibodies of this disclosure for

diagnostic purposes, and can include direct, indirect, and competitive ELISA assays, and adaptations thereof that will be apparent to those skilled in the art given the benefit of this disclosure.

[0075] Any diagnostic result described herein can be compared to any suitable control. Further, any diagnostic result can be fixed in a tangible medium of expression and communicated to a health care provider, or any other recipient. In one aspect the disclosure comprises diagnosing an individual as infected with hepatitis B virus and administering a composition of this invention to the individual.

[0076] In certain embodiments the disclosure includes one or more recombinant expression vectors encoding at least H and L chains of an antibody or antigen binding fragment of this disclosure, cells and cell cultures comprising the expression vectors, methods comprising culturing such cells and separating antibodies from the cell culture, the cell culture media that comprises the antibodies, antibodies that are separated from the cell culture, and kits comprising the expression vectors encoding an antibody and/or a polypeptide of this disclosure. Products containing the antibodies and/or the polypeptides are provided, wherein the antibodies and/or the polypeptides are provided as a pharmaceutical formulation contained in one or more sealed containers, which may be sterile and arranged in any manner by which such agents would be suitable for administration to a human or non-human subject. The products / kits may further comprise one or more articles for use in administering the compositions.

[0077] The following Examples are intended to illustrate but not limit the invention.

Example 1

[0078] Serologic Responses Against HBV

[0079] To select individuals with outstanding antibody responses to HBsAg, we performed ELISA assays on serum obtained from 159 volunteers. These included 15 uninfected and unvaccinated controls (HBsAg⁻, anti-HBs⁻, anti-HBc⁻), 20 infected and spontaneously recovered (HBsAg⁻, anti-HBs^{+/-}, anti-HBc⁺), and 124 vaccinated (HBsAg⁻, anti-HBs^{+/-}, anti-HBc⁻) volunteers. These individuals displayed a broad spectrum of anti-HBs titers (x-axis in Figure 1A and Figure 8B; Table S1). To determine their neutralizing activity, we tested their ability to block HBV infection in sodium taurocholate co-transporting polypeptide (NTCP)-overexpressing HepG2 cells (Michailidis et al., 2017; Yan et al., 2012) (y-axis in Figure 1A and Figure 8B and 8C; Table S1). Sera or antibodies purified from individuals with high levels of neutralizing activity were then compared across a wide range

of dilutions (Figure 1B and 1C). Although anti-HBs ELISA titers positively correlated with neutralizing activity ($r_s=0.492$, $p<0.001$, Spearman's rank correlation), there were notable exceptions as exemplified by volunteers #99 and #49, whose sera failed to neutralize HBV despite high anti-HBs ELISA titers (Figure 1A). Thus, ELISA titers against HBsAg are not entirely predictive of neutralizing activity *in vitro*.

[0080] The HBV surface protein, HBsAg can be subdivided into PreS1-, PreS2- and S-regions (Figure 1D). To determine which of these regions is the dominant target of the neutralizing response in the selected top neutralizers, we used S-protein to block neutralizing activity *in vitro*. The neutralizing activity in volunteers that received the HBV vaccine, which is composed of S-protein, was completely blocked by S-protein (black lines in Figure 1E). The same was true for the spontaneously recovered individuals in our cohort despite a reported ability of this population to produce anti-PreS1 or anti-PreS2 antibodies (Coursaget et al., 1988; Li et al., 2017; Sankhyani et al., 2016) (red lines in Figure 1E). These results suggest that the neutralizing antibody response in the selected individuals is directed primarily against the S-protein irrespective of immunization or infection.

Example 2

[0081] Human Monoclonal Antibodies to HBV

[0082] To characterize the antibodies responsible for neutralizing activity in the selected individuals, we purified S-protein binding class-switched memory B cells (Escolano et al., 2019; Scheid et al., 2009a). Unexposed naïve controls and vaccinated individuals with low anti-HBs ELISA titers showed background levels of S-protein specific memory B cells (Figure 2A and 9A). In contrast, individuals with high neutralizing activity displayed a distinct population of S-antigen binding B cells constituting 0.03-0.07% of the IgG⁺ memory compartment (CD19-MicroBeads⁺ CD20-PECy7⁺ IgG-Bv421⁺ S-protein-PE⁺ S-protein-APC⁺ ovalbumin-Alexa Fluor 488⁻) (Figure 2A and 9A). Consistent with the findings in elite HIV-1 neutralizers (Rouers et al., 2017), the fraction of S-protein specific cells was directly correlated to the neutralization titer of the individual ($r_s=0.699$, $p=0.0145$, Spearman's rank correlation) (Figure 2B).

[0083] Immunoglobulin heavy (*IGH*) and light (*IGL* or *IGK*) chain genes were amplified from single memory B cells by PCR (Robbiani et al., 2017; Scheid et al., 2009b; von Boehmer et al., 2016). Overall, we obtained 244 paired heavy and light chain variable regions from S-protein-binding memory B cells from eight volunteers with high anti-HBs ELISA titers (Figure 9B and 9C; Table S2). Expanded clones composed of cells producing

antibodies encoded by the same *Ig* variable gene segments with closely related CDR3s were found in each of the top neutralizers #146, #60 and #13 (Figure 2C). Moreover, IGHV3-30/IGLV3-21 was present in #146 and #60; IGHV3-33/IGLV3-21 in #146 and #13; and IGHV3-23/IGLV3-21 in #146, #60 and #13. The variable diversity and joining (V(D)J) region of these antibodies was approximately 80% identical at the amino acid level (Figure 2D). Antibodies with related *Ig* heavy and light chains were also identified between volunteer #55 (HBV infected but recovered) and vaccinated individuals (Figure 2C and 9B). We conclude that top HBV neutralizers produce clones of antigen-binding B cells that express related *Ig* heavy and light chains.

Example 3

[0084] Breadth of Reactivity

[0085] Twenty representative antibodies from 5 individuals, designated as H001 to H020, were selected for expression and further testing (Figure 9B). All 20 antibodies showed reactivity to the S-protein antigen used for B cell selection (HBsAg *adr* CHO) by ELISA with 50% effective concentration (EC₅₀) values ranging from 18-350 ng/ml (Figure 3A). These antibodies carried somatic mutations that enhanced antigen binding as determined by reversion to the inferred unmutated common ancestor (UCA) (Figure 3B). Thus, affinity maturation was essential for their high binding activity.

[0086] Four major serotypes of HBV exist as defined by a constant “a” determinant and two variable and mutually exclusive determinants “d/y” and “w/r” (Bancroft et al., 1972; Le Bouvier, 1971) with a highly statistically significant association between serotypes and genotypes (Kramvis et al., 2008; Norder et al., 2004). To determine whether our antibodies cross-react to different HBsAg serotypes, we performed ELISAs with 5 additional HBsAg antigens: yeast-expressed serotype “*adr*”, “*adw*”, and “*ayw*”, as well as “*ad*” and “*ay*” antigen purified from human blood (Figure 3C). Many of the antibodies tested displayed broad cross-reactivity and EC₅₀ values lower than libivirumab, a human anti-HBs monoclonal antibody that was isolated from HBV-immunized humanized mice and then tested clinically (Eren et al., 2000; Eren et al., 1998; Galun et al., 2002). These antibodies were not polyreactive or autoreactive when tested in polyreactivity ELISA and Hep-2 immunofluorescence assays respectively (Figure 10A and 10B). We conclude that the antibodies tested are broadly cross-reactive with different HBV serotypes.

Example 4

[0087] Antigenic Epitopes on S-protein

[0088] To determine whether the selected antibodies bind to overlapping or non-overlapping epitopes, we performed competition ELISA assays, in which the S-protein was pre-incubated with a selected antibody followed by a second biotinylated antibody.

Antibodies that showed weak levels of binding in ELISA (H002, H012, H013, H014, H018) were excluded. As expected, all of the antibodies tested blocked the binding of the autologous biotinylated monoclonal (yellow boxes in Figure 4A), while control human anti-HIV antibody 10-1074 failed to block any of the anti-HBs antibodies. The competition ELISA identified three mutually exclusive groups of monoclonal antibodies, suggesting that there are at least three dominant non-overlapping antigenic sites on HBsAg (red box for Group-I, blue box for Group-II, and H017 in Group-III, Figure 4A). Each of the individuals that had 2 or more antibodies tested in the competition ELISA expressed monoclonal antibodies that targeted 2 of the 3 non-overlapping epitopes (Figure 4A and 9B).

[0089] To further define these epitopes, we produced a series of alanine mutants spanning most of the predicted extracellular domain of the S-protein with the exception of cysteines, alanines, and amino acid residues critical for S-protein production (Salisse and Sureau, 2009) (Figure 1D). ELISA assays with the representative antibodies from each antibody group and the mutant proteins revealed a series of binding patterns partially corresponding to the three groups defined in the competition assays (Figure 4B and 11). For example, mutations I110A and T148A interfered with binding by Group-I antibodies exemplified by H004, H006, H019, and H020, but had little measurable effect on Group-II antibodies exemplified by H007, H015, and H016 or Group-III antibody H017 (Figure 4B and 11).

[0090] However alanine scanning suggested that some residues such as D144 and G145 are critical for binding of monoclonals in both Group-I and Group-II despite their inability to compete with each other for binding to the native antigen (Figure 4B and 11). Without intending to be constrained by any particular theory, it is considered that D144A and G145A mutations alter the overall structure of HBsAg thereby interfering with binding of antibodies that normally target independent sites on the protein.

[0091] In addition to alanine scanning, we also produced 44 common naturally occurring escape variants found in chronically infected individuals (Hsu et al., 2015; Ijaz et al., 2012; Ma and Wang, 2012; Salpini et al., 2015). Whereas alanine scanning showed that some of the antibodies in Group-I and -II were resistant to G145A, the corresponding naturally occurring mutations at the same position, G145E and G145R, revealed decreased binding by most antibodies (Figure 4C). Among the antibodies tested, H017 and H019, in

Groups-I and -III respectively, showed the greatest resistance to G145 mutations and the greatest breadth and complementarity (Figure 4C). We conclude that human anti-HBs monoclonals obtained from the selected individuals recognize distinct epitopes on HBsAg, most of which appear to be non-linear conformational epitopes spanning different regions of the protein.

Example 5

[0092] *In Vitro* Neutralizing Activity

[0093] To determine whether the new monoclonals neutralize HBV *in vitro*, we performed neutralization assays using HepG2-NTCP cells (Figure 5A and 5B). The 50% inhibitory concentration (IC₅₀) values were calculated based on HBsAg/HBeAg ELISA or immunofluorescence staining for HBcAg expression (Michailidis et al., 2017) (Figure 5C). Neutralizing activity was further verified by *in vitro* neutralization assays using primary human hepatocytes (Michailidis et al., 2020) (Figure 5C and 5D). Fourteen of the 20 antibodies tested showed neutralizing activity with IC₅₀ values as low as 5 ng/ml (Figure 5C). By comparison, libivirumab had an IC₅₀ of 35 and 128 ng/ml in the neutralization assays based on ELISA and immunofluorescence assays respectively (Figure 5C). Somatic mutations were essential for potent neutralizing activity as illustrated by the reduced activity of the inferred UCAs (Figure 12A and 12B). In addition, optimal activity required bivalent binding since the IC₅₀ values for Fab fragments were 2 orders of magnitude higher than intact antibodies (Figure 5E). Finally, there was no overt synergy when Group-I, -II, and -III antibodies were combined (Figure 12C). We conclude that half of the new monoclonals were significantly more potent than libivirumab including Group-I H004, H005, H006, H008, H009, H019, and H020 and Group-II H007, H015, and H016 (Figure 5C).

Example 6

[0094] Structure of the H015 Antibody/Peptide Complex

[0095] H015 differed from other antibodies in that its binding was inhibited by 5 consecutive alanine mutations spanning positions K141-G145 indicating the existence of a linear epitope. This idea was verified by ELISA against a series of overlapping peptides comprising the predicted extracellular domain of S-protein (Figure 6A and 13A). The data showed that H015 binds to KPSDGN (SEQ ID NO: 23), which is near the center of the putative extracellular domain and contains some of the most frequently mutated amino acids during natural infection.

[0096] To examine the molecular basis for H015 binding, its Fab fragment was co-crystallized with the target peptide epitope PSSSSTKPSDGNSTS (SEQ ID NO: 24), where all cysteine residues that flank the recognition sequence were substituted with serine to avoid non-physiological cross-linking. The 1.78 Å structure (Figure 6B and 13B) revealed that the peptide is primarily bound to the immunoglobulin heavy chain (Figure 6B and 6C), interacting with residues from CDR1 (R31), CDR2 (W52, F53) and CDR3 (E99, P101, L103, L104) of IgH with only one contact with CDR3 (P95) of IgL. The peptide adopts a three-residue beta hairpin (class 3) of the 3:5 type involving residues K141 through G145 as only one hydrogen bond is seen, between K141 and G145 (Milner-White and Poet, 1986), and they are not part of a beta sheet. The peptide is further stabilized by a salt-bridge formed between K141 and D144 (Figure 6D and 13C). Interestingly, the distance between the Cαs of the two residues (C139 and C147) flanking the recognition residues is 6.4 Å and are poised to form a disulfide bond between C139 and C147 found in the native HBsAg structure (Ito et al., 2010). The H015 Fab appears to stabilize the conformation of the peptide via the Fab-peptide contacts (Figure 13D) including a large binding surface (866 Å²; antibody-antigen buried surface of 600-900 Å² (Braden and Poljak, 1995)) comprised primarily of a single salt-bridge (lysine to aspartate; 0.9± 0.3 Kcal/mol) (White et al., 2013) and five hydrogen bonds (1-2 Kcal/mol/bond) (Sheu et al., 2003). Moreover, the peptide further restricts loop through intra-peptide contacts (Figure 13D) even in the absence of the disulfides.

[0097] The residues that form the hairpin are important for anti-HBs antibody recognition as determined by alanine scanning (Figure 4B and 11). In addition, each of these residues has been identified as important for immune recognition during natural infection (Ma and Wang, 2012). G145R, the most common naturally occurring S-protein escape mutation substitutes a large positively charged residue for a small neutral residue (circled residue in Figure 6E) potentially altering the antigenic binding surface. G145 adopts a positive phi angle of 77.9 and by doing so introduces a kink in the beta-strand, a structure that would be disrupted with the substitution to arginine.

[0098] HBsAg can be glycosylated at N146 and this site is also strictly conserved. However, some studies have suggested that this glycosylation site is never fully occupied, resulting in a nearly 1:1 ratio of glycosylated and non-glycosylated isoforms on the surface of viral envelope (Julithe et al., 2014). The glycosylation may be either NAG-NAG-MAN or NAG-(FUC)-NAG-MAN (Hyakumura et al., 2015). We have modeled both fucosylated and non-fucosylated options by grafting a 7mer and 11mer glycan conjugated at N146 of peptide

in the presence of the Fab. We found that both glycosylation forms are tolerated at that location with only minimal torsional adaptations without clashes with the Fab, though the fucosylated (branched) glycan required some additional torsional angle changes to the Fab, as well.

5

Example 7

[0099] Protection and Therapy in Humanized Mice

[0100] HBV infection is limited to humans, chimpanzees, tree shrews, and human liver chimeric mice (Sun and Li, 2017). To determine whether our anti-HBs bNAbs prevent infection *in vivo* we produced human liver chimeric *Fah*^{-/-}NOD*Rag1*^{-/-}*IL2rg*^{null} (huFNRG) mice (de Jong et al., 2014) and injected them with control or H020 (Group-I) or H007 (Group-II) antibodies before infection with HBV (Figure 7A-7D). These two antibodies were chosen because they bind to non-overlapping sites, and have broad and potent neutralizing activity. Whereas all six control animals in two independent experiments were infected, pre-exposure prophylaxis with either H007 or H020 was fully protective (Figure 7B-7D). We conclude that single anti-HBs bNAbs targeting different epitopes on the major virus surface antigen can prevent infection *in vivo*.

[0101] To determine whether bNAbs can also control established infections, we infused control antibody or bNAb H020 (Group-I) or H007 (Group-II) into huFNRG mice with HBV viral loads of 10⁶-10⁸ copies/ml of serum (Figure 7E-7H and Figure 14A). *Fah*^{-/-}NOD*Rag1*^{-/-}*IL2rg*^{null} mice are highly immunodeficient and unable to mount adaptive immune responses due to absence of T and B lymphocytes. In addition, the *IL2rg*^{null} mutation prevents cytokine signaling through multiple receptors, leading to a deficiency in innate immune function including antibody-dependent cellular cytotoxicity. Thus, elimination of viremia of 10⁶-10⁸ DNA copies/ml in huFNRG mice by antibody therapy alone would not be expected.

[0102] Animals that received the control antibodies further increased viremia to as high as ~10¹¹ DNA copies/ml (Figure 7F). In contrast, the 5 mice that received H020 maintained stable levels of viremia for around 30 days (Figure 7G), after which time 2 mice showed increased viremia (arrow-1/3 in Figure 7G). A similar result was observed in the 5 mice that received H007 (Figure 7H), where only one showed a slight increase viremia at around day 50 (arrow-5 in Figure 7H).

[0103] To determine whether the animals that showed increased HBV DNA levels during antibody monotherapy developed escape mutations, we sequenced the viral DNA recovered from mouse blood. All three mice that escaped H020 (Group-I) or H007 (Group-II)

monotherapy developed viruses that carried a G145R mutation in the S-protein (arrow-1/3 in Figure 7G, arrow-5 in Figure 7H, Figure 7I, and Figure 14). This mutation represents a major immune escape mutation in humans (Zanetti et al., 1988). Furthermore, mutations at the same position in the S-protein were also identified in mice that maintained low level viremia (arrow-2/4 in Figure 7G, arrow-6/7 in Figure 7H, Figure 7I, and Figure 14), but not in control animals (Figure 14). These results show that anti-HBs bNAb monotherapy leads to the emergence of escape mutations that are consistent with bNAb binding properties *in vitro* (Figure 4C).

[0104] To determine whether a combination of bNAbs targeting 2 separate epitopes would interfere with the emergence of resistant strains, we co-administered H006 + H007 (Group-I and -II, respectively) to 8 HBV-infected huFNRG mice (Figure 7J). H006 (Group-I) was chosen for this purpose because of its resistance to D144A and G145A mutation (Figure 4B). Similar to H007 monotherapy, there was only a slight increase in viremia in animals treated with the H006 + H007 anti-HBs bNAb combination during the 60-day observation period (Figure 7J and 14A). However, sequence analysis revealed that 3 of the mice developed resistance mutations including K122R/G145R, C137Y, and C137Y/D144V (arrow-8/9/10 in Figure 7J, Figure 7I, and Figure 14). These mutations confer loss of binding to both H006 (Group-I) and H007 (Group-II) (Figure 4C). Thus, the combination of 2 anti-HBs bNAbs targeting separate epitopes but susceptible to the same clinical escape variants is not sufficient to inhibit emergence of escape mutations.

[0105] To attempt to block the emergence of escape mutations, we combined H017 + H019 (Group-III and -I, respectively) bNAbs because they displayed complementary sensitivity to commonly occurring natural mutations (Figure 4C). None of 7 mice treated with the combination of showed increased viremia or escape mutations as assessed by sequence analysis (Figure 7K and 14A). Similar effects were also observed in the 9 animals treated with the H016, H017 and H019 (Group-II, -III, -I, respectively) triple antibody combination (Figure 7L and 14A). Moreover, both these combinations dramatically reduced the HBsAg levels in serum (Figure 14C and 14D). Altogether, these findings suggest that control of HBV infection by bNAbs requires a combination of antibodies targeting non-overlapping groups of common escape mutations.

[0106] RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Experimental Models: Cell Lines		

Human Hepatocytes, Cryopreserved, Plateable and Interaction Qualified	Lonza Bioscience	Cat#HUCPI
Hepatocyte Defined Medium	Corning	Cat#05449
HepG2-NTCP	(Michailidis et al., 2017)	N/A
HEK293-6E	National Research Council of Canada	NRC file 11565
HepDE19 cells	(Cai et al., 2012)	N/A
Huh-7.5	(Robbani et al., 2017)	N/A
Experimental Models: Mouse Strains		
<i>Fah</i> ^{-/-} <i>NODRag1</i> ^{-/-} <i>IL2rg</i> ^{-/-} mouse (huFNRG)	(de Jong et al., 2014)	N/A
Bacteria and Viruses		
Subcloning Efficiency™ DH5α™ Competent Cells	Thermo Fisher Scientific	Cat#18265017
HBV viruses	(Cai et al., 2012)	N
Antibodies		
Human recombinant 10-1074	(Mouquet et al., 2012)	N/A
Human recombinant ED38	(Wardemann et al., 2003)	N/A
Human recombinant mG053	(Yurasov et al., 2005)	N/A
Goat anti-Human IgG (H+L) Secondary Antibody, HRP	Thermo Fisher Scientific	Cat#31410
Alexa Fluor 488 Mouse anti-Human CD19	BD Biosciences	Cat#557697
BV421 Mouse Anti-Human CD19	BD Biosciences	Cat#562440
anti-CD20-PECy7	BD Biosciences	Cat#335811
Anti-CD27-PE	BD Biosciences	Cat#555441
APC Mouse Anti-Human IgG	BD Pharmingen	Cat#550931
Bv421 Mouse Anti-Human IgG	BD Biosciences	Cat#562581
Anti-Hepatitis B virus core antigen IgG	AUSTRAL Biologicals	Cat#HBP-023-9
Alexa Fluor® 488 AffiniPure Goat Anti-Human IgG, F(ab') ₂ fragment specific	Jackson ImmunoResearch	Cat#109-545-006
Goat anti-Rabbit IgG (H+L) Alexa Fluor 594	Thermo Fisher Scientific	Cat#A11037
Chemicals and Proteins		
Streptavidin HRP	BD Biosciences	Cat#554066
APC Streptavidin	BD Biosciences	Cat#554067
Strep-PE	eBioscience	Cat#12-4317-87
Streptavidin, Alexa Fluor™ 488	Thermo Fisher Scientific	Cat#S32354
Human BD Fc Block™	BD Biosciences	Cat#564220
Ovalbumin (257-264) chicken	Sigma-Aldrich	Cat#S7951
HBsAg adr CHO	ProSpec	Cat#HBS-875
HBsAg adw	ProSpec	Cat#HBS-872

HBsAg protein adr	Fitzgerald	Cat#30-AH37
HBsAg protein ay	Fitzgerald	Cat#30-1816
HBsAg protein ad	Fitzgerald	Cat#30-AH15
HBsAg protein ayw	Fitzgerald	Cat#30R-AH018
RNAasin Plus RNase inhibitor	Promega	Cat#N2615
Random Primers	Thermo Fisher Scientific	Cat#48190011
Lipopolysaccharides from <i>E. coli</i> O55:B5	Sigma-Aldrich	Cat#L2637
Insulin solution human	Sigma-Aldrich	Cat#I1927
Deoxyribonucleic acid from calf thymus	Sigma-Aldrich	Cat#4522
Hemocyanin from Megathura crenulata (keyhole limpet)	Sigma-Aldrich	Cat#H8283
Poly(ethylene glycol)	Sigma-Aldrich	Cat#81268
Normal Goat Serum	Jackson ImmunoResearch	Cat#005-000-121
DAPI, FluoroPure™ grade	Thermo Fisher Scientific	Cat#D21490
Paraformaldehyde 4% Aqueous Solution	Electron Microscopy Sciences	Cat#157-4
Phusion High-Fidelity DNA Polymerase	Thermo Fisher Scientific	Cat#F-530L
Commercial Assays		
ARCHITECT Anti-HBs	Abbott Laboratories	Cat#B7C180
ARCHITECT HBsAg Qualitative	Abbott Laboratories	Cat#B1P970
ARCHITECT Anti-HBc II	Abbott Laboratories	Cat#B8L440
HBsAg CLIA kit	Autobio Diagnostics Co.	Cat#CL0310-2
HBeAg CLIA kit	Autobio Diagnostics Co.	Cat#CL0312-2
Anti-HBs CLIA kit	Autobio Diagnostics Co.	Cat#CL0311-2
LS magnetic columns	Miltenyi Biotech	Cat#130-042-401
CD19 MicroBeads, human	Miltenyi Biotech	Cat#130-097-055
EZ-Link™ Micro NHS-PEG4-Biotinylation Kit	Thermo Fisher Scientific	Cat#21955
Superscript III Reverse Transcriptase	Thermo Fisher Scientific	Cat#18080044
QIAamp DNA blood mini kit	Qiagen	Cat#51104
TaqMan Universal PCR Master Mix	Applied Biosystems	Cat#4304437
Antinuclear antibodies (HEp-2) Kit	MBL International	Cat#ANK-120
Centricon Plus-70 Ultracel PL-100	Millipore Sigma	Cat#UFC710008
X-tremeGENE 9 DNA Transfection Reagent	Sigma-Aldrich	Cat#6365787001
Plasmids		
IGγ1 expression vector	(von Boehmer et al., 2016)	N/A
IGκ expression vector	(von Boehmer et al., 2016)	N/A
IGλ expression vector	(von Boehmer et al., 2016)	N/A
p1.3xHBV-WT	Laboratory of Charles M. Rice	N/A

Softwares and Websites		
PRISM	GraphPad	www.graphpad.com
IgBlast	(Ye et al., 2013)	www.ncbi.nlm.nih.gov/igblast/
IMGT/V-QUEST	(Lefranc et al., 2015)	www.imgt.org/IMGT_vquest/vquest
Geneious Prime	Geneious	www.geneious.com/

Example 8

[0107] This Example provides a description of materials, methods, and subjects used to obtain the foregoing results.

5 [0108] EXPERIMENTAL MODELS AND SUBJECTS

[0109] Human Subjects

[0110] Volunteer recruitment and blood draws were performed at the Rockefeller University Hospital under a protocol approved by the institutional review board (IRB QWA-0947). Study participants ranged in age from 22-65 with a mean of 43, the female:male ratio
10 was 81:78 (Figure 8D and 8E; Table S1).

[0111] Animals

[0112] *Fah*^{-/-}NODRag1^{-/-}IL2rg^{null} (FNRG) female mice were produced as reported (de Jong et al., 2014) and maintained in the AAALAC-certified facility of the Rockefeller University. Animal protocols were in accordance with NIH guidelines and approved by the
15 Rockefeller University Institutional Animal Care and Use Committee under protocol #18063. Female littermates were randomly assigned to experimental groups.

[0113] Cell Lines

[0114] HepG2-NTCP cells (Michailidis et al., 2017) and HepDE19 cells (Cai et al., 2012) were maintained in collagen-coated flasks in Dulbecco's Modified Eagle Medium
20 (DMEM) supplemented with 10% or 3% fetal bovine serum (FBS) and 0.1 mM non-essential amino acids (NEAA). Huh7.5-NTCP cells were maintained in DMEM supplemented with 10% FBS and 0.1 mM NEAA. All liver cell lines were cultured at 37°C in 5% CO₂. Human embryonic kidney HEK293-6E suspension cells were cultured at 37°C in 8% CO₂ with shaking at 120 rpm.

25 [0115] Viruses

[0116] HBV-containing supernatant from HepDE19 cells was collected and concentrated as previously described (Michailidis et al., 2017). The concentrated virus stock was aliquoted and stored at -80°C. For *in vivo* experiments one aliquot of mouse-passaged

genotype C HBV virus, originally launched from patient serum (Billerbeck et al., 2016), was stored at -80°C and thawed for mouse infection experiments. For protection and treatment experiments, animals were challenged intravenously using 1×10^4 DNA copies per mouse.

[0117] Bacteria

5 **[0118]** *E. coli* DH5-alpha were cultured at 37°C with shaking at 230 rpm.

[0119] METHODS

[0120] Collection of Human Samples

[0121] Samples of peripheral blood were collected from volunteers at the Rockefeller University Hospital. Serum was isolated by centrifugation of coagulated whole blood, and
10 aliquoted for storage at -80°C. PBMCs were isolated using a cell separation tube with frit barrier and cryopreserved in liquid nitrogen in 90% heat-inactivated FBS supplemented with 10% dimethylsulfoxide (DMSO).

[0122] HBV Stock

[0123] HepDE19 cells (Cai et al., 2012) were cultured in the absence of tetracycline
15 to induce HBV replication. After seven days, supernatant was collected every other day for two weeks and fresh medium was added. After each collection, medium was spun down to remove cell debris, passed through a 0.22 µm filter, and kept at 4°C. Collected medium was concentrated 100-fold via centrifugation using Centricon Plus-70 centrifugal filter devices (Millipore-Sigma, Billerica, MA). Mouse-passaged genotype C HBV virus (Billerbeck et al.,
20 2016) was used for *in vivo* mouse experiment.

[0124] *In Vitro* HBV Neutralization Assay

[0125] *In vitro* HBV infection was performed as previously described (Michailidis et al., 2017). Briefly, HepG2-NTCP cells were seeded in 96-well collagen-coated plates in DMEM supplemented with 10% FBS and 0.1 mM NEAA. The medium was changed to
25 DMEM with 3% FBS, 0.1 mM NEAA, and 2% DMSO the next day and cultured for an additional 24 hours before infection. The inoculation was in DMEM supplemented with 3% FBS and 0.1 mM NEAA 4% PEG and 2% DMSO. Antibodies or serum samples were incubated with the virus in the inoculation medium for one hour at 37°C before adding to cells. Serum neutralization capacity (y-axis in Figure 1A and 8B) was calculated as the
30 reciprocal of the relative percentage of infected HepG2-NTCP cells immunostained by rabbit anti-HBV core antibody (AUSTRAL Biologicals). For example, if the relative percentage of infected cells were 100% (no serum added or the sera from unexposed naïve control donors), the serum neutralization capacity would be calculated as 1; but if the relative percentage of

infected cells were 50% or 10%, the serum neutralization capacity would be 2 or 10. For the blocking neutralization assay, S-protein antigen at different concentration was incubated with purified polyclonal antibodies for one hour at 37°C before incubation with HBV virus. The cells were then spinoculated for one hour by centrifugation at 1,000 g at 37°C. After a 24-hour incubation, supernatant was removed, cells were washed five times with PBS, and 100 µl of fresh DMEM supplemented with 3% FBS, 0.1 mM NEAA, and 2% DMSO. Both supernatant and cells were harvested 7 days after infection for analysis. Neutralization assays in primary human hepatocytes were performed as above using hepatocytes from livers of highly humanized mice that were harvested and seeded on collagen-coated plates in hepatocyte defined medium (Corning) (Michailidis et al., 2020).

[0126] Chemiluminescence Immunoassay

[0127] For quantitative analysis of secreted antigen HBsAg or HBeAg, 50 µl of the collected supernatant was loaded into 96-well plates of a chemiluminescence immunoassay (CLIA) kit (Autobio Diagnostics Co., Zhengzhou, China) according to the manufacturer's instructions. Plates were read using a FLUOstar Omega luminometer (BMG Labtech). The absolute concentrations were measured and the relative values were calculated by normalizing to the virus-only control well in the same lane. For example, the absolute HBsAg/HBeAg level in virus-only control well (considered as reference) was 20 NCU/ml (national clinical units per milliliter), while adding one neutralizing serum sample might reduce this to 5 NCU/ml. Therefore, after normalization, the relative HBsAg/HBeAg level were calculated as 100% in control and 25% for this neutralizing serum. Since many factors (virus concentration, cell concentration, immunofluorescence reading, etc.) vary between different plates or different rounds of experiments, normalization is necessary for combining data for comparison.

[0128] Immunofluorescence

[0129] Cells were fixed in 4% paraformaldehyde for 20 minutes at room temperature, washed with PBS and permeabilized with 0.1% Triton X-100 in PBS. After blocking with 5% goat serum, the cells were incubated with rabbit anti-HBV core antibody (AUSTRAL Biologicals) overnight at 4°C and visualized with goat anti-rabbit Alexa Fluor 594 (Thermo Fisher Scientific). Nuclei were stained with DAPI. Cells were imaged using a Nikon Eclipse TE300 fluorescent microscope and processed with ImageJ. For high-content imaging analysis ImageXpress Micro XLS (Molecular Devices, Sunnyvale, CA) was used. The absolute HBc⁺ percentages were obtained and the relative percentage of HBc⁺ cells was calculated by

normalizing to the virus-only control well in the same lane. For example, the absolute HBc⁺ cell percentage in virus-only control well (considered as reference) was 40%, while adding one neutralizing serum sample might reduce this to 10%. Therefore, after normalization, the relative percentages of HBc⁺ cells were calculated as 100% in control well and 25% for this neutralizing serum sample. Since many factors (virus concentration, cell concentration, immunofluorescence reading, etc.) vary between different plates or different rounds of experiments, normalization is necessary for combining data for comparison.

[0130] ELISA Assays

[0131] Blood samples were submitted to Memorial Sloan Kettering Cancer Center for clinical testing. The presence of HBsAg protein and anti-HBc antibody, as well as anti-HBs titers, were determined by ELISA (Abbott Laboratories) as per the manufacturer's instructions.

[0132] The binding of serum or recombinant IgG antibodies to HBsAg proteins (see KEY RESOURCES TABLE) was measured by coating ELISA plates with 10 µg/ml of antigen in PBS. Plates were blocked with 2% BSA in PBS and incubated with antibody for one hour at room temperature. Visualization was with HRP-conjugated goat anti-human IgG (Thermo Fisher Scientific). The 50% effective concentration (EC₅₀) needed for maximal binding was determined by non-linear regression analysis in software PRISM.

[0133] For competition ELISAs plates were coated with 0.12 µg/ml HBsAg (*adr* CHO) and incubated with 16.7 µg/ml primary antibody for two hours, followed by directly adding 0.25 µg/ml biotinylated secondary antibody and incubation for 30 minutes all at room temperature. Detection was with streptavidin-HRP (BD Biosciences).

[0134] Autoreactivity and Polyreactivity

[0135] Autoreactivity and polyreactivity assays were performed as described (Gitlin et al., 2016; Mayer et al., 2017; Robbiani et al., 2017). For the autoreactivity assays, monoclonal antibodies were tested with the Antinuclear antibodies (HEp-2) Kit (MBL International). Antibodies were incubated at 100 µg/ml and were detected with Alexa Fluor 488 AffiniPure F(ab')₂ Fragment Goat Anti-Human IgG (H+L) (Jackson ImmunoResearch) at 10 µg/ml. Fluorescence images were taken with a wide-field fluorescence microscope (Axioplan 2, Zeiss), a 40x dry objective and a Hamamatsu Orca ER B/W digital camera. Images were analyzed with Image J. Human serum containing antinuclear antibodies (MBL International) was used as a positive control. For the polyreactivity ELISA assays, antibody binding to five different antigens, double-stranded DNA (dsDNA), insulin, keyhole limpet

hemocyanin (KLH), lipopolysaccharides (LPS), and single-stranded DNA (ssDNA), were measured. ED38 (Wardemann et al., 2003) and mG053 (Yurasov et al., 2005) antibodies were used as positive and negative controls, respectively.

[0136] Synthetic Peptides

5 **[0137]** Eighteen peptides spanning the antigenic loop region of S-protein antigen were synthesized at the Proteomics Resource Center of The Rockefeller University. For peptide ELISAs plates were coated with 10 µg/ml peptide in PBS.

[0138] HBsAg-Binding Memory B cells

[0139] S-protein (*adr* serotype) expressed and purified from Chinese hamster ovary
10 (CHO) cells (ProSpec) and ovalbumin (Sigma-Aldrich) were biotinylated using EZ-Link™ Micro NHS-PEG4-Biotinylation kit (Thermo Fisher Scientific). S-protein-PE and S-protein-APC were prepared by incubating 2-3 µg of biotin-S-protein with streptavidin-PE (eBioscience) or streptavidin-APC (BD Biosciences) in PBS respectively overnight at 4°C in the dark. Ovalbumin-Alexa Fluor 488 was generated by incubating biotin-ovalbumin
15 with streptavidin-Alexa Fluor 488 (Thermo Fisher Scientific).

[0140] B cell purification, labeling, and sorting were as previously described (Escolano et al., 2019; Robbiani et al., 2017; Tiller et al., 2008; von Boehmer et al., 2016). Briefly, PBMCs were thawed and washed with RPMI medium at 37°C. B lymphocytes were positively selected using CD19 MicroBeads (Miltenyi Biotec) followed by incubation
20 with human Fc block (BD Biosciences) and anti-CD20-PECy7 (BD Biosciences), anti-IgG-Bv421 (BD Biosciences), S-protein-PE at 10 µg/ml, S-protein-APC at 10 µg/ml, and ovalbumin-Alexa Fluor 488 at 10 µg/ml at 4°C for 20 minutes. Single CD20⁺ IgG⁺ S-protein-PE⁺ S-protein-APC⁺ Ova-Alexa Fluor 488⁻ memory B cells were sorted into 96-well plates using a FACS Aria II (Becton Dickinson) and stored at -80°C.

25 **[0141] Antibody Cloning, Sequencing and Production**

[0142] Antibody cloning, sequencing and production were done as previously reported (Robbiani et al., 2017; Tiller et al., 2008; von Boehmer et al., 2016). Primers are listed in Table S3. Unmutated common ancestor (UCA) antibody sequences of H006, H019 and H020 were synthesized by gBlock IDT (Table S3) and were inserted into antibody
30 vectors for expression. V(D)J gene segment and CDR3 sequences were determined by IgBlast (Ye et al., 2013) and/or IMGT/V-QUEST (Brochet et al., 2008).

[0143] S-protein Mutagenesis

[0144] Oligonucleotides fragments with the target point mutations were synthesized by gBlock IDT (Table S3), and were substituted into the antigenic loop region in plasmid p1.3xHBV-WT by Sequence and Ligation-Independent Cloning (SLIC) (Jeong et al., 2012). Mutant plasmids were transfected into Huh-7.5-NTCP cells using X-tremeGENE 9 DNA Transfection Reagent (Sigma-Aldrich) and the culture medium was changed to serum-free DMEM after 24 hours. Supernatants were collected 2 days later and stored at -80°C. Serum-free medium (50 µl) was directly used to coat ELISA plates.

[0145] Crystallization, X-ray Data Collection, Structure Determination and Refinement

[0146] Antibody Fab (25 mg/ml) in 50 mM Tris 8.0, 50 mM NaCl was mixed with peptide (5 mg/ml) in the same buffer at 5:1 v/v. Molar ratio of Fab:peptide is around 1:2. Crystals were obtained upon substitution of all peptide-11 cysteine residues with serine in the peptide synthesis (Proteomics Resource Center, RU). The crystallization condition for Fab15/peptide-11Ser was identified from a commercial screen (Morpheus by Molecular Dimensions) by the sitting-drop vapor-diffusion method at room temperature. The crystal used for data collection was obtained directly from the initial setup (position E1) in a precipitant solution consisting of 0.12 M Ethylene glycols (Di, Tri, Tetra and Penta-ethylene glycol), 0.1 M Buffer Mix 1 (Imidazole/MES) at pH 6.5 and 30% Precipitant Mix 1 (20% v/v PEG 500* MME; 10 % w/v PEG 20000). The crystals were flash-cooled in liquid nitrogen directly from the mother liquor without additional cryoprotectant. X-ray diffraction data were collected from a single crystal on the Advanced Photon Source (APS) beamline 24-ID-E to 1.78 Å resolution. The data were integrated and scaled with the program XDS (Kabsch, 2010a, b) and other data processing utilities from the CCP4 suite (Collaborative Computational Project, 1994) using RAPD, the software available at the beam-line. Initial phase estimates and electron-density maps were obtained by molecular replacement with Phaser (McCoy et al., 2007) using a single FAB molecule from (PDB: 5GGU) as an initial search model in Phenix (Adams et al., 2010). Iterative model building and structural refinement were manually performed using COOT (Emsley et al., 2010) and Phenix, respectively. The peptide density was well defined, and refined to 90% occupancy, for residues STKPSDGNST (SEQ ID NO: 25). All other residues were not visible and the area where they would be is fully solvent, with no crystal contacts involving any of the peptide atoms. The quality of the final model was good as noted in a Ramachandran of 96% of the observed residues within the allowable region. Data-collection and refinement statistics are

summarized (Figure 13B). All molecular graphics were prepared with PyMOL (Version 2.0 Schrödinger, LLC). Atomic coordinates and experimental structure factors have been deposited in the PDB under accession code 6VJT.

[0147] Humanized Mice and *In Vivo* Studies

5 [0148] Six to eight week old *Fah*^{-/-}*NODRag1*^{-/-}*IL2rg*^{null} (FNRG) female mice were transplanted with one million human hepatocytes from a pediatric female donor HUM4188 (Lonza Bioscience) as previously described (de Jong et al., 2014). Briefly, during isoflurane anesthesia mice underwent skin and peritoneal incision, exposing the spleen. One million hepatocytes were injected in the spleen using a 28-gauge needle. The peritoneum was then
10 approximated using 4.0 VICRYL sutures (Johnson & Johnson), and skin was closed using MikRon Autoclip surgical clips (Becton Dickinson). Mice were cycled off the drug nitisinone (Yecuris) on the basis of weight loss and overall health. Humanization was monitored by human albumin quantification in mouse serum using a human-specific ELISA (Bethyl Labs). Humanized FNRG mice with human albumin values greater than 1 mg/ml were used for
15 infection experiments. The human liver chimeric (huFNRG) mice are extremely immunodeficient. The *Rag1*^{-/-} renders the mice B and T cell deficient and the *IL2rg*^{null} mutation prevents cytokine signaling through multiple receptors, leading to a deficiency in functional NK cells. Moreover, the genetic background is NOD background, with suboptimal antigen presentation, defects in T and NK cell function, reduced macrophage cytokine
20 production, suppressed wound healing, and C5 complement deficiency. Thus the mice would be unable to produce antibody-dependent effector functions, including antibody-dependent cell-mediated cytotoxicity (ADCC), or passive antibody-enhanced adaptive immunity.

[0149] Mice were challenged intravenously with 1x10⁴ genome equivalent (GE) of mouse-passaged genotype C HBV viruses diluted in PBS. For prophylaxis experiments, 500
25 µg of monoclonal antibody was administered intraperitoneally at 20 and again at 6 hours before infection. For therapy experiments, huFNRG mice with established HBV infections (<10⁸ DNA copies/ml of serum) were injected with 500 µg of each monoclonal antibody intraperitoneally 3 times per week.

[0150] DNA in mouse serum collected weekly was extracted using a QIAamp DNA
30 Blood Mini Kit (Qiagen). Total HBV DNA was determined by quantitative PCR (Michailidis et al., 2017). PCR was performed using a TaqMan Universal PCR Master Mix (Applied Biosystems), primers and probe (Table S3).

[0151] To obtain HBV DNA from serum for sequence analysis the S domain was amplified using primers (Table S3), and Phusion DNA polymerase (Thermo Fisher Scientific). Initial denaturation was at 98°C for 30 s, followed by 40 amplification cycles (98°C for 10 s, 60°C for 30 s, and 72°C for 30 s), followed by one cycle at 72°C for 5 min. A ~700 bp fragment was gel extracted for Sanger sequencing. Sequence alignments were performed using MacVector.

[0152] QUANTIFICATION AND STATISTICAL ANALYSIS

[0153] The detailed information of statistical analysis could be found in the Result and Figure Legends. Correlation was evaluated by Spearman's rank correlation method (Figure 1A and 2B). Statistical significance was calculated by Dunn's Kruskal-Wallis multiple comparisons with p values corrected with the Benjamini-Hochberg procedure (Figure 8C). The 50% effective concentration (EC₅₀) values by ELISA assays (Figure 3A and 3C) and 50% inhibitory concentration (IC₅₀) values by neutralization assays (Figure 5C) were calculated by nonlinear regression analysis in PRISM software.

[0154] Discussion of Examples

[0155] Previous studies have identified several anti-HBs neutralizing antibodies from a small number of otherwise unselected spontaneously recovered or vaccinated individuals (Cerino et al., 2015; Colucci et al., 1986; Eren et al., 1998; Heijtkink et al., 2002; Heijtkink et al., 1995; Jin et al., 2009; Kim and Park, 2002; Li et al., 2017; Sa'adu et al., 1992; Sankhyan et al., 2016; Tajiri et al., 2007; Tokimitsu et al., 2007; Wang et al., 2016). In contrast, in the present disclosure, sera from 144 exposed volunteers was screened to identify elite neutralizers. Serologic activity varied greatly among the donors with a small number of individuals demonstrating high levels of neutralizing activity. To understand this activity, we isolated 244 anti-HBs antibodies from single B cells obtained from the top donors. Each of the elite donors tested showed expanded clones of memory B cells expressing bNAbs that targeted 3 non-overlapping sites on the S-protein. Moreover, the amino acid sequence of several of the bNAbs was highly similar in different individuals. These closely related antibodies target the same epitope.

[0156] The near identity of clones of HBV bNAbs in unrelated elite individuals is akin to reports for elite responders to HIV-1 (Scheid et al., 2011; West et al., 2012), influenza (Laursen and Wilson, 2013; Pappas et al., 2014; Wrammert et al., 2011), Zika (Robbiani et al., 2017), and malaria (Tan et al., 2018). However, none of the elite anti-HBs bNAbs shares both IgH and IgL with previously reported HBV neutralizing antibodies, the best of which have been tested in the clinic but are less potent than some of the bNAbs of this disclosure

(libivirumab IC₅₀: 35 ng/ml, tuvirumab IC₅₀: ~100 ng/ml) (Galun et al., 2002; Heijtkink et al., 2001; van Nunen et al., 2001).

[0157] The described alanine scanning and competition binding analyses are consistent with the existence of at least 3 domains that can be recognized concomitantly by bNAbs (Gao et al., 2017; Tajiri et al., 2010; Zhang et al., 2016). However, the domains do not appear to be limited to either of two previously defined circular peptide epitopes, 123-137 and 139-148 (Tajiri et al., 2010; Zhang et al., 2016). Instead, residues spanning most of the external domain can contribute to binding by both Group-I and -II antibodies. For example, alanine scanning indicates that Group-I H020 binding is dependent on I110, K141, D144, G145 and T148, while Group-II H016 binding depends on T123, D144, and G145. Thus, despite having non-overlapping binding sites some of the essential residues are shared by Group-I and II suggesting that the epitopes are conformational. Moreover, the antibody epitopes on S-protein identified using mouse and human antibodies may be distinct (Chen et al., 1996; Ijaz et al., 2003; Paulij et al., 1999; Zhang et al., 2019; Zhang et al., 2016). Finally, G145, a residue that is frequently mutated in infected humans (Ma and Wang, 2012; Tong et al., 2013), is believed to be essential for binding by all the Group-II but not all Group-I or -III antibodies tested.

[0158] Crystallization of the Group-II bNAb H015 and its linear epitope revealed a loop that includes P142, S/T143, D144, and G145, all of which are frequently mutated during natural infection to produce well-documented immune escape variants (Hsu et al., 2015; Ijaz et al., 2012; Ma and Wang, 2012; Salpini et al., 2015). In addition to immune escape, the residues that form this structure are also essential for infectivity, possibly by facilitating virus interactions with cell surface glycosaminoglycans (Sureau and Salisse, 2013). Mutations in K141, P142 as well as C139 and C147, all of which contribute to the stability of the structure, decrease viral infectivity (Salisse and Sureau, 2009). Without intending to be bound by any particular theory, it is considered that drugs that destabilize the newly elucidated H015-peptide loop structure may also interfere with infectivity.

[0159] The G145R mutation, which is among the most frequent immune escape variants, replaces a small neutral residue with a bulky charged residue that would likely interfere with antigenicity by destroying the salt bridge between K141 and D144 that anchors the peptide loop. However, this drastic structural change does not alter infectivity (Salisse and Sureau, 2009), possibly because the additional charge compensates for otherwise altered interactions between HBV and cell surface glycosaminoglycans (Sureau and Salisse, 2013).

Thus, the additional charge may allow G145R to function as a dominant immune escape variant while preserving infectivity.

[0160] The present disclosure describes antibodies directed at S-protein antigen in part because this is the antigen used in the currently FDA-approved vaccines, and because purified S-protein blocked nearly all of the neutralizing activity in the serum of the elite neutralizers irrespective of whether they were vaccinated or spontaneously recovered. Nevertheless, individuals who recover from infection also produce antibodies to the PreS1 domain of HBsAg (Li et al., 2017; Sankhyan et al., 2016). The PreS1 domain is essential for the virus to interact with the entry factor NCTP on hepatocytes and potent neutralizing antibodies to PreS1 have been described (Li et al., 2017). However, these are not naturally occurring antibodies but rather randomly paired IgH and IgL chains derived from phage libraries obtained from unexposed or vaccinated healthy donors (Li et al., 2017). Moreover, the phage antibodies required further engineering to enhance their neutralizing activity (Li et al., 2017). Thus, whether the human immune system also produces potent anti-PreS1 bNAbs has not been determined.

[0161] Chronic HBV infection remains a major global public health problem in need of an effective curative strategy (Graber-Stiehl, 2018; Lazarus et al., 2018; Revill et al., 2016). Chronically infected individuals produce an overwhelming amount of HBsAg that is postulated to incapacitate the immune system. Consequently, immune cells, which might normally clear the virus, are unable to react to antigen, a phenomenon referred to as exhaustion or anergy (Ye et al., 2015). The appearance of anti-HBs antibodies is associated with spontaneous recovery from the disease, perhaps because they can clear the antigen and facilitate the emergence of a productive immune response (Celis and Chang, 1984; Zhang et al., 2016; Zhu et al., 2016). These findings led to the hypothesis that passively administered antibodies might be used in conjunction with antiviral drugs to further decrease the antigenic burden while enhancing immune responses that maintain long-term control of the disease. The presently described results in huFNRG mice infected with HBV indicate that antibody monotherapy with a potent bNAb can lead to the emergence of the very same escape mutations commonly found in chronically infected individuals. Moreover, not all bNAb combinations are effective in preventing escape by mutation. Combinations that target separate epitopes but have overlapping sensitivity to commonly occurring escape mutations such as H006 and H007 are ineffective. In contrast, combinations with complementary sensitivity to common escape mutations prevent the emergence of escape mutations in huFNRG mice infected with HBV. Thus, as described above, the present disclosure provides

immunotherapy for HBV infection with combinations of antibodies with complementary activity to avert this potential problem.

[0162] The following reference listing is not an indication that any particular reference(s) is material to patentability.

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[0163] Supplemental Table S1. Detailed information of donors, Related to Figure 1.

[0164] The anti-HBs ELISA titer (x-axis in Figure 1A and 8B) and relative infection rate (y-axis in Figure 1A and 8B) of each donor's serum sample were determined by ELISA assay and *in vitro* neutralization assay, respectively.

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DONO R ID	ANTI- HBs ELISA TITE R	STAT UE	BIG BLOOD DRAW	INFECTION RATE (1:5 SERUM) PERCENTAGE OF HBcAg+ CELLS			AVE RAG E	NEU TRA CAP ACI TY	INFECTION RATE (1:50 SERUM) PERCENTAGE OF HBcAg+ CELLS			AVE RAG E	NEU TRA CAP ACI TY
QWA- 0947- 001	9.08	Vaccin ated		11 4.0 0	12 7.1 2	13 3.6 4	124. 92	0.80	11 8.0 6	12 8.9 0	12 2.1 9	123. 05	0.81
QWA- 0947- 002	516.1 2	Vaccin ated		65. 28	77. 58	75. 13	72.6 6	1.38	13 1.6 0	13 7.0 4	13 3.4 4	134. 03	0.75
QWA- 0947- 003	0	Vaccin ated		10 8.5 9	11 8.3 1	11 8.5 3	115. 14	0.87	13 2.8 1	13 6.6 5	13 2.2 2	133. 89	0.75
QWA- 0947- 004	267.1	Vaccin ated		11 3.3 9	12 1.9 1	12 1.6 7	118. 99	0.84	14 2.6 9	14 6.6 9	15 3.2 4	147. 54	0.68
QWA- 0947- 005	113.0 1	Vaccin ated		82. 91	87. 48	95. 39	88.5 9	1.13	14 8.2 4	14 9.3 6	14 6.7 5	148. 12	0.68
QWA- 0947- 006	325.7 7	Vaccin ated		81. 19	85. 97	96. 43	87.8 6	1.14	11 7.4 8	11 6.8 3	11 9.7 4	118. 02	0.85
QWA- 0947- 007	63.54	Vaccin ated		10 0.3 7	10 5.5 3	11 0.7 3	105. 54	0.95	13 4.1 1	13 5.1 5	13 8.5 1	135. 92	0.74
QWA- 0947- 008	21.8	Vaccin ated		40. 86	35. 60	42. 82	39.7 6	2.52	78. 64	84. 09	84. 79	82.5 1	1.21
QWA- 0947- 009	>100 0	Vaccin ated	BIG BLOOD DRAW	12. 84	14. 39	17. 20	14.8 1	6.75	34. 66	38. 81	33. 48	35.6 5	2.81
QWA- 0947- 010	0.33	Vaccin ated		93. 33	93. 42	10 4.9 1	97.2 2	1.03	10 5.4 1	11 6.7 2	11 5.5 8	112. 57	0.89
QWA- 0947- 011	1.29	Vaccin ated	BIG BLOOD DRAW	10 9.4 0	11 3.8 7	94. 10	105. 79	0.95	95. 79	93. 25	81. 95	90.3 3	1.11

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QWA-0947-012	12.87	Vaccinated		10 2.0 4	10 2.9 4	10 8.8 1	104. 60	0.96		14 2.9 5	13 7.9 5	12 5.1 2	135. 34	0.74
QWA-0947-013	>100 0	Vaccinated	BIG BLOOD DRAW	9.2 4	8.3 1	8.3 3	8.63	11.5 9		19. 95	20. 81	17. 29	19.3 5	5.17
QWA-0947-014	248.3 1	Vaccinated		80. 90	80. 65	79. 88	80.4 8	1.24		11 7.5 8	12 0.1 7	11 5.3 7	117. 71	0.85
QWA-0947-015	76.1	Vaccinated		97. 26	91. 48	86. 95	91.9 0	1.09		11 2.7 9	10 9.8 2	10 1.1 9	107. 93	0.93
QWA-0947-016	0.36	Non-Vaccinated		10 0.2 2	96. 77	95. 84	97.6 1	1.02		11 8.0 4	12 0.0 5	11 7.3 4	118. 48	0.84
QWA-0947-017	0.63	Vaccinated		10 0.3 0	10 2.9 8	10 1.5 5	101. 61	0.98		12 2.2 7	11 9.4 2	11 0.9 3	117. 54	0.85
QWA-0947-018	3.24	Vaccinated		10 1.6 5	11 3.3 8	96. 98	104. 00	0.96		11 8.1 8	12 1.2 6	10 7.0 5	115. 50	0.87
QWA-0947-019	>100 0	Vaccinated		47. 62	43. 35	40. 11	43.6 9	2.29		10 5.8 6	10 0.4 6	89. 54	98.6 2	1.01
QWA-0947-020	1.21	Non-Vaccinated		77. 13	75. 25	60. 04	70.8 1	1.41		11 6.2 8	11 3.7 2	10 8.6 5	112. 88	0.89
QWA-0947-021	15.81	Vaccinated		33. 85	41. 39	34. 98	36.7 4	2.72		89. 74	89. 87	88. 60	89.4 0	1.12
QWA-0947-022	2.17	Vaccinated		83. 52	94. 22	93. 88	90.5 4	1.10		10 0.0 8	11 9.8 8	11 0.1 9	110. 05	0.91
QWA-0947-023	183.3 7	Vaccinated		93. 15	11 9.5 7	11 6.0 8	109. 60	0.91		11 3.4 3	11 7.9 1	10 3.4 5	111. 60	0.90
QWA-0947-024	256.8 5	Vaccinated		55. 70	60. 03	49. 13	54.9 5	1.82		10 4.6 8	11 6.2 1	10 5.1 7	108. 69	0.92
QWA-0947-025	709.2 9	Vaccinated		76. 18	77. 38	75. 01	76.1 9	1.31		10 0.5 8	10 5.5 7	11 6.8 2	107. 66	0.93
QWA-0947-026	0.49	Non-Vaccinated		83. 02	10 2.4 2	96. 98	94.1 4	1.06		10 4.2 4	11 7.0 9	10 5.7 3	109. 02	0.92
QWA-0947-027	0.3	Non-Vaccinated	BIG BLOOD DRAW	10 3.5 1	12 8.7 9	11 4.8 2	115. 71	0.86		10 5.9 1	12 6.6 8	11 7.0 3	116. 54	0.86
QWA-0947-028	6.51	Non-Vaccinated		84. 03	90. 88	87. 77	87.5 6	1.14		10 7.2 3	11 7.8 9	10 8.2 1	111. 11	0.90
QWA-0947-029	1.67	Non-Vaccinated		10 3.7 2	98. 68	83. 74	95.3 8	1.05		96. 06	10 2.2 5	10 0.2 0	99.5 0	1.00
QWA-0947-030	0.09	Vaccinated	BIG BLOOD DRAW	86. 06	84. 44	91. 73	87.4 1	1.14		11 1.7 4	11 5.7 3	10 2.2 6	109. 91	0.91

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QWA-0947-031	488.3	Core Ab +		71.30	66.21	56.71	64.74	1.54		94.99	10.287	94.27	97.38	1.03
QWA-0947-032	>1000	Vaccinated		71.12	67.87	56.53	65.17	1.53		97.45	10.781	10.659	103.95	0.96
QWA-0947-033	330.93	Vaccinated		99.61	93.60	87.25	93.49	1.07		10.628	11.665	10.845	110.46	0.91
QWA-0947-034	588.26	Core Ab +		40.92	41.19	35.30	39.14	2.56		99.54	11.16	10.528	105.32	0.95
QWA-0947-035	365.7	Vaccinated		10.152	11.383	94.76	103.37	0.97		12.977	13.160	12.119	127.52	0.78
QWA-0947-036	108.83	Vaccinated		87.55	85.69	77.65	83.63	1.20		12.228	12.203	10.769	117.33	0.85
QWA-0947-037	>1000	Vaccinated		23.79	21.09	18.46	21.11	4.74		66.02	59.97	52.64	59.54	1.68
QWA-0947-038	11.76	Vaccinated		94.89	95.53	96.87	95.76	1.04		11.979	12.509	11.527	120.05	0.83
QWA-0947-039	230.99	Vaccinated		10.208	99.23	91.54	97.62	1.02		11.301	11.504	98.95	109.00	0.92
QWA-0947-040	0.26	Vaccinated		54.12	57.38	45.32	52.27	1.91		10.243	10.789	95.37	101.90	0.98
QWA-0947-041	0.42	Non-Vaccinated		77.09	78.29	84.91	80.09	1.25		87.59	10.125	10.119	96.68	1.03
QWA-0947-042	128.75	Core Ab +		97.03	10.651	11.026	104.60	0.96		11.407	14.901	12.198	128.35	0.78
QWA-0947-043	229.75	Core Ab +		78.56	94.35	95.71	89.54	1.12		95.18	14.423	12.382	121.08	0.83
QWA-0947-044	222.48	Core Ab +		45.85	56.61	65.34	55.93	1.79		94.00	13.396	10.986	112.60	0.89
QWA-0947-045	>1000	Core Ab +		51.82	66.02	61.55	59.80	1.67		10.436	12.203	12.096	115.78	0.86
QWA-0947-046	350.93	Vaccinated		89.57	99.40	11.155	100.17	1.00		10.098	12.950	11.179	114.09	0.88
QWA-0947-047	0.33	Vaccinated		12.688	13.830	14.237	135.85	0.74		11.235	15.677	12.772	132.28	0.76
QWA-0947-048	>1000	Vaccinated	BIG BLOOD DRAW	35.94	44.44	46.02	42.14	2.37		83.08	10.989	94.60	95.86	1.04
QWA-0947-049	>1000	Core Ab +	BIG BLOOD DRAW	94.21	12.065	11.957	111.48	0.90		11.333	13.910	12.642	126.28	0.79

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QWA-0947-050	6.2	Vaccinated		93.10	114.26	113.58	106.98	0.93		93.34	121.07	112.91	109.10	0.92
QWA-0947-051	228.35	Vaccinated		111.78	112.69	115.97	113.48	0.88		104.71	102.64	83.60	96.98	1.03
QWA-0947-052	2.77	Vaccinated		116.53	115.59	110.83	114.32	0.87		113.48	114.25	125.60	117.78	0.85
QWA-0947-053	48.25	Vaccinated		114.90	112.78	98.40	108.69	0.92		105.04	116.61	119.01	113.55	0.88
QWA-0947-054	24.06	Vaccinated		121.56	125.13	111.71	119.47	0.84		99.64	118.99	122.11	113.58	0.88
QWA-0947-055	772.43	Core Ab +	BIG BLOOD DRAW	8.79	9.33	5.78	7.97	12.55		82.33	95.93	87.80	88.69	1.13
QWA-0947-056	441.12	Vaccinated		86.57	86.67	79.10	84.12	1.19		98.81	120.31	116.13	111.75	0.89
QWA-0947-057	91.37	Vaccinated		120.46	113.18	110.80	114.82	0.87		111.45	107.08	116.80	111.78	0.89
QWA-0947-058	>1000	Vaccinated		27.66	27.74	26.37	27.26	3.67		82.86	83.73	74.74	80.44	1.24
QWA-0947-059	83.28	Vaccinated		110.69	109.95	99.34	106.66	0.94		115.21	115.69	99.96	110.29	0.91
QWA-0947-060	>1000	Vaccinated	BIG BLOOD DRAW	5.68	6.72	5.17	5.86	17.08		25.39	26.65	24.93	25.66	3.90
QWA-0947-061	104.78	Vaccinated		109.98	120.25	131.62	120.61	0.83		107.59	134.01	124.63	122.08	0.82
QWA-0947-062	2.56	Vaccinated		113.16	140.19	143.78	132.38	0.76		120.58	139.98	135.32	131.96	0.76
QWA-0947-063	246.16	Vaccinated		101.93	112.01	141.39	118.44	0.84		114.71	134.13	143.18	130.67	0.77
QWA-0947-064	Not Available	Vaccinated		128.17	114.29	147.09	129.85	0.77		133.50	133.31	133.32	133.35	0.75
QWA-0947-065	0.28	Core Ab +		112.39	133.12	155.43	133.65	0.75		131.76	134.78	150.74	139.09	0.72
QWA-0947-066	265.6	Vaccinated		50.87	68.37	86.59	68.61	1.46		129.24	133.43	119.16	127.28	0.79
QWA-0947-067	0	Vaccinated		106.36	120.57	150.56	125.83	0.79		122.57	142.42	139.51	134.84	0.74
QWA-0947-068	0.25	Vaccinated		58.26	87.26	105.25	83.59	1.20		123.65	128.77	124.58	125.67	0.80

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QWA-0947-069	>1000	Vaccinated	BIG BLOOD DRAW	11.42	27.20	22.32	20.31	4.92		50.80	55.44	64.27	56.84	1.76
QWA-0947-070	7.01	Vaccinated		107.39	113.96	138.16	119.84	0.83		118.06	116.97	118.95	117.99	0.85
QWA-0947-071	638.24	Vaccinated		56.39	48.55	55.42	53.45	1.87		94.83	111.19	117.23	107.75	0.93
QWA-0947-072	15.55	Vaccinated		128.74	135.08	126.34	130.05	0.77		137.00	132.93	122.94	130.96	0.76
QWA-0947-073	225.34	Vaccinated		131.87	122.33	137.50	130.57	0.77		137.43	128.35	124.59	130.12	0.77
QWA-0947-074	159.52	Core Ab +		120.51	119.04	128.75	122.76	0.81		140.98	130.18	124.00	131.72	0.76
QWA-0947-075	0.37	Vaccinated		131.78	125.05	159.51	138.78	0.72		133.08	135.29	117.74	128.70	0.78
QWA-0947-076	27.37	Vaccinated		137.32	145.89		141.60	0.71		132.06			132.06	0.76
QWA-0947-077	52.77	Vaccinated		112.72	121.48		117.10	0.85		137.12			137.12	0.73
QWA-0947-078	181.6	Vaccinated		116.16	107.29		111.72	0.90		138.30	131.27		134.79	0.74
QWA-0947-079	>1000	Vaccinated		54.73	59.28	71.14	61.72	1.62		130.53	128.66	118.32	125.84	0.79
QWA-0947-080	>1000	Vaccinated		62.38	53.55	69.34	61.76	1.62		122.37	106.42		114.40	0.87
QWA-0947-081	7.23	Vaccinated		113.81	111.55	142.59	122.65	0.82		109.38	105.63	116.78	110.60	0.90
QWA-0947-082	24.98	Vaccinated		120.69	124.58	118.10	121.12	0.83		106.45	118.55	117.79	114.26	0.88
QWA-0947-083	90.5	Vaccinated		84.79	87.62	99.65	90.69	1.10		91.86	99.93	105.67	99.15	1.01
QWA-0947-084	880.92	Core Ab +		112.81	125.10	114.29	117.40	0.85		106.78	117.78	147.46	124.01	0.81
QWA-0947-085	82.25	Vaccinated		120.45	148.83	159.96	143.08	0.70		114.14	114.33	136.45	121.64	0.82
QWA-0947-086	19.16	Vaccinated		147.29	173.59	166.75	162.55	0.62		110.03	128.28	120.46	119.59	0.84
QWA-0947-087	88.6	Vaccinated		126.58	146.46	145.74	139.59	0.72		105.86	119.12	119.22	114.74	0.87

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QWA-0947-088	288.42	Core Ab +		108.25	120.39	140.09	122.91	0.81		90.55	101.28	115.15	102.33	0.98
QWA-0947-089	15.74	Vaccinated		101.12	94.87	98.43	98.14	1.02		75.70	96.65	111.21	94.52	1.06
QWA-0947-090	>1000	Vaccinated		54.59	47.73	53.63	51.99	1.92		71.09	87.31	99.22	85.87	1.16
QWA-0947-091	>1000	Vaccinated		18.28	23.05	19.85	20.39	4.90		48.17	59.50	53.15	53.61	1.87
QWA-0947-093	2.64	Vaccinated		155.82	147.87	143.25	148.98	0.67		126.83	113.67	124.04	121.51	0.82
QWA-0947-094	127.58	Vaccinated		160.76	145.63	119.61	142.00	0.70		105.84	110.91	114.14	110.30	0.91
QWA-0947-095	23.74	Vaccinated		176.74	160.65	159.27	165.55	0.60		110.83	103.36	112.17	108.78	0.92
QWA-0947-096	>1000	Vaccinated		51.24	50.60	36.36	46.07	2.17		109.95	99.89	100.76	103.54	0.97
QWA-0947-097	25.97	Vaccinated		151.86	144.37	127.26	141.16	0.71		109.63	109.86	98.50	106.00	0.94
QWA-0947-098	>1000	Vaccinated		73.82	83.70	70.82	76.11	1.31		88.55	95.98	100.28	94.94	1.05
QWA-0947-099	688.28	Vaccinated	BIG BLOOD DRAW	110.48	112.47	90.05	104.33	0.96		100.29	103.59	94.65	99.51	1.00
QWA-0947-100	366.05	Vaccinated		85.68	99.38	86.23	90.43	1.11		97.85	101.09	85.62	94.85	1.05
QWA-0947-101	1.22	Vaccinated		88.54	96.48	92.77	92.60	1.08		107.51	104.47	106.69	106.22	0.94
QWA-0947-102	0.65	Vaccinated		96.90	94.97	99.88	97.25	1.03		109.63	101.73	102.43	104.60	0.96
QWA-0947-103	45.53	Core Ab +		100.38	104.13	93.37	99.29	1.01		103.40	95.77	93.83	97.67	1.02
QWA-0947-104	95.76	Vaccinated		95.99	87.67	79.38	87.68	1.14		111.24	105.95	113.01	110.07	0.91
QWA-0947-105	1.48	Vaccinated		42.47	43.05	47.61	44.38	2.25		102.15	99.45	98.24	99.95	1.00
QWA-0947-106	>1000	Vaccinated		16.40	16.66	16.15	16.40	6.10		64.77	68.47	66.59	66.61	1.50
QWA-0947-107	32.84	Vaccinated		148.16	141.65	127.35	139.05	0.72		123.79	119.06	104.81	115.89	0.86

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QWA-0947-108	352.99	Vaccinated		78.23	81.50	84.50	81.41	1.23		109.31	116.46	103.38	109.72	0.91
QWA-0947-109	15.04	Vaccinated		112.45	103.15	97.70	104.43	0.96		110.85	121.08	117.28	116.40	0.86
QWA-0947-110	26.27	Vaccinated		86.31	102.24	99.68	96.08	1.04		115.57	130.13	116.61	120.77	0.83
QWA-0947-111	40.79	Vaccinated		81.44	86.98	87.80	85.40	1.17		109.93	98.54	91.77	100.08	1.00
QWA-0947-112	260.82	Core Ab +		35.62	36.63	32.67	34.97	2.86		69.44	65.66	65.06	66.72	1.50
QWA-0947-113	1.97	Vaccinated		93.25	98.77	81.76	91.26	1.10		101.75	104.27	100.12	102.05	0.98
QWA-0947-114	>1000	Vaccinated		32.49	27.64	25.33	28.49	3.51		80.93	61.56	71.59	71.36	1.40
QWA-0947-115	798.12	Core Ab +		13.86	14.67	15.02	14.52	6.89		45.62	46.82	42.16	44.87	2.23
QWA-0947-116	459.84	Vaccinated		99.96	93.67	81.32	91.65	1.09		107.55	108.08	109.31	108.31	0.92
QWA-0947-117	0.46	Vaccinated		98.06	92.72	95.42	95.40	1.05		106.12	104.66	111.74	107.51	0.93
QWA-0947-118	20.87	Vaccinated		15.182	146.04	144.65	147.50	0.68		112.36	109.15	112.429	115.26	0.87
QWA-0947-119	91.47	Vaccinated		114.36	109.63	108.87	110.96	0.90		108.91	112.79	110.489	108.86	0.92
QWA-0947-120	13	Core Ab +		44.97	45.06	40.30	43.44	2.30		102.35	110.61	97.70	103.55	0.97
QWA-0947-121	175.21	Vaccinated		91.44	91.91	96.95	93.43	1.07		166.31	164.27	144.97	158.52	0.63
QWA-0947-122	51.51	Vaccinated		95.47	92.45	100.97	96.30	1.04		180.79	174.92	143.73	166.48	0.60
QWA-0947-123	36.81	Vaccinated		145.77	156.75	146.88	149.80	0.67		180.84	176.71	135.18	164.24	0.61
QWA-0947-124	1.3	Vaccinated		147.11	133.31	131.87	137.43	0.73		170.89	169.84	127.57	156.10	0.64
QWA-0947-125	1.44	Vaccinated		110.99	111.85	118.19	113.68	0.88		178.09	178.48	149.45	168.67	0.59
QWA-0947-126	359.06	Core Ab +		79.16	76.31	85.67	80.38	1.24		167.98	161.85	154.57	161.47	0.62

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QWA-0947-127	1.23	Non-Vaccinated		12 8.7 5	12 5.4 0	14 3.5 4	132. 56	0.75		16 2.0 1	15 7.2 2	13 9.0 8	152. 77	0.65
QWA-0947-128	>100 0	Vaccinated		30. 63	25. 86	36. 31	30.9 4	3.23		69. 73	82. 09	84. 44	78.7 6	1.27
QWA-0947-129	0.17	Non-Vaccinated		16 6.5 6	15 6.8 6	15 7.8 9	160. 44	0.62		16 2.2 4	16 8.1 8	15 4.5 2	161. 65	0.62
QWA-0947-131	11.81	Vaccinated		14 3.1 4	12 9.6 7	11 4.9 8	129. 26	0.77		15 6.9 4	14 4.3 7	11 9.2 6	140. 19	0.71
QWA-0947-132	0	Non-Vaccinated		14 3.3 7	14 8.5 1	13 4.4 1	142. 09	0.70		17 0.7 2	14 6.0 3	12 6.5 6	147. 77	0.68
QWA-0947-133	731.2 7	Core Ab +		86. 48	85. 37	78. 16	83.3 4	1.20		15 7.6 4	13 7.8 7	13 1.0 7	142. 20	0.70
QWA-0947-134	>100 0	Vaccinated		31. 62	30. 52	27. 60	29.9 2	3.34		14 4.3 6	13 7.8 2	11 5.1 4	132. 44	0.76
QWA-0947-135	796.9 3	Core Ab +		81. 56	81. 84	88. 25	83.8 8	1.19		15 7.5 8	14 2.4 2	11 6.8 4	138. 95	0.72
QWA-0947-136	0	Non-Vaccinated		12 8.1 9	13 2.9 5	13 9.9 1	133. 68	0.75		16 5.8 5	14 0.5 6	13 7.5 8	148. 00	0.68
QWA-0947-137	1.56	Non-Vaccinated		15 5.0 9	15 1.9 3	13 7.0 5	148. 02	0.68		17 5.5 1	15 5.2 2	12 8.7 5	153. 16	0.65
QWA-0947-138	0.74	Non-Vaccinated		16 0.7 6	15 9.8 7	13 5.6 1	152. 08	0.66		16 5.3 0	13 7.9 6	11 9.5 2	140. 93	0.71
QWA-0947-139	0	Non-Vaccinated		14 3.9 6	14 5.7 1	12 3.9 8	137. 88	0.73		14 3.8 2	12 5.6 0	11 4.2 2	127. 88	0.78
QWA-0947-140	609.4 6	Core Ab +		93. 61	96. 21	89. 99	93.2 7	1.07		12 5.4 2	13 5.9 2	10 6.5 8	122. 64	0.82
QWA-0947-141	>100 0	Vaccinated		35. 14	37. 74	36. 31	36.4 0	2.75		90. 32	87. 71	83. 80	87.2 8	1.15
QWA-0947-142	0.01	Non-Vaccinated		72. 39	72. 79	69. 24	71.4 7	1.40		85. 86	89. 49	80. 98	85.4 4	1.17
QWA-0947-143	51.9	Vaccinated		83. 85	74. 96	78. 42	79.0 7	1.26		89. 70	83. 02	81. 24	84.6 5	1.18
QWA-0947-144	192.4 1	Vaccinated		99. 03	10 3.7 5	10 4.6 9	102. 49	0.98		88. 00	80. 96	10 0.2 1	89.7 3	1.11
QWA-0947-145	>100 0	Vaccinated		35. 23	36. 75	36. 99	36.3 2	2.75		91. 40	83. 04	84. 37	86.2 7	1.16
QWA-0947-146	>100 0	Vaccinated	BIG BLOOD DRAW	3.2 1	3.1 7	3.4 7	3.28	30.4 5		4.6 6	4.4 5	3.8 2	4.31	23.1 8

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QWA-0947-147	>1000	Vaccinated		74.42	79.63	70.02	74.69	1.34		96.43	89.82	90.93	92.39	1.08
QWA-0947-149	>1000	Vaccinated		48.09	53.38	53.47	51.65	1.94		85.58	89.74	84.49	86.60	1.15
QWA-0947-150	>1000	Vaccinated		45.84	50.91	49.78	48.84	2.05		97.27	93.55	92.90	94.57	1.06
QWA-0947-151	24.03	Vaccinated		76.16	78.93	83.53	79.54	1.26		104.49	103.12	97.68	101.76	0.98
QWA-0947-152	32.89	Vaccinated		76.50	74.31	58.42	69.75	1.43		80.82	81.72	78.43	80.33	1.24
QWA-0947-153	0.36	Vaccinated		92.38	95.06	83.56	90.33	1.11		81.13	82.29	70.79	78.07	1.28
QWA-0947-154	8.02	Vaccinated		81.20	78.04	61.49	73.58	1.36		89.89	80.29	72.54	80.90	1.24
QWA-0947-155	271.68	Vaccinated		83.98	86.99	69.06	80.01	1.25		79.14	80.93	74.47	78.18	1.28
QWA-0947-156	>1000	Vaccinated		23.65	20.82	15.97	20.15	4.96		78.25	75.10	58.66	70.67	1.42
QWA-0947-157	93.05	Vaccinated		93.75	95.02	83.23	90.67	1.10		77.02	80.62	70.27	75.97	1.32
QWA-0947-158	261.09	Vaccinated		78.75	78.50	64.50	73.92	1.35		88.22	86.79	71.09	82.03	1.22
QWA-0947-159	61.12	Vaccinated		87.14	91.02	76.00	84.72	1.18		80.77	86.19	74.40	80.45	1.24
QWA-0947-160	381.69	Vaccinated		72.70	68.79	62.46	67.98	1.47		81.13	74.64	66.11	73.96	1.35
QWA-0947-161	3.62	Vaccinated		91.93	85.42	72.87	83.40	1.20		85.76	80.35	74.62	80.24	1.25
QWA-0947-162	198.58	Vaccinated		91.35	92.25	79.20	87.60	1.14		112.63	106.14	95.29	104.69	0.96

[0165] Supplemental Table S2. Detailed information about cloned antibodies with paired heavy and light chains, Related to Figure 2.

[0166] Variable (V), diversity (D) and joining (J) genes, mutation on the variable gene (V MUT), and CDR3 amino acid sequences of cloned immunoglobulin heavy, kappa light and lambda light chains are listed. These antibodies are grouped by their IGHV genes, with our selected H001-H020 antibodies indicated. H021 antibody used for sequence alignment in Figure 2D is also indicated. The amino acid length of IGH CDR3 was between 5 and 27 amino acids, with the highest peak at 16 amino acids and the average around 15 amino acids. There are 16 of IGH CDR3 containing cysteines.

HEAVY CHAIN				KAPPA LIGHT CHAIN				LAMBDA LIGHT CHAIN			
DO NO R ID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	SEQ ID NO:
9	IG H V1										
	-	IGH D6-13*									
	18*0	1	01	2	IGHJ 6*0	GYT FTT	ISTY NRN T	27	26	28	29
55	IG H V1										
	-	IGH D2-15*									
	18*0	1	01	2	IGHJ 4*0	GYS FNT	ISTY NGK T	32	31	33	34
55	IG H V1										
	-	IGH D2-15*									
	18*0	1	01	2	IGHJ 4*0	GYS FNT	ISTY NGK T	37	36	38	39
55	IG H V1										
	-	IGH D2-15*									
	18*0	1	01	2	IGHJ 4*0	GYS FNT	ISTY NGK T	40	39	41	42

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 1							LEK LTL DY																	
55	IG H V1	IGH D2- 15* 01	IGHJ 4*0 2	GYS FNT YG	43	ISTY NGK T	44				IGK V3- 11* 01	IGKJ 1*0 1	QSV SSY	46	DAS	47	QH RS NS WT								
55	IG H V1	IGH D4- 17* 01	IGHJ 4*0 2	GYT FSS YG	48	ISA HSG NT	49												IGL V3- 25* 02	IG LJ 3* 02	ALP VQF	51	KD S	QSA DST ATY WV	52
99	IG H V1	IGH D3- 16* 01	IGHJ 6*0 3	GYS FSS YG	53	ISAY NGD T	54												IGL V3- 19* 01	IG LJ 3* 02	SLR TTY	56	GK N	GSR DNS GYS	57
99	IG H V1	IGH D6- 13* 01	IGHJ 4*0 2	GYT FGS FG	58	ISGY SGK T	59				IGK V3- 11* 01	IGKJ 4*0 1	QSV GSY	61	DAS	62	QQ YN DW LT								
14 6	IG H V1	IGH D1- 01	IGHJ 1*0 1	DYR SINS G	63	ISPF NGN T	64	AGD TTS	65		IGK V4- 01	IGKJ 3*0 1	ESV FFS	66	WAS	67	QQ YY								

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	- 18 *0 1	1*0 1				SAA LTF				1*0 1		PHN RNY			TT PS									
14 6	IG H V1	IGH D1- 26* 01	IGHJ 6*0 2	GYN FISY A	68	ISPY NGK K		ARF FGG ATM TVY FYG LDV	69	IGK V1- 5*0 1	IGKJ 1*0 1	QSI KT W	71	DAS T	QQ YN SYS GW T	72								
14 6	IG H V1	IGH D6- 19* 01	IGHJ 4*0 2	GYK FTN YG	73	INA YNG HT		TRS EQ WRS RGE Y	74								IGL V1- 44* 01	IG LJ 3* 02	NSN VG NN V	76	AN S		ASW DDS LSG SWV	77
14 6	IG H V1	IGH D1- 26* 01	IGHJ 5*0 2	GYT FSN YG	78	ISAS SGN T		GRD DSG SYP MSP	79	IGK V3- 20* 01	IGKJ 4*0 1	QSV SGS Y	81	GAS LA	QQ YX SSP LA	82								
14 6	IG H V1	IGH D1- 20* 01	IGHJ 4*0 2	GYT FRN YG	83	INA HNG DT		VRD INFI FDY	84								IGL V7- 43* 01	IG LJ 3* 02	TGA VTS SYV	86	RT N		LLY XWS SSA LG	87
69	IG H V1	IGH D3- 01	IGHJ 6*0 3	GYS FTS YG	88	INV YNA NT		ARE GWF GEF	89	IGK V3- 01	IGKJ 1*0 1	LSV SSN	91	DAS EW	QQ YH EW	92								

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	HEAVY CHAIN											KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN						
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	- 18 *0 4	10* 01					RRN YNY NYY MD V			15* 01						PR T								
49	IG H V1	IGH D4- 11* 01	IGHJ 3*0 1	GYT LTE LS	93	FDP DEG EV	94	TLV TRV DAF DV	95	IGK V1- 39* 01	IGKJ 2*0 1	QSV RTY	96	AAS	QQ SYF AP YT	97								
49	IG H V1	IGH D4- 11* 01	IGHJ 3*0 1	GYS HTE LP	98	FDP DEG ET	99	TLV TRV DAF EV	100	IGK V1- 39* 01	IGKJ 2*0 1	QNI RNY	101	AAS	QQ SYF AP YT	102								
49	IG H V1	IGH D2- 21* 02	IGHJ 3*0 1	GYT LTE LP	10	FDP DEG ET	10	TLV TGV DAF AV	105	IGK V1- 39* 01	IGKJ 2*0 1	QNI RTY	106	TAS	QQ SYF AP YT	107								
49	IG H V1	IGH D3- 16* 01	IGHJ 3*0 1	GYIF SEL S	10	FDP DEG ET	10	TSVI KAD AFE V	110	IGK V1- 39* 01	IGKJ 2*0 1	QNI RTY	111	VAS	QQ SYF AP YT	112								

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
13	IG H V1	IGH																						
	- 3*	D2- 21*	IGHJ 6*0	GYT FTH	11 3	LNG GND	11 4			IGK V3- 20*	IGKJ 4*0	QSV SSS	116 Q		QH YN NP	117	IGL V3- 21*	IG LJ 2*	NIR NK		AD	118	QV WD GGS YHV	119
	01	01	2	YA	3	DR	4	V	115	01	1	Q	116	GAS	VA	117	02	01	N		S	118	I	119
13	IG H V1	IGH																						
	- 3*	D3- 10*	IGHJ 4*0	GYT FTR	12 0	INA ANG	12 1										IGL V2- 11*	IG LJ 2*	SSD VGG		DV	123	CSY AGN YILV	124
	01	01	2	YP	0	DT	1	FDN	122								01	01	YNY		N	123		124
69	IG H V1	IGH																						
	- 3*	D2- 2*0	IGHJ 3*0	GYN FQR	12 5	INV GNG	12 6			IGK V1- 5*0	IGKJ 2*0	ENI GG	128 W	KAS		QQ YN SYS RY								
	01	1	1	SA	6	NT	6	FDF	127	3	1	W	128		T	129								
99	IG H V1	IGH																						
	- 3*	D3- 10*	IGHJ 4*0	GYT FTS	13 0	INP ANG	13 1										IGL V2- 11*	IG LJ 3*	NSD VGG		DV	133	SSY AGK YTL	134
	01	01	2	YP	0	DT	1	FDL	132								01	02	YNY		T	133	V	134
14 6	IG H V1	IGH																						
	- 3*	D1- 1*0	IGHJ 3*0	GYT LTS	13 5	INA GSG	13 6			IGK V1- 39*	IGKJ 4*0	QSV STY	138	TAS	QQ SSS VP	139								
	01	1	2	YA	6	LT	6	I	137	01	1	1	138		LT	139								
14 6 H 0	IG H V1	IGH																						
	- 3*	D3- 10*	IGHJ 3*0	GYT FTT	14 0	INA GNG	14 1			IGK V1- 1	IGKJ 4*0	QSV STY	143	SAS	QQ SYS	144								
	01	01	2	YA	0	IT	1	VRG	142	V1- 1	1	1	143		SYS	144								

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		HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
01	-	16* 01						AGG SPF DI			39* 01						TP LT								
	IG H V1	IGH						ARV GIL VRG			IGK V1- 39* 01	IGKJ 4* 01	QSI TY 148			QQ SYS TP LT 149									
146	-	D3- 16* 01	IGHJ 3* 02	GYT FTT 14 5	INA GNG IT 14 6			AGG SPF DI 147			IGK V1- 5* 03	IGKJ 4* 01	QSV STW 153			QL YN SYS GT T 154									
	IG H V1	IGH						ARE DYT GNY YDA FDF 152			IGK V1- 5* 03	IGKJ 4* 01													
146	-	D4- 11* 01	IGHJ 3* 01	GYT FSR HA 15 0	INIG NGN T 15 1			ARD GVK EQL VYY YFG MD V 157																	
	IG H V1	IGH																	IGL V1- 40* 01	IG LJ 2* 01	SSN IGK NY D 158		GD T	QSY DSN LSG SVV 159	
146	-	D6- 13* 01	IGHJ 6* 02	GYS FSN YA 15 5	INA AYG NT 15 6			ARG ALL WF RDD FDF 162			IGK V1- 27* 01	IGKJ 3* 01	QGI SNY 163			QK YD SA PY T 164									
	IG H V1	IGH																	IGL V1- 51* 01	IG LJ 1* 01	SSN IGK NY TY 165		DN N	GSW DSS LYS FYV 166	
99	-	D2- 2* 01	IGHJ 1* 01	GYT FSN YH 16 7	INPS GDS T 16 8			ASR LDA IPF QV 169			IGK V3- 20* 01	IGKJ 2* 01	PNA NSG S 170			QQ YG GL PF T 171									
	IG H V1	IGH																							

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
99	IG H V1	IGH D4- 23* 01 01	IGHJ 6*0 4	GYI VTS YR	17 2	IDPS DTY T	17 3	ARK GNY GSR YD WYF DV	174									IGL V2- 14* 01	IG LJ 3* 02	SSD VG DYS Y	175	DV N	SSY TSS STG V	176
55	IG H V1	IGH D3- 9*0 1	IGHJ 3*0 1	GYT FTN FN	17 7	INP GAG TT	17 8	YFD WQS RDA FDV	179	IGK V1- 17* 01	IGKJ 3*0 1	QGI RND	180	AAS	LQ HN GY PIT	181								
60	IG H V1	IGH D3- 10* 01	IGHJ 6*0 1	GGT FSS YS	18 2	IVPI FGIP	18 3	AM DV	184	IGK V1- 39* 01	IGKJ 3*0 1	QSI NY	185	GAS	QQ SYS TL FS	186	IGL V2- 14* 01	IG LJ 1* 01	SSD VGG YKY	187	EV T	SSY TGS STR YV	188	
14 6	IG H V1	IGH D3- 3*0 1	IGHJ 4*0 2	GGK FIAY G	18 9	TIPI YGT A	19 0	YPN QFF DH	191	IGK V1- 17* 03	IGKJ 1*0 1	QGI SNS	192	GAS	LQ HN TY PW T	193								
13	IG H V2	IGH D3- 9*0 1	IGHJ 5*0 2	GFS FST GGV G	19 4	IYG DGD E	19 5	LLT AYY DH	196	IGK V1- 5*0 3	IGKJ 1*0 1	QSI RW	197	KAS	QQ YN SYS WA	198								

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HEAVY CHAIN														KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:	
55	IG H V2 - 5* 02	IGH D6- 13* 01	IGHJ 5*0 2	GFS LST FGV G	19 9	IYW DDD K	20 0	AHT VAA AAT FWF DP	201								IGL V1- 44* 01	IG LJ 2* 01	SSN IGS NT	202 N	ST N	AT WD DSL NGL V	203		
	69	IG H V2 - 5* 02	IGH D2- 21* 02	IGHJ 3*0 2	GFS LST TAV G	20 4	IYG DDD K	20 5	AHS SYF DCG GDC SDV AFD I	206							IGL V3- 10* 01	IG LJ 3* 02	ALP RKY	207 N	ED N	YST DSS GDP V	208		
14 6		IG H V2 - 5* 02	IGH D2- 15* 01	IGHJ 3*0 1	GFS LTT NG MG	20 9	IYW DDD K	21 0	ARS YCR GGN CYS TAF NV	211							IGL V2- 11* 01	IG LJ 2* 01	SSD VGG YDY	212 N	GV N	CSY AGA YTY VA	213		
H 0 0 2	14 6	IG H V2 - 70 D* 04	IGH D7- 27* 01	GFS LST NT MR	21 4	IDW DDE K	21 5	ARS NH WGS HFD Y	216								IGL V3- 21* 02	IG LJ 1* 01	NIG GKT	217 S	DN S	QV WD TSG DHL YV	218		
55	IG H V3 - 11 *0 1	IGH D2- 21* 01	IGHJ 3*0 1	GFT FSD YY	21 9	IRGS HSS V	22 0	ARD LPG DEY LDA FDL	221	IGK V4- 1*0 1	IGKJ 4*0 1	QSL LYS SNN KNY	222	WAS	QQ FY TA PL T	223									

		HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:		V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:		V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
60	IG H V3 - 11 *0 1	IGH D6- 13* 01 01	IGHJ 6*0 2	GLT LSD YY 4	22 4	ISH DGS TI 5	22 5	ASG AAV PYF YYG VDV 226											IGL V3- 1*0 1	IG LJ 2* 01		KLG DAY 227	QD T		QA WGS SPA KV 228	
99	IG H V3 - 13 *0 1	IGH D3- 22* 01 01	IGHJ 4*0 2	GFT FSS YD 9	22 9	IGA ATD T 23	23 0	ARA VHY YDS SGH YSG YYF DY 231											IGL V1- 44* 01	IG LJ 2* 01		SSN IGS NT 232	SN N		AT WD ASL KGV V 233	
55	IG H V3 - 15 *0 1	IGH D1- 1*0 1	IGHJ 4*0 2	GFT FSN AW 4	23 4	IRSK TDG GTA 5	23 5	TTQ NAF ES 236											IGL V3- 21* 01	IG LJ 1* 01		NIG SKS 237	YD S		QV WD SSS DHY V 238	
55	IG H V3 - 15 *0 1	IGH D2/ OR1 5- 2a*0 1	IGHJ 6*0 2	GFT FSN AY 9	23 9	IKSI TDG GTI 0	24 0	HTL STT HYY GM DV 241			IGK V3- 20* 01	IGKJ 4*0 1	QSV TSN Y 242		GAS	QQ YIN SPL T 243										
14 6	IG H V3 - 15 *0 1	IGH D6- 25* 01 01	IGHJ 4*0 2	GFT FSN TY 4	24 4	IQR KTD GGT A 246	24 5	AAH NRA AY 247			IGK V1- 5*0 1	IGKJ 2*0 1	QSI NW 247		DAS	QQ YY SY PL T 248										

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		HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
	DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	9	IG H V3	IGH D3- 3*0 1 2	IGHJ 4*0 2 2	GLT FST HS	24 9	ISGS SDYI	25 0	ARA RPP GTA FGF DH	251									IGL V1- 40* 01	IG LJ 2* 01	SSN IGA GYD	252 N	DN N	QSY DSS LSG AL	253
	13	IG H V3	IGH D3- 16* 01 01	IGHJ 4*0 2 2	GFT FSS YV	25 4	VSS SSYS I	25 5	VRT FYF DY	256	IGK V3- 15* 01	IGKJ 1*0 1 1	QSV RTN	257	SAS	QQ YDI WP PR T	258								
	55	IG H V3	IGH D4- 17* 01 01	IGHJ 1*0 1 1	GFT FSS FS	25 9	ISSS SRYI	26 0	VRD MTT VTT CXX QH	261								IGL V1- 44* 01	IG LJ 2* 01	SSN IGS HT	262 S	TN S	AA WD DSL NGL V	263	
	55	IG H V3	IGH D4- 17* 01 01	IGHJ 1*0 1 1	GFT FSS FS	26 4	ISSS SRYI	26 5	VRD MTT VTT CYL QH	266								IGL V1- 44* 01	IG LJ 2* 01	SSN IGS HT	267 S	TN S	AA WD DSL NGL V	268	
	14 6	IG H V3	IGH D4- 17* 01 01	IGHJ 4*0 2 2	GFS FSIY S	26 9	IGN RGN PK	27 0	ARG RTY GDS N	271	IGK V3- 15* 01	IGKJ 1*0 1 1	RSIS SN	272	RAS	QQ YD NW HT	273								

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	HEAVY CHAIN											KAPPA LIGHT CHAIN					LAMBDA LIGHT CHAIN									
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:	
14 6	IG H V3	IGH D3- 3*0 1 1	IGHJ 4*0 2	GFS FNA YS	27 4	ISS SSYI	27 5	ARV PILL AQG VPT FDL	276	IGK V3- 15* 01	IGKJ 2*0 1	QSV NSN	277	SAS YT	278		QQ YS DW PR YT									
9	IG H V3	IGH D2- 2*0 1 2	IGHJ 6*0 3	GFT FTR YT	27 9	VSG SGS ST	28 0	AKA AIL GNY NYY MD V	281									IGL V3- 21* 02	IG LJ 2* 01	NIA SKS	282 N	DD N		QV WD SSA DHL VV	283	
13	IG H V3	IGH D1- 1*0 1 1	IGHJ 4*0 1	EFR FGS YA	28 4	IIAT GAK T	28 5	VKD AIY MSN WP WYF DY	286									IGL V3- 21* 02	IG LJ 2* 01	NIG SKS	287 N	DD N				
13	IG H V3	IGH D6- 13* 01 01	IGHJ 4*0 2	GFT FTN YA	28 8	ISGS GGS T	28 9	AKD PIYS SSW PYY FDY	290									IGL V3- 21* 02	IG LJ 2* 01	NIG SRG	291 S	ED S		QV WD SSS DHP EVV	292	
H 0 2 1	13	IGH D6- 13* 01 01	IGHJ 4*0 2	GFR FSS YA	29 3	ISGS GGS T	29 4	AKD PIYT SRW PYY FDY	295	IGK V1- 39* 01	IGKJ 2*0 3	QSS SY	296	AAS LYS	297		QQ SYS LYS		IGL V3- 21* 02	IG LJ 2* 01	NIG SKS	298 S	DD S		QV WH SSS DHS EVI	299

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HEAVY CHAIN													KAPPA LIGHT CHAIN					LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:		
13	IG H V3	IGH D3- 10* 01	IGHJ 4*0 2	GFR	30	ISGR DAS T	30	AKD GVL GSY HQY YFQ Y	302								IGL V3- 21* 02	IG LJ 2* 01	NIG SKS	303	DD T		QV WD NSS DHP GVV	304		
	FSS			30																						
	YA			0																						
13	IG H V3	IGH D5- 12* 01	IGHJ 4*0 2	GFT	30	ISGS GGS T	30	AKG SRN GPYI VAT LHF DY	307	IGK V3- 15* 01	IGKJ 4*0 1	QSV SSN	308	GAF	QH YN HW SL T	309										
	FSS			30																						
	YA			5																						
55	IG H V3	IGH D6- 13* 01	IGHJ 4*0 2	GFT	31	VSG NGG ST	31	VLS SSW MD NPF DF	312								IGL V5- 45* 02	IG LJ 3* 02	SGI NV GTY R	313	YK SD SD K		MIW HSS AW V	315		
	FNN			31																						
	YA			0																						
55	IG H V3	IGH D1- 26* 01	IGHJ 4*0 2	GFT	31	ASA SGR NT	31	AGF PSG THF FDY	318	IGK V3- 11* 01	IGKJ 1*0 1	QSV SNH	319	DAS	QQ RS NW WT	320										
	FSS			31																						
	YA			6																						
55	IG H V3	IGH D1- 26* 01	IGHJ 4*0 2	GFT	32	ASA SGR NT	32	AGF PSG THF FDY	323	IGK V3- 20* 01	IGKJ 4*0 1	QSV SNS Y	324	GAS	QQ FG SSP LT	325	IGL V2- 8*0 1	IG LJ 1* 01	SSD IGG YNY	326	EV N		NSY AGN NNF V	327		
	FSS			32																						
	YA			1																						

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R3	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:		
55	IG H V3 - 23 *0 1	IGH D2- 2*0 1	IGHJ 6*0 2	EFT	32 8	ISGS GDT T	32 9	ARP	330	IGL V1- 44* 01	IG LJ 3* 02	SSN IGT NT	331 N	SN N	AA WD DRL IGW V						
				FSS				YGM												DV	
				YA																	
55	IG H V3 - 23 *0 1	IGH D1- 26* 01	IGHJ 4*0 2	GFT	33 3	ISG NGG FT	33 4	AKR	335	IGK V3- 20* 01	IGKJ 2*0 1	QSV SNS Y	336 GVS	QQ YG SSP PY T							
				FSS				RYF												MVE	
				HG				DY												ATN	
55	IG H V3 - 23 *0 1	IGH D1- 26* 01	IGHJ 4*0 2	GFT	33 8	ISA NGI YT	33 9	ARD	340	IGL V2- 11* 01	IG LJ 2* 01	SSD VGG YNY	341 N	DV N	CSY AGS YTV V						
				FIN				GID												SSE	
				YA				F												WVL	
60	IG H V3 - 23 *0 1	IGH D4/ OR1 5- 4a*0 1	IGHJ 2*0 1	GFT	34 3	ITGS GGS T	34 4	AKD	345	IGL V3- 21* 02	IG LJ 2* 01	NIG IKS	346 T	DD T	QV WD SNS DHP KVV						
				FSS				WYF												AVR	
				YA				DF												SAN	
																				HA	
60	IG H V3 - 23 *0 1	IGH D5- 12* 01	IGHJ 4*0 2	GFT	34 8	ISSN GAG T	34 9	AKG	350	IGK V3- 15* 01	IGKJ 1*0 1	QSL VTN	351 GAS	QQ YIN WP PW S							
				FSS				YGL												AKG	
				TA				FDS												YGL	

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HEAVY CHAIN													KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 1																							
H 60 0 23 0 21* 3 1 01	IG H V3	IGH D2- 21* 01	IGHJ 2*0 1	GFT FSS YA	35 3	LTA TGG NT	35 4	AKD AIR NSN HA WYF DV	355								IGL V3- 21* 02	IG LJ 2* 01	NIG SKS	356	DD N		QV WD PTS DQV	357
	IG H V3	IGH D2- 8*0 1	IGHJ 4*0 2	GFT FSS YG	35 8	ISGR GDE T	35 9	AKS RVT NSG SID H	360	IGK V1- 39* 01	IGKJ 5*0 1	QTI GTU	361	AAS	QQ SYS TSI T									
60	IG H V3	IGH D4/ OR1	IGHJ 2*0 1	GFR FNN YA	36 3	ISGG DGY T	36 4	AKD AILS ANH PWY FDF	365	IGK V4- 1*0 1	IGKJ 4*0 1	QSV LYS SNN KNY	366	WAS	QQ YY ST PL T		IGL V3- 21* 02	IG LJ 3* 02	NIG TNS	368	ED S		QV WD SSS DHP KVV	369
60	IG H V3	IGH D2- 21* 01	IGHJ 2*0 1	GFT FSS YA	37 0	IVN SGG ST	37 1	AKD AIRS SNH PWY FHV	372								IGL V3- 21* 02	IG LJ 2* 01	NIG SES	373	DD S		QV WD GSS DHP KVL	374
60	IG H V3	IGH D4/ OR1	IGHJ 2*0 1	GFR FNN YA	37 5	ITG GEG YT	37 6	AKD AILS ANH PWY FDF	377								IGL V3- 21* 02	IG LJ 3* 02	NIG TNS	378	ED S		QV WD RSS DQS KVV	379

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 1	4a*0 1																						
14 6	IG H V3	IGH D3/ OR1	IGHJ 4*0 2	GFT FST HA	38 0	ISGG SEW S	38 1	AKG YGL FDF	382	IGK V3- 15* 01	IGKJ 1*0 1	QSV SSN	383	GPS	QQ YIN RP PW T	384								
9	IG H V3	IGH D1- 1*0 1	IGHJ 4*0 2	GFT FSN YA	38 5	IYT GGS KT	38 6	AKV LLG GW NGV FDH	387	IGK V3- 11* 01	IGKJ 4*0 1	QSV DSY	388	DAS	QQ RS TW PP S	389								
14 6	IG H V3	IGH D3- 10* 01	IGHJ 6*0 2	GFR FNN YG	39 0	FSG SGS NI	39 1	AKD GYF GSG SLY GID V	392								IGL V3- 21* 02	IG LJ 2* 01	NIG SKS	393	ED S	QV WD SNH DHP GVV	394	
14 6	IG H V3	IGH D3- 10* 01	IGHJ 6*0 2	GFT FTS YA	39 5	ISGS GGS T	39 6	AKD GYG GSG SLY GM DV	397								IGL V3- 21* 02	IG LJ 2* 01	NIG SKS	398	DD S	QV WD STS DHP GVV	399	
14 6	IG H V3	IGH D3- 9*0 1	IGHJ 6*0 2	GFT FSS YA	40 0	FSG SGS ST	40 1	AKV IQY PRG FWF	402								IGL V1- 51* 01	IG LJ 3* 02	SSN IGN NY	403	DN N	GT WD SSL NNC V	404	

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 4							YGM DV															
	IG H V3																						
	- 30	IGH	IGHJ 6*0 2	GFT		ISYD		ARD PGV PYY HYA MD V															
	- 3*	D3- 10*			40 5	GST H	40 6																
60	01	01	2	YA	40 5																		
	IG H V3																						
	- 30	IGH	IGHJ 4*0 2	EFT		ISA		VRD ETD WEI GVV VAT PEF DY															
	- 3*	D3- 3*0			41 0	DGN NR	41 1																
14 6	01	1	2	YA	41 0																		
	IG H V3																						
	- 30	IGH	IGHJ 4*0 2	GFP		LSF		VTG IRA RDY GGS TFD L															
	- 3*	D4- 23*			41 7	NGD YI	41 8																
	02	01	2	HA	41 7																		
	IG H V3																						
	- 30	IGH	IGHJ 3*0 1	GFR		IRY		AKD GR WFG ESG GFD V															
	0 2	D3- 10			42 2	DGS KK	42 3																
9	2	01	1	YG	42 2																		

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
9	IG							ARD																	
	H							YCS																	
	V3							RTN																	
	-	IGH						CIN									QQ								
30	D2-		IGHJ	GFT		MSY										YG									
*0	2*0		2*0	FTS	42	DGS	42	WIF					PSV			SSP									
3	1	1	1	YS	7	YE	8	DL	429		IGK	IGKJ	SSSY	430	GVS	LT	431								
60	IG																								
	H							AKD																	
	V3							GYL																	
	-	IGH						SAA																	
30	D2-		IGHJ	GFR		ISN																			
*0	8*0		6*0	FTG	43	DGS	43	GM																	
3	2	2	2	YG	2	KK	3	DV	434																
146	IG																								
	H																								
	V3																								
	-	IGH																							
30	D4-		IGHJ	GFT		ISYD		ARD																	
0	17		4*0	FSN	43	GSN	43	DYY																	
3	01	2	2	YD	7	K	8	FDY	439																
9	IG																								
	H							ARG																	
	V3							GGY																	
	-	IGH						TYG																	
30	D5-		IGHJ	KFT		TSY																			
0	18		6*0	FSK	44	NGG	44	YSM																	
4	01	2	2	YA	2	SK	3	DV	444		IGK	IGKJ	KNY	445	WAS	T	446								
9	IG																								
	H							ARG																	
	V3							GGY																	
	-	IGH						TYG																	
30	D5-		IGHJ	RFT		ISYD																			
0	18		6*0	FSK	44	GSS	44	YAM																	
4	01	2	2	YA	7	K	8	DV	449		IGK	IGKJ	KNY	450	WAS	T	451								

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		HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
	DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	55	IG H V3	IGH D1- 26* 01	IGHJ 4*0 2	GFT FSS YS	45 2	MSN TGS TK	45 3	ARA LLS VVG SKS YYF DF	454 3	IGK V3- 11* 01	IGKJ 1*0 1	QSV SSY	455	DAS	QH RS NS WT	456								
	55	IG H V3	IGH D1- 26* 01	IGHJ 4*0 2	GFT FSS YS	45 7	MSN TGS TK	45 8	ARA LLS VVG SKS YYF DF	459	IGK V3- 11* 01	IGKJ 1*0 1	QSV SSY	460	DAS	QH RS NS WT	461								
	55	IG H V3	IGH D1- 26* 01	IGHJ 6*0 2	GFN FNV YA	46 2	ISYD GSK K	46 3	ARD EKY SGL YSG RTG DYY YGM DV	464		IGL V1- 51* 01	IG LJ 2* 01	NSN IGN NF	465	NS D								GT WD SSLS LGV	466
	55	IG H V3	IGH D3- 22* 01	IGHJ 6*0 2	GFT FSA YS	46 7	ISYD GSN R	46 8	ARD GKL GRT YHD SRQ SYF YIM DV	469		IGL V2- 14* 01	IG LJ 2* 01	SSD VGG YNY	470	DV N								SSY TSS TSL V	471
	13	IG H V3	IGH D3- 10* 01	IGHJ 6*0 2	GFR FSS YG	47 2	TSF DGS KT	47 3	AKD AAY FAS GSF	474		IGL V3- 21* 02	IG LJ 2* 01	NIG SKS	475	DD N								QV WGS GGV I	476

HEAVY CHAIN													KAPPA LIGHT CHAIN					LAMBDA LIGHT CHAIN						
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*1 8							FGM DV																
13	IG H V3	IGH D3- 10*	IGHJ 6*0 2	GFT	47 7	ISYD GSN K	47 8	AKD AYY YGS GYG MD V	479 3	IGK V1- 5*0 3	IGKJ 4*0 1	QSYS VW	480	KAS	QQ YT SFS T	481	IGL V1- 47*	IG LJ 1* 01	SSN IGS RN N	482 N	AA WD DRL SGY V	483		
	FSR YG																							
60	IG H V3	IGH D3- 10*	IGHJ 6*0 2	GFT	48 4	ISSD GSK K	48 5	AKD GYV VSG SGY GM DV	486								IGL V3- 21*	IG LJ 2* 01		487 S	QV WD SSS DHV V	488		
	FRS YG																							
60 H 0 0 9	IG H V3	IGH D1- 26*	IGHJ 6*0 2	RFS FNT YG	48 9	ISYD GSH E	49 0	AKT DIK WG ATN YGM DV	491								IGL V3- 21*	IG LJ 2* 01		492 N	QV WD GTR DHL VV	493		
	FNT YG																							
60	IG H V3	IGH D5- 12*	IGHJ 4*0 2	GFT FSN YA	49 4	TLY DGS HS	49 5	AKD SAG YGL HY	496	IGK V1- 17* 01	IGKJ 1*0 1	QGI RTD	497	AAS	LQ HN SY PW T	498	IGL V3- 19*	IG LJ 2* 01		499 D	NSR DSI GNH VV	500		
	FSN YA																							
60	IG H V3	IGH D3- 22*	IGHJ 6*0 2	GFR FTG YG	50 1	ISN DGS KK	50 2	AKD GYL SAA RGY	503								IGL V3- 21*	IG LJ 2* 01		504 S	QV WD TTT DQL V	505		
	FTG YG																							

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN										
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:		V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:		V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:	
	*1 8							GM DV																			
60	IG H V3	IGH D3- 22* 01	IGHJ 6*0 2	GFR FTG YG	50 6	ISN DGS KT	50 7	AKD GYL SAA RGY GM DV	508											IGL V3- 21* 02	IG LJ 2* 01	NIG GKS	509	DD S		QV WD TTS DQL V	510
60	IG H V3	IGH D3- 22* 01	IGHJ 6*0 2	GFR FTG YG	51 1	ISN DGS KK	51 2	AKD GYL SAA RGY GM DV	513											IGL V3- 21* 02	IG LJ 2* 01	NIG ALS	514	DD N		QV WD TSS DQL V	515
H 0 0 5	IG H V3	IGH D3- 16* 01	IGHJ 6*0 2	GFR FTG YG	51 6	ISN DGS KK	51 7	AKD AYL SAA RGY GM HV	518											IGL V3- 21* 02	IG LJ 2* 01	NIG GKS	519	DD S		QV WD TAS DQL V	520
60	IG H V3	IGH D3- 22* 01	IGHJ 6*0 2	GFR FTG YG	52 1	ISN DGS KK	52 2	AKD GYL SAA RGY GM DV	523											IGL V3- 21* 02	IG LJ 2* 01	NIG GKS	524	DD R		QV WD TTS DQL V	525
60	IG H V3	IGH D3- 22* 01	IGHJ 6*0 2	GFR FTG YG	52 6	ISN DGS KK	52 7	AKD GYL SAA RGY	528											IGL V3- 21* 02	IG LJ 2* 01	NIG GKS	529	DD T		QV WD TTS DQL V	530

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HEAVY CHAIN												KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R3	SEQ ID NO:	CDR 2	SEQ ID NO:	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R3	SEQ ID NO:	
60	*1 8							YGM DV																		
	IG H V3	IGH						AKT DIM WR																		
	- 30	D2-15*	IGHJ 6*0	RFS FST YG	58 1	ISYD GSE K	58 2	AVN YGM DV	583	IGL V3-21* 02	IG LJ 2* 01	NIG SKS	584 N	DD N												
	*1 8	01	2																							
60	IG H V3	IGH						AKT DIM WQ AVN YGM DV																		
	- 30	D2-21*	IGHJ 6*0	GFS FST YG	58 6	ISYD GSS K	58 7	AVN YGM DV	588	IGL V3-21* 02	IG LJ 2* 01	NIG SKS	589 N	DD N												
	*1 8	01	2																							
	IG H V3	IGH						AKD GYL SAA RGY GM DV	593	IGL V3-21* 02	IG LJ 2* 01	NIG GKS	594 R	DD R												
60	IG H V3	IGH						AKT DIM WR																		
	- 30	D2-15*	IGHJ 6*0	RFS FST YG	59 6	ISYD GSE K	59 7	AVN YGM DV	598	IGL V3-21* 02	IG LJ 2* 01	NIG SKS	599 N	DD N												
	*1 8	01	2																							
	IG H V3	IGH						AKD GYL SAA RGY	603	IGL V3-21* 02	IG LJ 2* 01	NIG GKS	604 R	DD R												

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:	
	*1 8							GM DV																
H 0 0 8	IG H V3	IGH						AKD GIL GAR																
	- 30 *1 8	D1- 26* 01	IGHJ 6*0 2	GFR FTM YG	60 6	IPF DGR TQ	60 7	RGL YGI DV	608															
H 0 0 7	IG H V3	IGH						AKD IGG FDF RSG																
	- 30 *1 8	D3- 3*0 1	IGHJ 6*0 2	GFT FNN YA	61 1	ISYD GSN K	61 2	SQR SYY YYG VDV	613															
14 6	IG H V3	IGH						AKD IGG FDF RSG DQL TTY																
	- 30 *1 8	D3- 3*0 1	IGHJ 6*0 2	GFT FSR HG	61 6	ISYD GGN K	61 7	YYG MD V	618															
14 6	IG H V3	IGH						AKD AYI YAR																
	- 30 *1 8	D5- 18* 01	IGHJ 6*0 2	GFS FSN YG	62 1	ISYD GSN K	62 2	GSY YGM DV	623															

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		HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
	DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
		*1 8																							
	14 6	IG H V3 - 30 *1 8	IGH D1- 20* 01	IGHJ 4*0 2	GFT FSN YG 1	65 1	TSY DGI NK 2	65 2	AKD PVH RSN WFF FDH 653									IGL V3- 21* 02	IG LJ 2* 01	YIG SKT 654	654 R	DD		QV WYS NSE PVV 655	
	14 6	IG H V3 - 30 *1 8	IGH D3- 3*0 1	IGHJ 6*0 2	GTS FST SG 6	65 6	ISPN AFD K 7	65 7	AKG SPII RFL MM DV 658		IGK V1- 5*0 3	IGKJ 1*0 1	QSI DT W	659	KAS	QY YS VY ST 660		IGL V3- 21* 02	IG LJ 3* 02	NIG SKN 661	661 N	DD		QV WD NNS DHV V 662	
	13	IG H V3 - 33 *0 1	IGH D6- 13* 01	IGHJ 4*0 2	GFT FSS YG 3	66 3	IWS DGS NK 4	66 4	ARE AGI AAP ASL DF 665									IGL V3- 21* 02	IG LJ 2* 01	NIR GKS 666	666 S	AD		QV WD SSS DHV V 667	
	13	IG H V3 - 33 *0 1	IGH D6- 13* 01	IGHJ 4*0 2	GFT FSN YG 8	66 8	IWS DGT NK 9	66 9	TRE AGI AAP AAL DY 670									IGL V3- 21* 02	IG LJ 2* 01	NIG NK N 671	671 N	DD		QV WD SSSY HVV 672	
H 0 1 1	13	IG H V3 - 33	IGH D1- 7*0 1	IGHJ 3*0 1	GFT FSN YG 3	67 3	VW YDG SYK 4	67 4	VRD NW SYN AFD V 675		IGK V3- 11* 01	IGKJ 2*0 3	QSI SY	676	GTS	QH RN SW PY S 677									

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 1																				
13	IG H V3	IGH D3- 10* 01	IGHJ 3*0 2	GFT FSS YG	70 3	VW YDG SYK	70 3	VRD NW SYN AFD I	705 4	IGK V3- 11* 01	IGKJ 2*0 3	QSSS SY	706 3	QH RN SW PY S	707 S						
13	IG H V3	IGH D1- 20* 01	IGHJ 3*0 2	GFT FSN YG	70 8	IWY DGS YK	70 9	ARD NW KYN AFD I	710 9	IGK V3- 11* 01	IGKJ 2*0 3	QSSS SSY	711 3	QH RS NW PY S	712 S						
13	IG H V3	IGH D6- 19* 01	IGHJ 4*0 2	GFT FSR YG	71 3	IWS DGS NQ	71 4	ARE SSG WYY FDY	715 4							SSD VG NY NF	IG LJ 1* 01	EG S	716 S	CLY AGS SISY V	717 V
13	IG H V3	IGH D6- 13* 01	IGHJ 5*0 2	GFT FSS FG	71 8	IWY DGS NE	71 9	ARE ERI AAP ASL DL	720 9								IG LJ 2* 01	AD S	721 S	QV WD SST YHV V	722 V
13	IG H V3	IGH D6- 25* 01	IGHJ 4*0 2	GFT FSS YG	72 3	IWH DGT NQ	72 4	ARE LRI AAP AAL DY	725 4								IG LJ 2* 01	AD S	726 S	QV WD SGS DHV L	727 L

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	DO NO RID	HEAVY CHAIN						KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
		V	D	J	CDR 1	SEQ ID NO:	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 1	J	CDR 2	SEQ ID NO:
		*0 1																	
		IG H V3																	
		- 33	IGH D3- 16*	IGHJ 4*0 2	GFT FSS FN	72 8		ARQ MFT GHF DY	730 9	IGK V3- 15*	IGKJ 1*0 1	QGV SSN	731	QH YN NW PR T	732				
	49	1	01																
		IG H V3						ARE GRG QLL		IGK V3- 20*	IGKJ 3*0 1	QSV SSSY	736	QQ YG RS QG FT	737				
	60	1	2*0 1					FHG MD V	735 4										
		IG H V3						ARD GHC DGG											
		- 33	IGH D2- 21*	IGHJ 4*0 2	GFT FSG HG	73 8		CYS ALY DY	740 9										
	60	1	02																
		IG H V3						ARE DPH LLIA TLD L	745 4	IGK V1- 39*	IGKJ 4*0 1	QGL TSF	746	QQ SY GT PA LA	747				
		- 33	IGH D6- 6*0	IGHJ 4*0 2	GFS FSR HG	74 3													
	60	1	1																
		IG H V3						ARE TTIF NW YFD L	750 9	IGK V1- 39*	IGKJ 4*0 1	QSI NKY	751	QQ SFS IPP T	752				
	60	33	IGH D4- 11*	IGHJ 2*0 1	GFT FRS YG	74 8													

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN									
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:		V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:		V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 1																									
60	IG H V3																									
	- 33 *0 1	IGH D2- 21* 01	IGHJ 2*0 1	GFT FRN YG	77 8	IWA DGT NQ	77 9	ARE TTIF QW YFD L	780	IGK V1- 39* 01	IGKJ 4*0 1	QSI NNY	781	GAS	QQ SFS IPP T	782										
	IG H V3																									
69	- 33 *0 1	IGH D2- 15* 01	IGHJ 6*0 2	GFT FSS YG	78 3	IWY DGS LK	78 4	ARE TTF GRF CSG GSC YSD YYY GM DV	785	IGK V2- 24* 01	IGKJ 1*0 1	QSL VHS DGN TY	786	QIS	MQ AA QF PW T	787										
	IG H V3																									
	- 33 *0 1	IGH D6- 13* 01	IGHJ 4*0 2	GFV FSN YG	78 8	IWA DGT NS	78 9	ARE GGI VAA DK	790											IGL V1- 51* 01	IG LJ 1* 01	SSN IGN NY	791	DN N		
H 0 1 4 4	IG H V3	IGH																								
	- 33 *0 1	IGH D4/ OR1 5- 4a*0 1	IGHJ 4*0 2	GFS FSD YG	79 2	IWR DGS NS	79 3	ARE ARV AAP ASY DY	794										IGL V3- 21* 02	IG LJ 3* 02	KIV NK N	795	DD D	QV WD NGS NHV V	796	
	IG H V3	IGH	IGHJ 4*0 2	GFT FSS CG	79 7	IWA DGT NK	79 8	ARE ALI AAP	799										IGL V3- 02	IG LJ 02	NIR SKN	800	DD D	QV WD NNS	801	

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
	DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
		- 33 *0 1	13* 01						ATF DY									21* 02	2* 01					RHV V	
		IG H V3	IGH D6- 13* 01	IGHJ 5*0 2	GFT FRN YG	80 2	IWA DGS NK		ARE GHI AAP AAL DL	80 3								IGL V3- 21* 02	IG LJ 2* 01	NIR NK N	805	DD D		QV WD SSSE HVV	806
H 0 1 3	14 6	IG H V3	IGH D6- 13* 01	IGHJ 4*0 2	GFT FSG NG	80 7	IWS DGS NK		ARE ANI AAP AIY DH	80 8								IGL V3- 21* 02	IG LJ 2* 01	NIR SKN	810	DD N		QV WD SYS DHV V	811
	14 6	IG H V3	IGH D2- 15* 01	IGHJ 5*0 2	GFT FTT YG	81 2	IWA DGS NQ		ARE GHV ATP ILD	81 3	IGK V1- 39* 01	IGKJ 4*0 1		QSI ANY	815	VAS	QQ SYS MP TL T								
	14 6	IG H V3	IGH D3- 10* 01	IGHJ 3*0 1	GFT FSS YG	81 7	IWY DGS IK		VRD NFG LNA FDV	81 8	IGK V3- 11* 01	IGKJ 2*0 1		QSV TRY	820	EAT	QH RS NW PY T								
	14 6	IG H V3	IGH D6- 01	IGHJ 4*0 2	GFT FSN YG	82 2	IWH DGS NQ		ATE RRI AAP	82 3								IGL V5-	IG LJ	SGI SVD RSR	825	SX SD K	82 6	MIX HSS	827

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		HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN						
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	- 33 *0 1	13* 01						GCL DY									48* 02	2* 01					AM W	
14 6	IG H V3	IGH D6- 13* 01	IGHJ 4*0 2	GFT FSS HG	82 8	IWY DGS TK	82 9	ARE ALI AAP ATF DY		IGK V1- 5*0 3	IGKJ 1*0 1	QSI DT W	831	KAS	QY YS VY ST	832	IGL V3- 21* 02	IG LJ 3* 02	NIG SKN	833	DD N		QV WD NNS DHV V	834
60	IG H V3	IGH D5- 12* 01	IGHJ 6*0 2	GFS FSR YG	83 5	IWY DGS TR	83 6	AGG GYS SRG YYN YGL DV		IGK V1- 33* 01	IGKJ 4*0 1	QDI SNY	838	DAS	QQ YD NL PP LT	839	IGL V3- 10* 01	IG LJ 2* 01			ED N		YST DRS GDQ RV	840
99	IG H V3	IGH D2- 15* 01	IGHJ 4*0 2	GFT FSR YG	84 1	IWS DGS NK	84 2	AKA TCG DGS CGL YYF DY									IGL V1- 40* 01	IG LJ 3* 02	SSN IGA GYD	844	GN S		QSY DSN LSG WV	845
55	IG H V3	IGH D2- 21* 01	IGHJ 5*0 2			ING NGR DT	84 6	AKD IWI FDG RR WIA GSP DA		IGK V2- 30* 01	IGKJ 1*0 1	QSL VYS DGN TY	848	KVS	MQ QT HW PW A	849								
49	IG H V3	IGH D1-	IGHJ 6*0 2	GFS FSS YS	85 0	ITS NSA TI	85 1	ARA GPP SPP		IGK V4-	IGKJ 4*0 1	QSL LYR	853	WAS	QQ YY TA	854								

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	- 48 *0 3									1*0 1		SVN KNH			SP PIT									
55	IG H V3	IGH D2- 2*0 2	IGHJ 4*0 2	GFT FSN NE	88 1	ISS GSV M		AGH CSS NKC YKY	88 2								IGL V1- 40* 01	IG LJ 2* 01	SSN IGA GYD	884 S	RN S		QSY DSS LSG SI	885
69	IG H V3	IGH D3- 22* 01	IGHJ 4*0 2	GFT FGD YG	88 6	IKP KAY GGA T		ARD LTI NKII VAN DF	88 7	IGK V4- 1*0 1	IGKJ 5*0 1	QSL LYS SNN KNY	889	WAS	QQ YY ST PIT	890								
14 6	IG H V3	IGH D6- 13* 01	IGHJ 4*0 2	GFT FGD YA	89 1	IRSK GYG GTR		ARV PYS SSW YVA WA DY	89 2	IGK V4- 1*0 1	IGKJ 4*0 1	QSV LYS FNN KNY	894	WAS	QQ YY ST PL T	895								
99	IG H V3	IGH D3- 10* 01	IGHJ 4*0 2	GFT FGD YG	89 6	IRR KAN RG'T T		TRG DYY GSR NSY FWL FDY	89 7	IGK V2D - 29* 01	IGKJ 1*0 1	QSL LYS DGK TY	899	ELS	MQ SIQ LR T	900								
69	IG H V3	IGH D6-	IGHJ 4*0 2	GFT VIS NY	90 1	IYSG VNT		ARV IAV AGT	90 2								IGL V7-	IG LJ	SGT VTT	904 T	ST T		LLY CSG VRV	905

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	HEAVY CHAIN											KAPPA LIGHT CHAIN					LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	- 53 *0 1	19* 01						NRG GPR WRS TTY FDY									43* 01	3* 02	AN Y					
9	IG H V3	IGH D3- 3*0 1	IGHJ 4*0 2	GLT FSR YW	90 6	INE EGS HS	90 7	ASE LWT AFN KD WSG YND Y									IGL V1- 51* 01	IG LJ 3* 02	SSN VGK NY	909	DS Y		GT WD SSL KVV V	910
9	IG H V3	IGH D1- 26* 01	IGHJ 4*0 2	GFT FTN FK	91 1	IKQ DGS EK	91 2	TRD TW VDS	913	IGK V1- 17* 03	IGKJ 3*0 1	QGI SKY	914	ASS		LQ HQ SY PF T								
13	IG H V3	IGH D2- 21* 01	IGHJ 4*0 2	GFS FSN YW	91 6	IKE DGS EK	91 7	ASS HYS AGD VSY NFD Y	918								IGL V1 0- 54* 01	IG LJ 3* 02	NK NV GN KG	919	RH N		SAW DFS LRA WV	920
55	IG H V3	IGH D6- 13* 01	IGHJ 5*0 2	GFIF SSS W	92 1	IKQ DGS DK	92 2	ARS HVA AGV TR WF DP	923	IGK V3- 11* 01	IGKJ 2*0 1	QSV SSY	924	DAS		QH RS K								
55	IG H V3	IGH D6- 13* 01	IGHJ 5*0 1	SFT FST SW	92 6	INQ DGS ER	92 7	ARS HVA AGG TR	928	IGK V3- 11* 01	IGKJ 2*0 1	QNI NSO	929	DAS		HH RI N								

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HEAVY CHAIN														KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:	
	7*							WID S																	
55	IG H V3	IGH						ARL DRG TGE SGY RSS DV															AA WD DSL NGV V		
	- 7* 03	D3-16* 02	IGHJ 3*0 1	GFT FSD YW	93 1	INQ DGS EY	93 2											IGL V1-44* 01	IG LJ 2* 01	SSN IGS RS	934 N				
55	IG H V3	IGH						ARS HVA ASG TR WF DP																	
	- 7* 03	D1-7*0 1	IGHJ 5*0 2	GFIF SSN W	93 6	INQ DGS DI	93 7			IGK V3-11* 01	IGKJ 2*0 1	QSV SSY	939	DAS	QH RS Y	940									
55	IG H V3	IGH						ARD GYD ILN HFV RFD F																	
	- 72*0 1	D3-9*0 1	IGHJ 4*0 2	GFT FSD HF	94 1	TRN KAN SYT T	94 2			IGK V3-11* 01	IGKJ 2*0 1	QSV SSY	944	DAS	QH RS Y	945									
60	IG H V3	IGH						ARE GLG SPT SDA FDI															SSY TTS STL V		
	- 72*0 1	D3-16* 01	IGHJ 3*0 2	GFT FSD HY	94 6	IRN KAK SYT T	94 7											IGL V2-14* 01	IG LJ 3* 02	SSD VGG YNY	949 T				
60	IG H V3	IGH						TSQ YGD GYY YAM DV																	
	- 73*0 2	D4-17* 01	IGHJ 6*0 2	GFT LSG SA	95 1	IRSK ANN YAT	95 2			IGK V3-15* 01	IGKJ 3*0 1	QNI RNN	954	GAS	QH YN NW PL FT	955									

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	DO NO RID	HEAVY CHAIN								KAPPA LIGHT CHAIN								LAMBDA LIGHT CHAIN							
		V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	9	IG H V3 - 74 *0 1		IGHJ 6*0 2			ISD DER ST		VRG LNH AM DV	957								IGL V2- 14* 01	IG LJ 3* 02	NSD VGG YNF	958	DV T		CSF TTR NT WV	959
	13	IG H V3 - 74 *0 1	IGH D3- 22* 01	IGHJ 4*0 2	GFT FST YR	96 0	IKY DGS ST		ARV YRD SRD GSD FRH FDS	962	IGK V4- 1*0 1	IGKJ 4*0 1	QSL LYS SNK KNY	963	WAS	QQ YY DIP YT	964								
H 0 1 7	55	IG H V3 - 74 *0 1	IGH D3- 10* 01	IGHJ 4*0 2	GFT FSN YW	96 5	ISTD GSS T		ARG STY YFG SGS VDY	967								IGL V2- 14* 01	IG LJ 1* 01	SSD IGV YNY	968	DV T		SSY RGS STP YV	969
	55	IG H V3 - 74 *0 1	IGH D1- 26* 01	IGHJ 4*0 2	GFT FSD YW	97 0	IESD GSG T		ARG SLD F	972								IGL V2- 14* 01	IG LJ 2* 01	RSD VGA YNY	973	DV S		YSY TTS NTL V	974
	55	IG H V3 - 74 *0 1	IGH D1- 26* 01	IGHJ 4*0 2	GFT FSD YW	97 5	IDD GGS AT		SRG SLD Y	977								IGL V2- 14* 01	IG LJ 2* 01	RSD VGA YNY	978	DV S		YSY TTS NTL V	979

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
99	IG H V3	IGH D4/ OR1	IGHJ 4*0 2	GFT FSN YW	98 0	INS DGT NT	98 1	ACL RVP DRN	982								IGL V7- 46* 01	IG LJ 2* 01	TGA VTS GH Y	983	DA S	LLS YSG AQV	984	
	- 74 *0 1	5- 4a*0 1																						
13	IG H V3	IGH D2- 2*0 1	IGHJ 4*0 2	GFIF DDY S	98 5	ISW NSE FM	98 6	VKA NVK KGS TSC FDY	987	IGK V3- 20* 01	IGKJ 1*0 1	QSV SSSY	988	DAS	QQ YS GSS PR T	989								
	- 9* 01	2*0 1																						
60	IG H V3	IGH D6- 19* 01	IGHJ 4*0 1	GFN FNM YA	99 0	ISYN GGA R	99 1	VKD KSQ GIP VAG LEY	992								IGL V1- 51* 01	IG LJ 2* 01	NSN IGN NY	993	DD S	GT WD SSLS AA	994	
	- 9* 01	19* 01																						
60	IG H V3	IGH D6- 19* 01	IGHJ 4*0 2	GFT FNM YA	99 5	ISFN GGA R	99 6	VKD KSQ GIPL AGL EY	997								IGL V1- 51* 01	IG LJ 2* 01	SSN IGN NY	998	DD S	AT WD SSL TAA	999	
	- 9* 01	19* 01																						
H 0 1 1 8	IG H V3	IGH D6- 19* 01	IGHJ 4*0 1	GFN FNM YA	10 00	ISYN GGA R	10 01	VKD KSQ GIP VAG LEY	100 2								IGL V1- 51* 01	IG LJ 2* 01	NSN IGN NF	100 3	DD S	GT WD SSLS AA	100 4	
	- 9* 01	19* 01																						
69	IG H V4	IGH D2- 2*0 3	IGHJ 3*0 2	GGSI TTG DYY	10 05	IYYS GST	10 06	AIY MDE AW AFEI	100 7	IGK V1- 39* 01	IGKJ 2*0 1	QSI GNY	1008	AVS	QQ SY TIS	100 9								
	- 9* 01	2*0 3																						

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	DO NO RID	HEAVY CHAIN								KAPPA LIGHT CHAIN								LAMBDA LIGHT CHAIN							
		V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	13	IG H V4	IGH D3- 22* 01	IGHJ 4*0 2	GGSI SSG GYG	10 30	IYYS DTT YYS GST	10 31	ARV VSS GHR HYY FDY	103 2	IGK V1- 27* 01	IGKJ 1*0 1	QGI SNY	1033	SAS	QK YW T	103 4								
	60	IG H V4	IGH D1- 1*0 1	IGHJ 5*0 2	RGS VG WG ENF	10 35	ILN TGI D	10 36	AQS RRL VGP FVS	103 7	IGK V3- 15* 01	IGKJ 2*0 3	SINI N	1038	DAS	QQ YD KW PR S	103 9	IGL V6- 57* 01	IG LJ 3* 02	SGS IAS NY	104 0	ED N		QSY DSS NHG V	104 1
	99	IG H V4	IGH D2- 8*0 2	IGHJ 4*0 2	GGSI SSG GYG	10 42	ISYS GST	10 43	ARG VLV	104 4	IGK V3- 20* 01	IGKJ 2*0 1	QSV SRA Y	1045	GAS	QQ YD SSP YT	104 6								
	14 6	IG H V4	IGH D3- 10* 01	IGHJ 3*0 1	GGSI NSD DYY	10 47	IYY DGS A	10 48	ARV VHA SAN AFD V	104 9	IGK V1- 6*0 1	IGKJ 4*0 1	QGI RND	1050	AAS	LQ DY NY PL T	105 1	IGL V1- 51* 01	IG LJ 3* 02	SSN IGN TF	105 2	DN Y		GT WD SSL NG WV	105 3
	14 6	IG H V4	IGH D3- 10* 01	IGHJ 3*0 1	GGSI SND NYY	10 54	IYY DGS A	10 55	ARV VHA SAN AFD V	105 6	IGK V1- 39* 01	IGKJ 5*0 1	QSI NKF	1057	DAS	QQ TY ST PT	105 8								

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:		
14 6	IG H V4	IGH D4- 11* 01	IGHJ 3*0 2	GVP INN AGF Y	10 59	IHA SGA T	10 60	ARV PLR DFY SNY SPS AFD I	106 1	IGK V3- 15* 01	IGKJ 4*0 1	QSV SSD 1062	GAS LT	106 3	V	J	CDR 1	1067	CD R3	SEQ ID NO:	CDR 1	SEQ ID NO:	CDR 3	SEQ ID NO:
9	IG H V4	IGH D3- 16* 01	IGHJ 5*0 2	RGS FSD YY	10 64	INH SGS T	10 65	AGG RFT NDF VW GSY RYE S	106 6	IGK V2- 28* 01	IGKJ 4*0 1	QSL LHS NGY NY 1067	LGS T	106 8				1067	MQ AL QT LLL T					
60	IG H V4	IGH D6- 19* 01	IGHJ 4*0 2	GGS FIG HY	10 69	ISHS GSA	10 70	VRG GYS SAP YPR EW RY	107 1						IGL V1- 44* 01	IG LJ 3* 02	SSN IGS NT	107 2	SN N		AA WD DSL NG WV	107 3		
69	IG H V4	IGH D5- 24* 01	IGHJ 6*0 3	GGS FSG DF	10 74	INQ SGS T	10 75	ARG RDG YNY VGY YYY YYM DV	107 6	IGK V3- 11* 01	IGKJ 1*0 1	QSV TNY 1077	DGS T	107 8				1077	QQ RS NW QW T					
14 6	IG H V4	IGH D3- 3*0 1	IGHJ 6*0 2	GGT FSG YY	10 79	IDH SGG T	10 80	ARG IFEV VIIP YYS YRV DV	108 1	IGK V3- 15* 01	IGKJ 3*0 1	QTI SNN 1082	GAS FT	108 3	IGL V3- 19* 01	IG LJ 2* 01	SLR SYT SY	108 4	GR N		SSR SGN RLV	108 5		

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HEAVY CHAIN												KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	J	V	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	J	V	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:
9	IG	H	V4			GRG																			
	-	IGH				LGR																			
	34	D6-13*	IGHJ 5*0	GGP	10	INH	10	YGG	108																
2	*0	01	2	FSG YY	86	SGS T	87	RRF DP	8																
9	IG	H	V4																						
	-	IGH				ARD																			
	38	D3-22*	IGHJ 3*0	GYSI RNR	10	MYH	10	FYD	109																
2	*0	01	2	YY	91	SGS T	92	AFD I	3																
146	IG	H	V4																						
	-	IGH				RSG YVF																			
	38	D2-21*	IGHJ 4*0	GYSI SRD	10	FSH	10	VTR	109																
2	*0	02	2	YY	96	SGT T	97	ADY	8																
60	IG	H	V4																						
	-	IGH				ARR																			
	39	D2-8*0	IGHJ 4*0	GGSI SSSS	11	IDY	11	IQL	110																
1	*0	1	2	YY	01	YGS T	02	MVF DF	3																
60	IG	H	V4																						
	-	IGH				ARRH																			
	39	D3-3*0	IGHJ 2*0	GGSI SNS	11	IYYS	11	PYY	110																
1	*0	1	1	NY	06	GST	07	NF WY	8																

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D		J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 1									WYF DL											
99	IG H V4	IGH D3- 10* 01	IGHJ 3*0 1				VSS KGK T			TRH WLG GDK WSQ SPF LAV	111 3					IGL V1- 44* 01	IG LJ 3* 02	AN N		AV WD DSL NT WV	111 5
99	IG H V4	IGH D5- 12* 01	IGHJ 3*0 2				IYY GGS T			AKG RYS GYN DYN AFD I	111 8					IGL V1- 47* 02	IG LJ 3* 02	SN N		AA WD DSP EWL G	111 9
14 6	IG H V4	IGH D3- 10* 01	IGHJ 3*0 1				IYYS GTT			TRP ASG AHD YVS RSY YPG QGA FGV	112 2										
14 6	IG H V4	IGH D6- 13* 01	IGHJ 4*0 2				LYY TGI T			ARL LGI AAT GHF DS	112 7					IGL V1 0- 54* 01	IG LJ 3* 02	RN N		STW DSS LST WL	112 9
14 6	IG H V4	IGH D3- 10* 01	IGHJ 3*0 2				IYYS GTP			TRP ASG AHD YAS	113 2										

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN								
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:		V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	39 *0 1							RSY YPG LGA FGI																	
14 6	IG H V4	IGH D3- 3*0 1	IGHJ 3*0 2	GCSI TSL SYW	11 35	IYYS GTT	11 36			IGK V3- 20* 01	IGKJ 4*0 1	QSV SSK C	1138		QQ HD NS LS	113 9									
14 6	IG H V4	IGH D6- 6*0 1	IGHJ 4*0 2	GDS MSR NSF Y	11 40	INY NGI T	11 41	AAH RVS SSY PAD Y	114 2	IGK V1- 39* 01	IGKJ 1*0 1	QNI DDY	1143		QQ SY NT PT	114 4									
14 6	IG H V4	IGH D3- 3*0 1	IGHJ 3*0 2	GCSI SSLS YY	11 45	IYYS GTA	11 46	ARP LLN PSTI YGV TPG	114 7	IGK V3D -	IGKJ 1*0 1	QSI RSN	1148		QQ YIN WP PW T	114 9									
14 6	IG H V4	IGH D3- 16* 02	IGHJ 6*0 2	GYS VST SN W	11 50	IYHI GST	11 51	ARG NYD YV WGS YRS DQG	115 2	IGK V1- 39* 01	IGKJ 2*0 1	QSI DNY	1153		QR SYS TP YT	115 4									

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN											
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:			
49	IG	H V4	IGH	IGHJ 6*0 3	GASI 11 55	VHS 11 56	ARE 11 56	GGS 11 56	SYY 11 56	YYY 11 56	YMD 11 56	115 7							IGL 1 8*0 1	IG 1 01	SSD 115 8	VGS 115 8	YNY 115 8	DV 115 8	SSY 115 9	AGI 115 9	NSY 115 9	VI 115 9
	4*																											
13	IG	H V4	IGH	IGHJ 5*0 2	GCSI 11 60	IYY 11 61	ARS 11 61	KNQ 11 61	LLL 11 61	FDP 11 61	116 2	IGK 1 01	IGKJ 4*0 1	QSV 1163	GAS 1163		QQ 116 4											
	59*0 1																											
13	IG	H V4	IGH	IGHJ 5*0 1	GDS 11 65	VYH 11 66	ARS 11 66	KNQ 11 66	LLL 11 66	FEF 11 66	116 7	IGK 1 01	IGKJ 4*0 1	QDI 1168	DAS 1168		QQ 116 9											
	59*0 1																											
55	IG	H V4	IGH	IGHJ 3*0 1	GASI 11 70	MYS 11 71	ART 11 71	NW 11 71	AYD 11 71	PFN 11 71	117 2	IGK 1 01	IGKJ 1*0 1	QNI 1173	KAS 1173		QQ 117 4	IGL 1 01	IG 1 01	NN 117 5	NIG 117 5	RSA 117 5	ED 117 5	SAW 117 6	DFS 117 6	LSV 117 6	QV 117 6	
	59*0 1																											D7*27* 01
60	IG	H V4	IGH	IGHJ 6*0 2	GCSI 11 77	IYDS 11 78	ARD 11 78	RGY 11 78	CSG 11 78	GSC 11 78	LGG 11 78	117 9	IGK 1 01	IGKJ 4*0 1	QSI 1180	KAS 1180		QQ 118 1										
	59*0 1																											

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HEAVY CHAIN													KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	SEQ ID NO:	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:		
60	IG H V4	IGH D2- 8*0	IGHJ 6*0	GGSI SGS	11 82	IYDS GNT	11 83	MD V	118 4	IGK V1- 5*0	IGKJ 1*0	QSSS SW	1185	KAS RT	QQ YN SY	118 6								
60	IG H V4	IGH D2- 8*0	IGHJ 4*0	GGSI SNY	11 87	VYS SGT	11 88	GLT FDY	118 9												AA WD DSL NGP NVV	119 1		
69	IG H V4	IGH D3- 22*	IGHJ 6*0	GGSI RSY	11 92	IYYS GST	11 93	YMD V	119 4												QA WD SSV V	119 6		
14 6	IG H V4	IGH D1- 26*	IGHJ 6*0	GGSI SGY	11 97	IYYS GTT	11 98	YGL DV	119 9	IGK V1- 39*	IGKJ 2*0	QSSS SY	1200	ATS YT	HQ SYS SP	120 1								
55	IG H V4	IGH D5- 18*	IGHJ 4*0	GGSI SND	12 02	IHS KGD	12 03	RNY FDY	120 4	IGK V1- 12*	IGKJ 4*0	QGI SSG	1205	AAS LT	QQ AN SFP	120 6								

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HEAVY CHAIN												KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN						
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	*0 8																							
H 0 2 0	IG H V4	IGH D5- 18*	IGHJ 4*0 2	GGSI SND Y	12 07	IHS KGD T	12 08	ARH LYR YGY	120 9	IGK V1- 12*	IGKJ 4*0 1	QGI SSG	1210	AAS	QQ AN SFP LT	121 1								
	IG H V4	IGH D6- 13*	IGHJ 3*0 2	GGSI VRS TGY F	12 12	IYT GGA T	12 13	ARM TSF KQS GG WY	121 4	IGK V1- 5*0 1	IGKJ 2*0 1	QTI GTY	1215	EAS	QE YN SYS YT	121 6								
69	IG H V4	IGH D6- 19*	IGHJ 3*0 2	RGS VSN GGY Y	12 17	TGS S	12 18	ARL TSY KQR GG WY	121 9	IGK V1- 5*0 1	IGKJ 2*0 1	QSI TL	1220	DGS	QE YSS YS YT	122 1								
9	IG H V5	IGH D3- 22*	IGHJ 4*0 2	GYS FTS YW	12 22	IQS GDY NT	12 23	ARR ARN VGN YGT SDF	122 4								IGL V2- 14* 01	IG LJ 3* 02	SSD VGR YNY	122 5	DV T	SSYI SSN TLW V	122 6	
60	IG H V5	IGH D1-	IGHJ 3*0 2	GYT FAS YW	12 27	INP PNS DT	12 28	ARR RVS VTG	122 9								IGL V2- 14* 01	IG LJ 3* 02	SSD VGG YNY	123 0	EV N	SSY AGT	123 1	

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	HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN							
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	SEQ ID NO:	CDR 2	CD R3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 1	SEQ ID NO:	CD R2	SEQ ID NO:	CDR 3	SEQ ID NO:
	- 51*0 1	14* 01						TDA FDI							8*0 1	2* 01							NTF VV	
60	IGH V5	IGH						ARR RVS VTG TDA FDI	123 4						IGL V2-8*0 1	IG LJ 2* 01	SSD VGG YNY	123 5			EV N		SSY AGT NTF VV	123 6
69	IGH V5	IGH D1-1*0 1	IGHJ 4*0 2	GDT FGN YW	12 37	ILLS DSD T	12 38	ARA TPG NY Y FDS	123 9						IGL V2-14* 01	IG LJ 1* 01	SSD VGA YNY	124 0			DV T		SSY TDS SPN CV	124 1
99	IGH V5	IGH D2-2*0 1	IGHJ 1*0 1	GYS FSN FW	12 42	IYPG DSD T	12 43	ARP SRS RDI NK WYL STS EYF HY	124 4				QQ YA NS PL T				IGK V3-20* 01	IGKJ 4*0 1	QSV SSR S	1245				
9	IGH V6	IGH						AVG HH WH FKY	124 9						IGL V2-8*0 1	IG LJ 1* 01	SSD VGG YSH	125 0			EV S		SSH AGS NYG V	125 1
9	IGH V6	IGH D1-1*0 1	IGHJ 4*0 2	GDS VSN NTA V	12 47	TY Y RSK WF N	12 48	AVG HH WH FKY	125 4						IGL V2-1* 01	IG LJ	SSD VGG YSH	125 5			EV S		SSH AGS	125 6

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HEAVY CHAIN										KAPPA LIGHT CHAIN						LAMBDA LIGHT CHAIN					
DO NO RID	V	D	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	V	J	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:	CDR 3	SEQ ID NO:	CDR 1	SEQ ID NO:	CDR 2	SEQ ID NO:
	- 1* 01	1* 01		NTA V		WF N		WH FKY													
55	IG H V6 - 1* 01	IGH D3- 10* 01	IGHJ 4*0 2	GSSI FTN SAG	12 57	TYR RSK WY N	12 58	ARD TYR YTS ASY YNV DY	125 9	IGK V1- 39* 01	IGKJ 5*0 1	ESIR SN	1260	AAS		QQ SY RT PIT	126 1				
55	IG H V7 - 4- 1* 02	IGH D1- 7*0 1	IGHJ 4*0 2	GYT FTS YG	12 62	INT DTG NP	12 63	ARL GEY SW NSI GYF DY	126 4									IGL V1- 40* 01	IG LJ 2* 01	SSN IGA GYD	126 5
99	IG H V7 - 4- 1* 02	IGH D3- 10* 01	IGHJ 4*0 2	GYV FTN YA	12 67	INT NTG NP	12 68	ARS YAY GDF	126 9	IGK V1- 39* 01	IGKJ 1*0 1	QNI AIR	1270	EAS		QQ SD TL PW T	127 1				
99	IG H V7 - 4- 1* 02	IGH D3- 22* 01	IGHJ 4*0 2	GYT FSN YA	12 72	INT NTG NP	12 73	ARG ARS YYD SSG YYS WS DY	127 4	IGK V4- 1*0 1	IGKJ 1*0 1	QSV LYR SNN KNY	1275	WAS		QQ YY NT LT WA	127 6				

[0167] Table S3. Primers and synthesized nucleotide sequences.

Single-Cell Antibody Cloning Primers		SEQ ID NO:
A2		
F1-HC	5'-ACAGGTGCCCCACTCCCAGGTGCAG	1277
F2-HC	5'-AAGGTGTCCAGTGTGARGTGCAG	1278
F3-HC	5'-CCCAGATGGGTCCTGTCCCAGGTGCAG	1279
F4-HC	5'-CAAGGAGTCTGTTCCGAGGTGCAG	1280
R-1st-HC	5'-GGAAGGTGTGCACGCCGCTGGTC	1281
R-2nd-HC	5'-GTTCTGGGAAGTAGTCCTTGAC	1282
F1-Kappa	5'-ATGAGGSTCCCYGCTCAGCTGCTGG	1283
F2-Kappa	5'-CTCTTCCTCCTGCTACTCTGGCTCCCAG	1284
F3-Kappa	5'-ATTTCTCTGTTGCTCTGGATCTCTG	1285
F4-Kappa	5'-ATGACCCAGWCTCCABYCWCCCTG	1286
R-1st-Kappa	5'-GTTTCTCGTAGTCTGCTTTGCTCA	1287
R-2nd-Kappa	5'-GTGCTGTCCTTGCTGTCCTGCT	1288
F1-Lambda	5'-GGTCCTGGGCCCAGTCTGTGCTG	1289
F2-Lambda	5'-GGTCCTGGGCCCAGTCTGCCCTG	1290
F3-Lambda	5'-GCTCTGTGACCTCCTATGAGCTG	1291
F4-Lambda	5'-GGTCTCTCTCSCAGCYTGTGCTG	1292
F5-Lambda	5'-GTTCTTGGGCCAATTTTATGCTG	1293
F6-Lambda	5'-GGTCCAATTCYCAGGCTGTGGTG	1294
F7-Lambda	5'-GAGTGGATTCTCAGACTGTGGTG	1295
R-1st-Lambda	5'-CACCAGTGTGGCCTTGTTGGCTTG	1296
R-2nd-Lambda	5'-CTCCTCACTCGAGGGYGGGAACAGAGTG	1297
F-Vector Seq Primer	5'-GCTTCGTTAGAACGCGGCTAC	1298
Antibody Cloning Primers for Each Antibody		
F-H001-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTCCAGCTTGTGCAGTCTGG	1299
R-H001-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAAGAGACGGTGACCATTGTCCCTT	1300
F-H001-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GACATCCAGATGA CCCAGTCTCCA	1301
R-H001-Kappa	5'- GAAGACAGATGGTGCAGCCACCGTACG TTTGATCTCCACCTTG GTCCCTCC	1302
F-H002-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTCACCTTGAAGGAGTCTGG	1303

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-H002-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGGTG	1304
F-H002-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CCCAGGCGC	1305
F-H003-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAGATGCAGCTGCTGGAGTCTGG	1306
R-H003-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACAGTGACCAGGGTGC	1307
F-H003-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATATGCTGA CTCAGGCACCC	1308
F-H004-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAGATGCAACTGGTGGAGTCTGG	1309
R-H004-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGATGACCGTGGTCC	1310
F-H004-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1311
F-H005-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGCGTCTGGTGGAATCTGG	1312
R-H005-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCGGGGT	1313
F-H005-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1314
F-H006-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGCGTCTGGTGGAATCGGG	1315
R-H006-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCGGGATC	1316
F-H006-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1317
F-H007-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCACCTGGTGGAGTCTG	1318
R-H007-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCGTGGTC	1319
F-H007-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GAAATTGTGTTG ACGCAGTCTCCAG	1320
R-H007-Kappa	5'- GAAGACAGATGGTGCAGCCACCGTACG TTTGATCTCCAATTG GTCCCCTGG	1321
F-H008-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGCACCTATTGGAGTCTGGG	1322

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-H008-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGACGAGACGGTGACCCTGGTC	1323
F-H008-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1324
F-H009-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGAAGTTGGTGGAGTCTGGG	1325
R-H009-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCCTGGTC	1326
F-H009-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1327
F-H010-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGGTGGAGTCTG	1328
R-H010-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCAGGGTT	1329
F-H010-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1330
F-H011-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTTCACTTGGCGGAGTCTGG	1331
R-H011-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAAGAGACGGTGACCAATGTCCC	1332
F-H011-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GAAGTTGTGTTGA CACAGTCTCCAGC	1333
R-H011-Kappa	5'- GAAGACAGATGGTGCAGCCACCGTACG TTTGATCTCCAGCTTG GTCCCCTG	1334
F-H012-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGCTGCAGCTGGTGGAGTCTG	1335
R-H012-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCAGGGTTC	1336
F-H012-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1337
F-H013-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGGTGGAGTCTG	1338
R-H013-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCAGGGCT	1339
F-H013-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1340
F-H014-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTACAAGTATGGAGTCTGGG	1341

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-H014-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCAGGGCT	1342
F-H014-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC TCCTATGTGCTGA CTCAGACACCC	1343
F-H015-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGGTGGAGTCTG	1344
R-H015-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCAGGGTTC	1345
F-H015-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GACATCCAGGTGA CCCAGTCAC	1346
R-H015-Kappa	5'- GAAGACAGATGGTGCAGCCACCGTACG TTTGATGTCCACCTTG GTCCCTCC	1347
F-H016-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAGATGCACCTGGTGGAGTCTGG	1348
R-H016-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACAGTGACCAGGGTGC	1349
F-H016-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GAAATACTGCTGA CGCAGTCTCCAG	1350
R-H016-Kappa	5'- GAAGACAGATGGTGCAGCCACCGTACG TTTGATCTCCACCTTG GTCCCTCC	1351
F-H017-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAGGTGCAGCTGGTGGAGTCC	1352
R-H017-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCAGGGTTC	1353
F-H017-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC CAGTCTGCCCTGA CTCAGCCTG	1354
F-H018-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAAGGACAGCTGGTGGAGTCTGG	1355
R-H018-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAGGAGACGGTGACCAGGGTTC	1356
F-H018-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCC CAGTCTGTGTTGA CGCAGCCGC	1357
F-H019-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGGTGTCTGCAGGAGTCG	1358
R-H019-HC	5'-CCGATGGGCCCTTGGTTCGACGC TGAAGAGACGGCGACCAGTGTCC	1359
F-H019-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GACATCCAGATGA CCCAGTCTCCG	1360

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-H019-Kappa	5'- GAAGACAGATGGTGCAGCCACCGTACG TTTGATCTCCAGCTTG GTCCCTG	1361
F-H020-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGCAGGAGTCG	1362
R-H020-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGTTTCC	1363
F-H020-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GACATCCAGATGA CCCAGTCTCCA	1364
R-H020-Kappa	5'- GAAGACAGATGGTGCAGCCACCGTACG TTTGAACTCCACCTTG GTCCCTCC	1365
R-Lambda	5'-GGCTTGAAGCTCCTCACTCGAGGGYGGGAACAGAGTG	1366
gBlock Synthesis for Alanine Mutations		
101Q	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGG CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGCC AAATTTCGAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCTCTTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATGCAGGTATGTTGCCCGTTTGTCTCT AATTCAGGATCAACAACAACAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1367
102G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGG CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGCC AAATTTCGAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCTCTTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGCAATGTTGCCCGTTTGTCTCT AATTCAGGATCAACAACAACAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1368

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
103M	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTGCATTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1369
104L	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGGCACCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1370
105P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGGCAGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1371

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
106V	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCCGATGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1372
108P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCCGTTTGTGCACT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1373
109L	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCCGTTTGTCTCTGC AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1374

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
110I	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AGCACCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1375
111P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTGCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1376
112G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGCATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1377

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
113S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGAGCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1378
114T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAGCAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1379
115T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAGCAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1380

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
116T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAGCAAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1381
117S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCGCAACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1382
118T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACAGTGCAGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1383

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
119G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGCACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1384
120P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGAGCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1385
122K	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCGCAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1386

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
123T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAGCA TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1387
125T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAACCC TGCACGCACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1388
126T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAACCC TGCACGGCACCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1389

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
127P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTGCAGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1390
129Q	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTGCAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1391
130G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGCAAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1392

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
131N	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCGCATCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1393
132S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACGCAATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1394
133M	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTGCATTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1395

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
134F	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGGCACCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1396
135P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTGCATCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1397
136S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCGCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1398

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
140T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTGCAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1399
141K	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAGCACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1400
142P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAAGCAACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1401

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
143T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTGCAGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1402
144D	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGCAGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1403
145G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGCAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1404

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
146N	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAGCATGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1405
148T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCGCATGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1406
150I	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTGCACCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1407

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
151P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTGCAAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1408
152I	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCGC ACCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1409
153P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CGCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1410

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
154S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCAGCATCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1411
155S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGGCATGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1412
156W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCGCAGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1413

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
158F	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTGCAGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1414
160K	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAGCATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1415
161Y	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAAGCACTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1416

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
162L	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACGCATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1417
163W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTAGCAGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1418
164E	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGCATGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1419

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
165W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGGCAGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1420
167S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC GCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1421
168V	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGCACGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1422

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
169R	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCTCTTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCGCATTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1423
170F	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCTCTTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTGCATCTTGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1424
171S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCTCTTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTTCGCATGGCTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1425

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
172W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGAC CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTTCGAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCTGCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCTCTTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTGCACTCAGTTTACTAGTGCCATTTGTTT AGTGGTTTCGTAGGG	1426
gBlock Synthesis for Germline Antibodies		
H006- HC_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTCAGGTGCAGCTGG TGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAG ACTCTCCTGTGCAGCCTCTGGATTACCTTCAGTAGCTATGGC ATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGG TGGCAGTTATATCATATGATGGAAGTAATAAATACTATGCAG ACTCCGTGAAGGGCCGATTACACCATCTCCAGAGACAATTCCAA GAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGAC ACGGCTGTGTATTACTGTGCGAAAGATGCTTATCTTTCTGCAG CGAGAGGATACGGTATGGACGTCTGGGGCCAAGGGACCACGGT CACCGTCTCCTCAGCGTCGACCAAGGGCCCATCGG	1427
H006- Lambda_GL	5'- CTAGTAGCAACTGCAACCGGTTCTGGGCCTCCTATGTGCTGA CTCAGCCACCCTCGGTGTGAGTGGCCCCAGGACAGACGGCCAG GATTACCTGTGGGGGAAACAACATTGGAAGTAAAAGTGTGCAC TGGTACCAGCAGAAGCCAGGCCAGGCCCTGTGCTGGTTCGTCT ATGATGATAGCGACCGGCCCTCAGGGATCCCTGAGCGATTCTC TGGCTCCAACCTCTGGGAACACGGCCACCCTGACCATCAGCAGG GTCGAAGCCGGGGATGAGGCCGACTATTACTGTCAGGTGTGGG ATAGTAGTAGTGATCATGTGGTATTCGGCGGAGGGACCAAGCT GACCGTCTAGGTCAGCCCAAGGCTGCCCCCTCGGTCACTCTGT TCCCACCCTCGAGTGAGGAGCTTCAAGCC	1428

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
H019- HC_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTCAGGTGCAGCTGC AGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTGGTGAT TACTACTGGAGTTGGATCCGCCAGCCCCAGGGAAGGGCCTGG AGTGGATTGGGTACATCTATTACAGTGGGAGCACCTACTACAA CCCGTCCCTCAAGAGTCGAGTTACCATATCAGTAGACACGTCC AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACTGCCGCAG ACACGGCCGTGTATTACTGTGCCATCTACATGGATGAGGCCTG GGCTTTTGATATCTGGGGCCAAGGGACAATGGTCACCGTCTCT TCAGCGTCGACCAAGGGCCCATCGG	1429
H019- Kappa_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTGACATCCAGATGA CCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAA ATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGAT CTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTT AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCA GTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAG TTACAGTATTTCTTTATTTCACTTTTGGCCAGGGGACCAAGCTG GAGATCAAACGTACGGTGGCTGCACCATCTGTCTTC	1430
H020- HC_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTCAGGTGCAGCTGC AGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACT GGAGCTGGATCCGGCAGCCCCAGGGAAGGGACTGGAGTGGAT TGGGTATATCTATTACAGTGGGAGCACCAACTACAACCCCTCC CTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAACC AGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCAGACACGGC CGTGTATTACTGTGCGAGACACCTTTATCGCTATGGTTATAGG AACTACTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCT CCTCAGCGTCGACCAAGGGCCCATCGG	1431
H020- Kappa_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTGACATCCAGATGA CCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGT CACCATCACTTGTCGGGCGAGTCAGGGTATTAGCAGCTGGTTA GCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA TCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTT CAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC AGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGG CTAACAGTTTCCCGCTCACTTTTCGGCGGAGGGACCAAGGTGGA GATCAAACGTACGGTGGCTGCACCATCTGTCTTC	1432
HBV TaqMan PCR		
F-sense	5'-CCGTCTGTGCCTTCTCATCTG	1433

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-anti-sense	5'-AGTCCAAGAGTCCTCTTATGTAAGACCTT	1434
Probe	5-/56 FAM/ CCGTGTGCA/ZEN/CTTCGCTTC ACCTCT GC/3IABkFQ/-3	1435
S-protein PCR		
F-S-protein	5'-CCCTGCGCTGAACATGGAGAACA	1436
R-S-protein	5'-AAATGTATACCCAAAGACAAAAGAAAA	1437

[0168] It will be recognized from the foregoing that the present disclosure describes screening individuals who were either vaccinated or had spontaneously recovered from HBV infection. Antibody cloning from memory B cells revealed that all 5 of the top individuals produced clones of broadly neutralizing antibodies (bNAbs) that targeted 3 non-overlapping epitopes on the HBV S antigen (HBsAg). Clones with the same immunoglobulin variable, diversity and joining heavy and light chain genes were shared among elite neutralizers. Single bNAbs protected humanized mice against infection, but selected for resistance mutations in mice with established infection. In contrast, infection was controlled in the absence of detectable escape mutations by a combination of bNAbs targeting non-overlapping epitopes with complementary sensitivity to mutations that commonly emerge during human infection. The co-crystal structure of one of the bNAbs with a peptide epitope containing residues frequently mutated in human immune escape variants revealed a loop anchored by oppositely charged residues. The structure provides a molecular explanation for why immunotherapy for chronic HBV infection may require combinations of complementary bNAbs, as described herein.

[0169] While the disclosure has been described through specific embodiments, routine modifications will be apparent to those skilled in the art and such modifications are intended to be within the scope of the present disclosure.

What is claimed is:

1. An isolated or recombinant antibody or antigen binding fragment thereof, said isolated or recombinant antibody or antigen binding fragment thereof comprising
5 complementarity determining regions (CDRs), the CDRs comprising heavy and light chain amino acid sequences CDR1, CDR2 and CDR3 selected from the antibody heavy and light chain CDRs of Table S2.
2. The recombinant or isolated antibody or antigen binding fragment thereof of claim 1,
10 comprising the heavy and light chain CDR1, CDR2 and CDR3 sequences of antibody H017 from Table S2, or the heavy and light chain CDR1, CDR2 and CDR3 sequences of antibody H019 from Table S2, the heavy and light chain CDR1, CDR2 and CDR3 sequences of antibody H016 from Table S2.
3. The recombinant or isolated antibody or antigen binding fragment thereof of claim 1,
15 comprising the heavy and light chain CDR1, CDR2 and CDR3 sequences of H004 from Table S2, or the heavy and light chain CDR1, CDR2 and CDR3 sequences of H005 from Table S2, or the heavy and light chain CDR1, CDR2 and CDR3 sequences of H008 from Table S2, or the heavy and light chain CDR1, CDR2 and CDR3 sequences of H009 from Table S2.
4. The recombinant or isolated antibody of any one of claims 1–3, comprising at least
20 one modification of its constant region, wherein the modification increases in vivo half-life of the antibody, or alters the ability of the antibody to bind to Fc receptors, or inhibits aggregation of the antibodies, or a combination of said modifications, or wherein the antibody is attached to a detectable label or a substrate.
5. The recombinant or isolated antibody of claim 4, comprising the modification that increases in vivo half-life of the antibody.
- 25 6. The recombinant or isolated antibody of claim 4, comprising the modification that alters the ability of the antibody to bind to Fc receptors.
7. A pharmaceutical composition comprising an antibody or an antigen binding fragment thereof, or a combination of antibodies or antigen binding fragment thereof, of any one of claims 1-3.

8. The pharmaceutical composition of claim 7, comprising the combination of the antibodies.
9. The pharmaceutical composition of claim 8, wherein the combination of the antibodies includes the H017 and H019 antibodies.
- 5 10. The composition of claim 9, wherein the composition further comprises the H016 antibody.
11. A method for prophylaxis or therapy of a Hepatitis B virus infection comprising administering to an individual in need thereof an effective amount of at least one antibody or antigen binding fragment thereof of any one of claims 1–3, wherein optionally the at least one
10 antibody comprises at least one modification of the constant region.
12. The method of claim 11, wherein the administering comprises administering a combination of antibodies that include the H017 and H019 antibodies.
13. The method of claim 12, wherein the administration further comprises administering the H016 antibody.
- 15 14. The method of claim 11, comprising administering a combination of at least two of the antibodies, and wherein administering the combination of at the least two antibodies provides a therapeutic and/or prophylactic effect against infection by a hepatitis B virus that comprises one or more escape mutations in at least one of the HBsAg or the S-protein of the hepatitis B virus.
- 20 15. The method of claim 14, wherein the combination of at least two of the antibodies comprises the H017 and H019 antibodies.
16. The method of claim 15, wherein the combination of at least two of the antibodies further comprises the H016 antibody.
17. One or more recombinant expression vectors encoding the heavy chain and the light
25 chain of any one of the antibodies or antigen binding fragments thereof of any one of claims 1–3.
18. Cells comprising one or more recombinant expression vectors of claim 17.

19. A method comprising culturing cells of claim 18 and separating antibodies from the cells.
20. A kit comprising one or more expression vectors encoding according to claim 17.
21. A method for detecting Hepatitis B virus comprising:
5 contacting a biological sample from an individual with an antibody of any one of claims 1–3, and detecting the presence of a complex comprising the antibody and a Hepatitis B virus protein.
22. A method comprising testing one or more candidate drug agents for the capability to target an antigenic loop region of the hepatitis B virus S-protein by interfering with a
10 complex formed by the peptide and an antibody of any one of claims 1–3.
23. A vaccine comprising at least two non-overlapping epitopes from the Hepatitis B virus S antigen (HBsAg), wherein optionally at least one of the non-overlapping epitopes does not comprise a commonly occurring escape mutation.
24. The vaccine of claim 23, comprising at least three, non-overlapping epitopes from the
15 HBsAg.
25. A method for prophylaxis and/or therapy for Hepatitis B virus infection comprising administering a vaccine of claim 23 to an individual in need thereof.
26. The method of claim 25, wherein the administering comprises at least three, non-overlapping epitopes from the HBsAg.
- 20 27. The method of claim 26, wherein the Hepatitis B virus in the individual does not develop Hepatitis B virus comprising escape mutations subsequent to administering the vaccine.

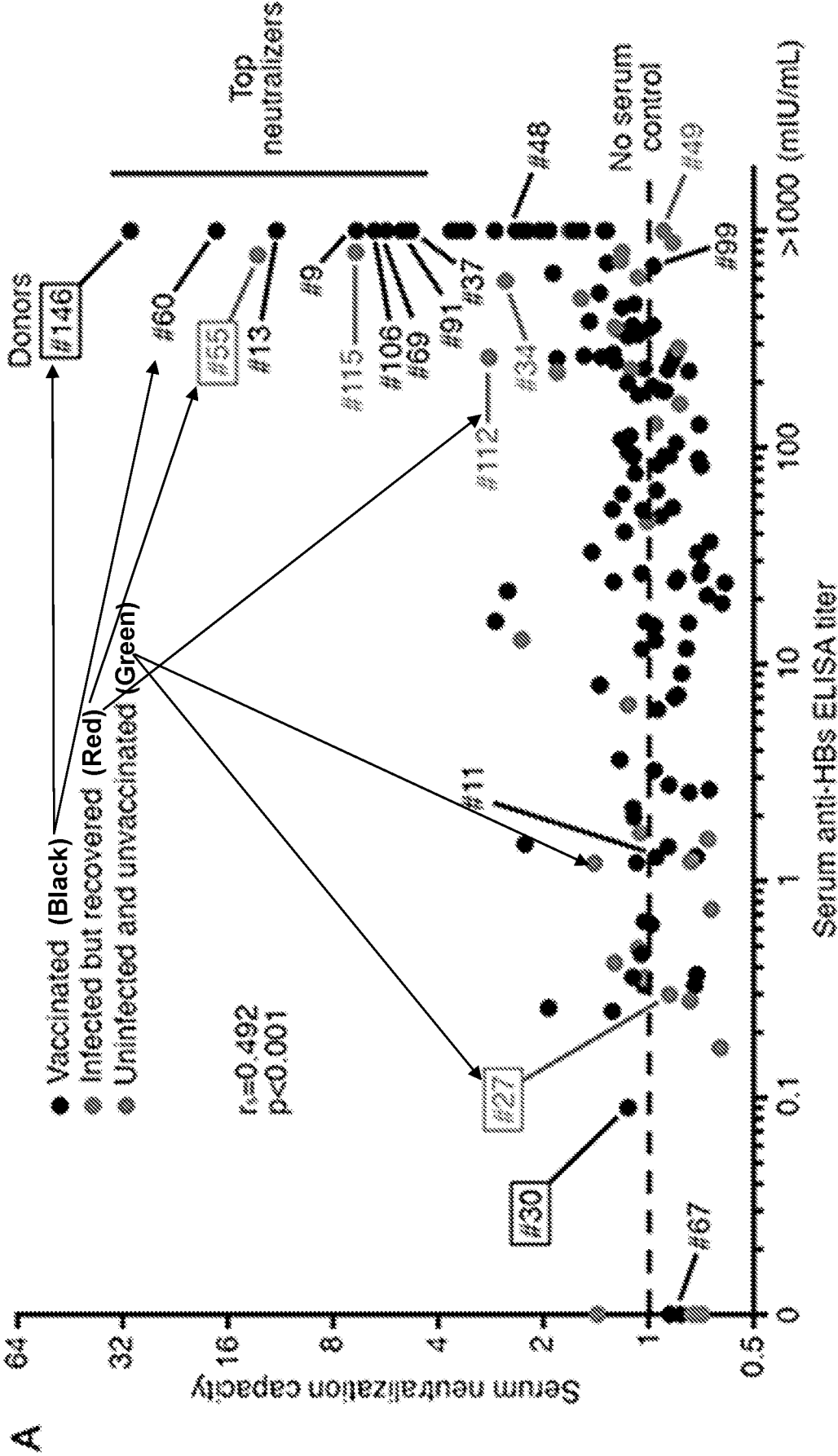


Fig. 1

8



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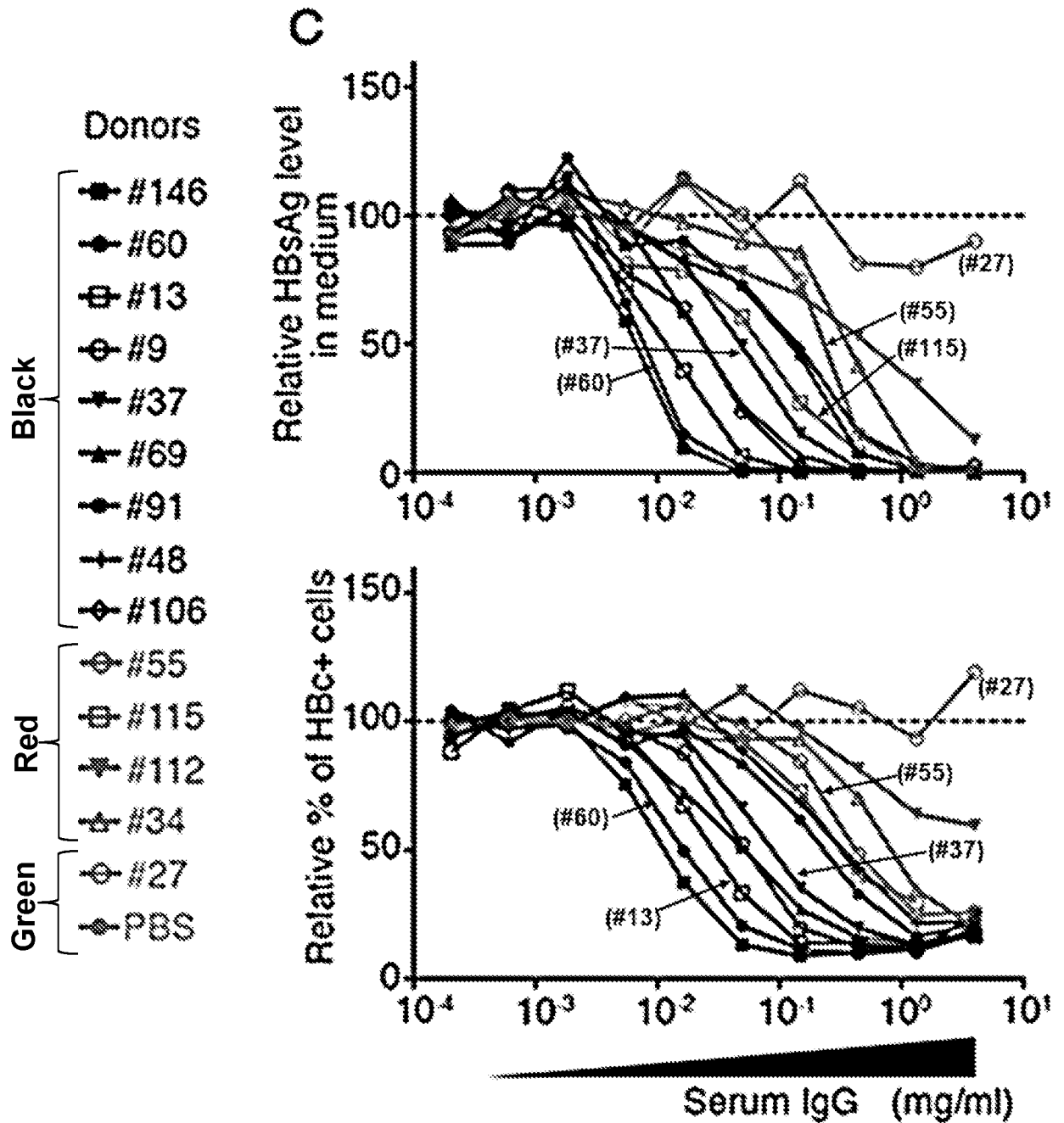


Fig. 1 (continued)

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D

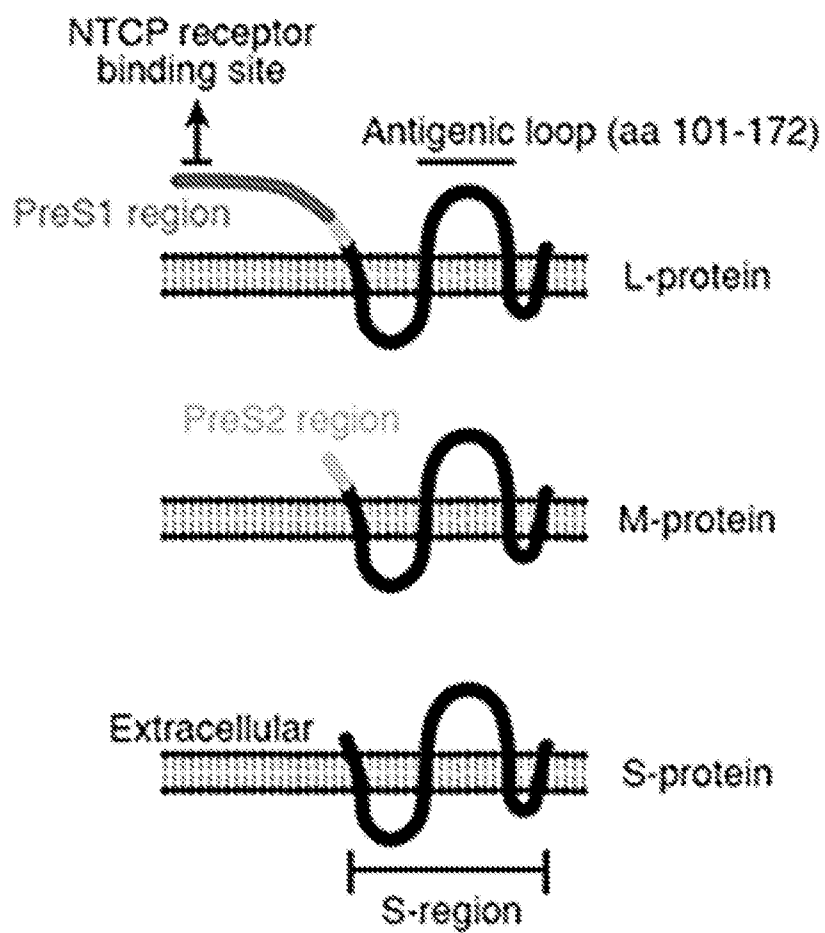


Fig. 1 (continued)

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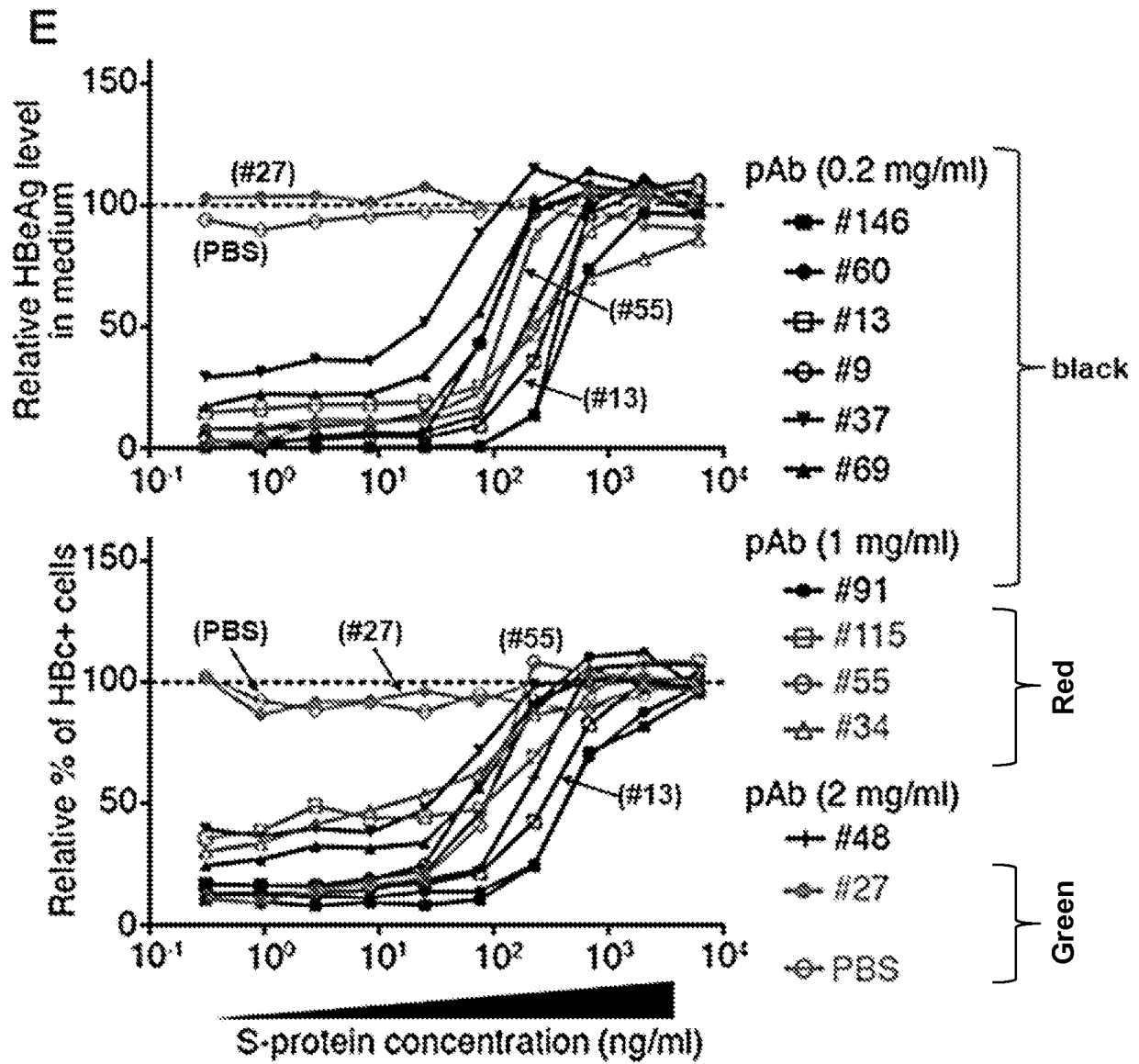


Fig. 1 (continued)

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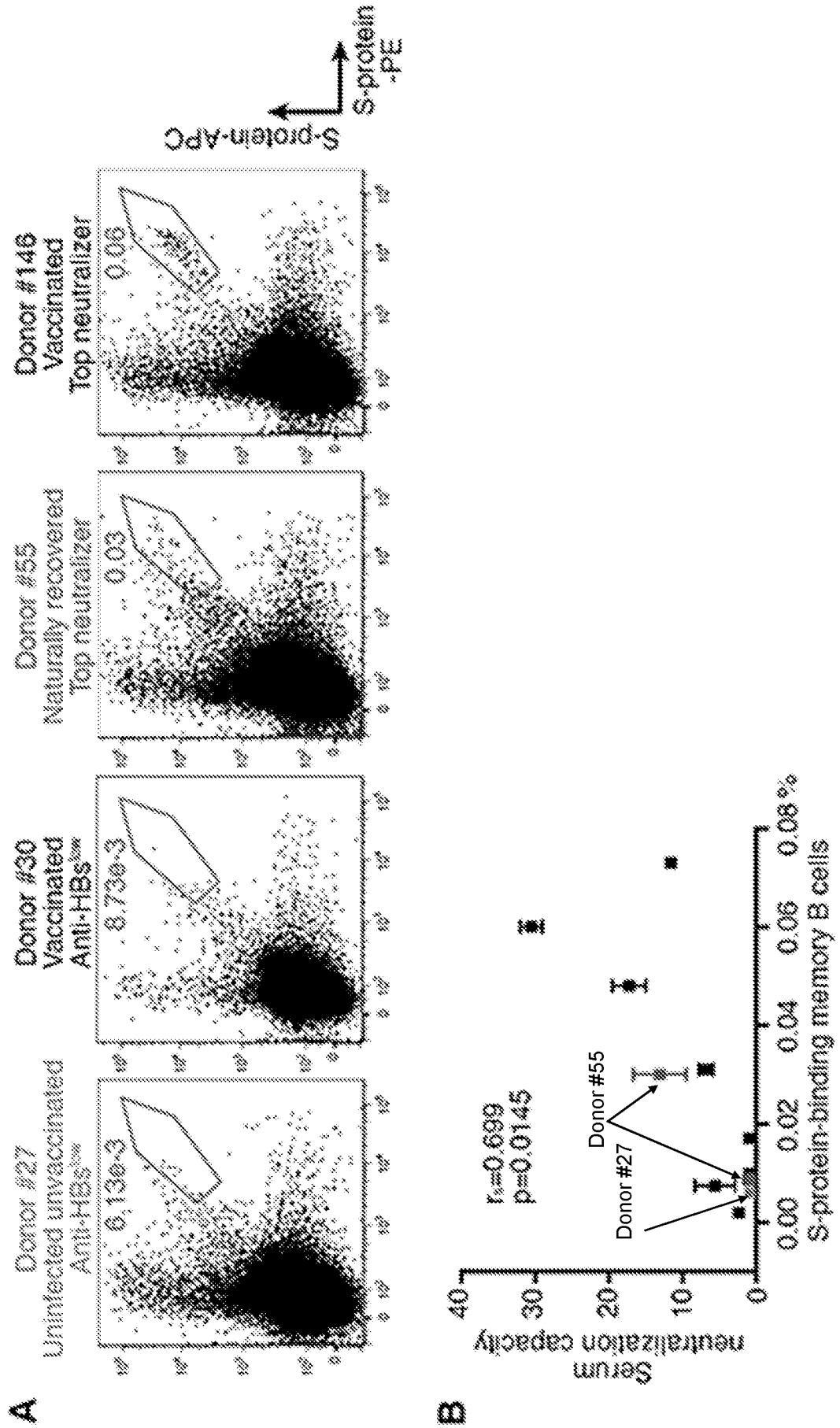


Fig. 2

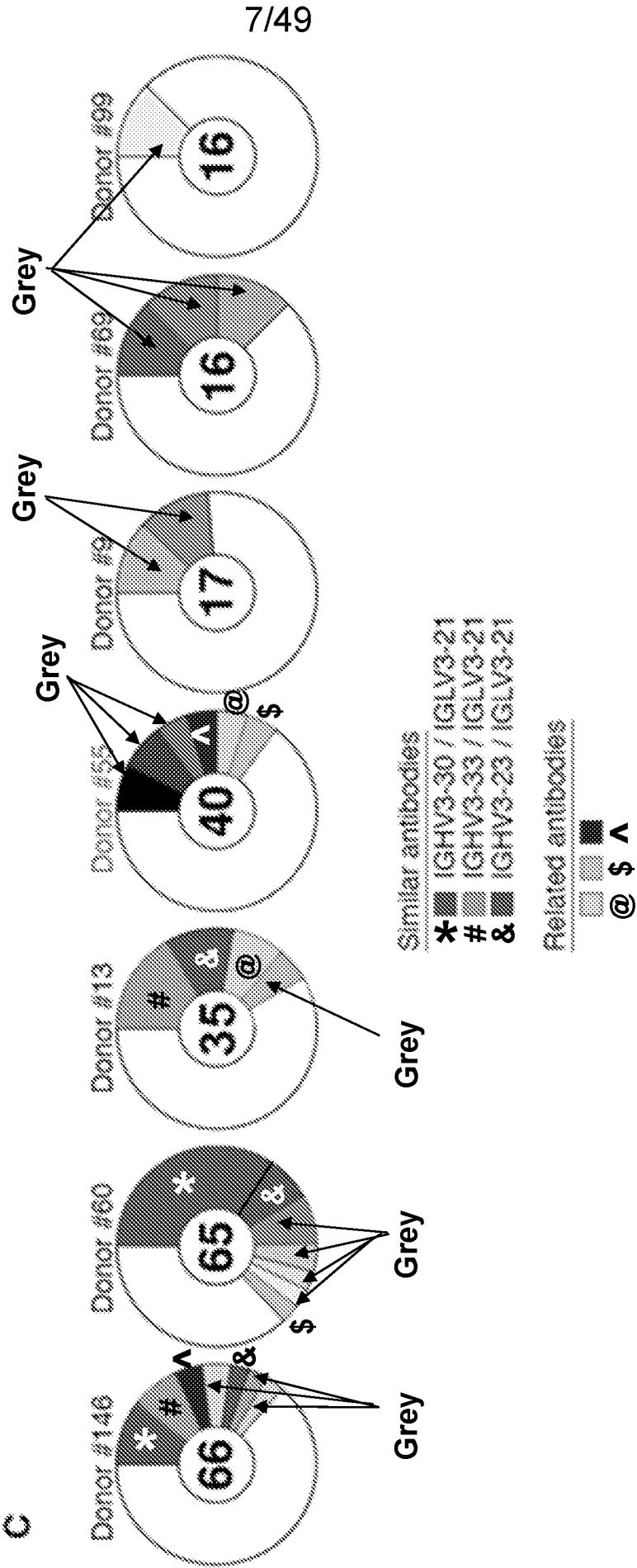


Fig. 2 (continued)

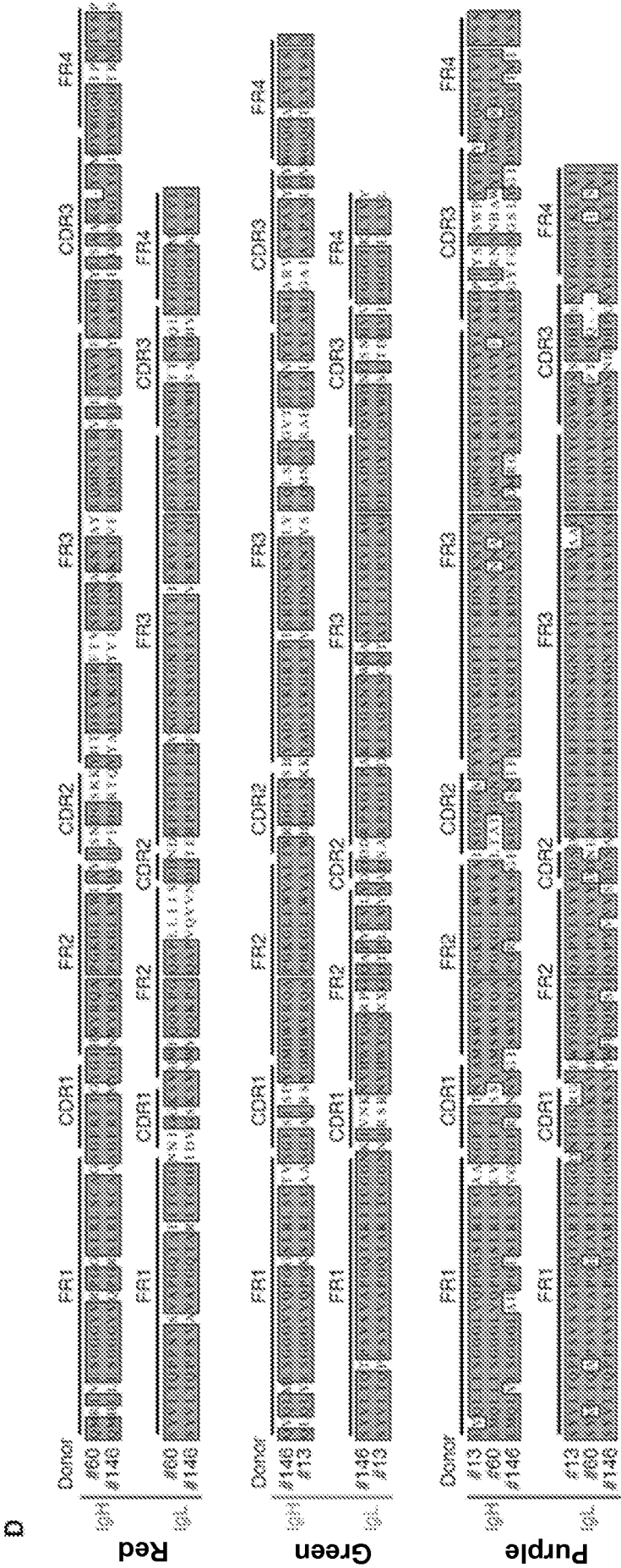


Fig. 2 (continued)

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A

Antibody	Donor ID	Heavy chain V gene	Light chain V gene	adr CHO cell
H001	146	IGHV1-3*01	IGKV1-39*01	27.1
H002	146	IGHV2-70D*04	IGLV3-21*02	30.78
H003	60	IGHV3-23*01	IGLV3-21*02	33.76
H004	146	IGHV3-23*04	IGLV3-21*02	24.65
H005	60	IGHV3-30*18	IGLV3-21*02	69.82
H006	60	IGHV3-30*18	IGLV3-21*02	49.56
H007	146	IGHV3-30*18	IGKV3-20*01	46.77
H008	146	IGHV3-30*18	IGLV3-21*02	48.27
H009	60	IGHV3-30*18	IGLV3-21*02	38.02
H010	60	IGHV3-30*18	IGLV3-21*03	35.17
H011	13	IGHV3-33*01	IGKV3-11*01	18.66
H012	13	IGHV3-33*01	IGLV3-21*02	170.9
H013	146	IGHV3-33*01	IGLV3-21*02	351.2
H014	146	IGHV3-33*01	IGLV3-21*02	111.1
H015	60	IGHV3-33*01	IGKV1-39*01	74.87
H016	69	IGHV3-48*02	IGKV3-15*01	33.58
H017	55	IGHV3-74*01	IGLV2-14*01	40.87
H018	60	IGHV3-9*01	IGLV1-51*01	b.d.
H019	69	IGHV4-30-4*01	IGKV1-39*01	34.9
H020	55	IGHV4-59*08	IGKV1-12*01	29.58
libivirumab	(positive control)			105
10-1074	(negative control)			not binding

Red

Orange

Red

Yellow

White

Fig. 3

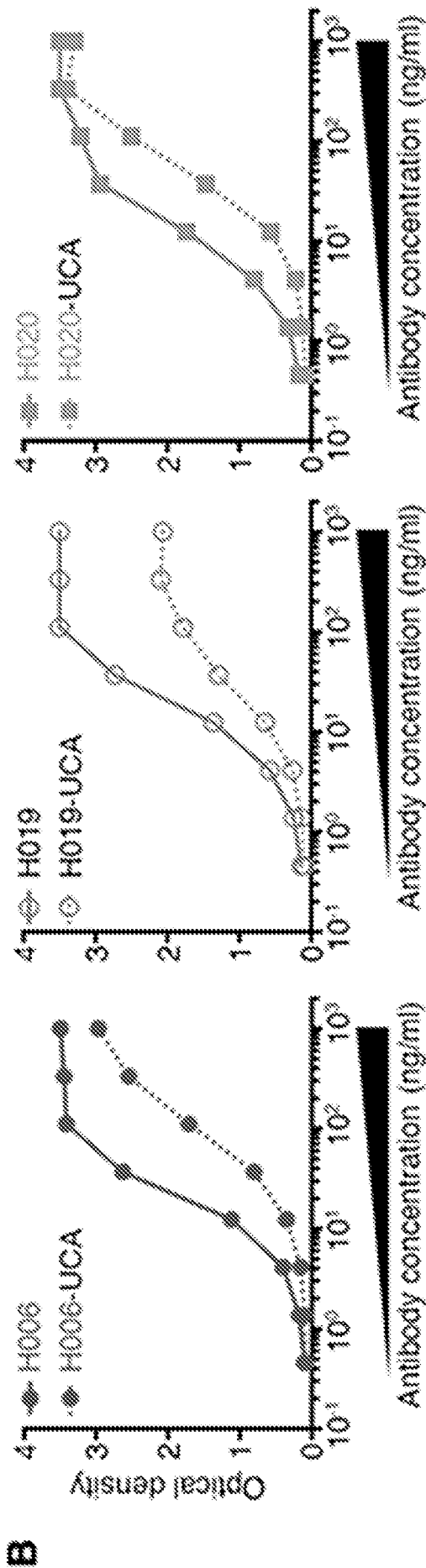


Fig. 3 (continued)

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C

adr Yeast	adw Yeast	ad Human blood	ayw Yeast	ay Human blood
26.89	30.36	42.84	18.76	63.09
24.01	40.77	53.6	b.d.	167.4
21.99	25.27	40.17	159.5	42.75
16.07	23	25.51	27.75	13.39
25	27.83	40.43	17.38	130.6
50.61	40.2	28.98	17.57	115.5
47.33	40.63	43.26	16.57	197.1
46.62	36.83	49.28	18.1	115.3
40.41	41.26	25.49	20.82	40.49
44.93	42.59	22.69	232	38.76
21.95	19.41	609.4	29.52	b.d.
111.5	45.47	82.29	57.74	78.01
133.1	82.14	52.14	72.54	120.2
167.2	50	61.45	70.64	b.d.
23.07	b.d.	103.6	34.08	129.4
25.68	68.46	46.89	23.83	102.6
28.61	74.08	66.17	25.15	207.1
b.d.	b.d.	135.1	b.d.	b.d.
33.31	37.55	36.77	35.85	38.18
35.14	40.37	30.72	34.95	34.66
116.8	123.2	112.6	40.34	119.5
not binding	not binding	not binding	not binding	not binding

Red

Orange

Yellow

White

Fig. 3 (continued)

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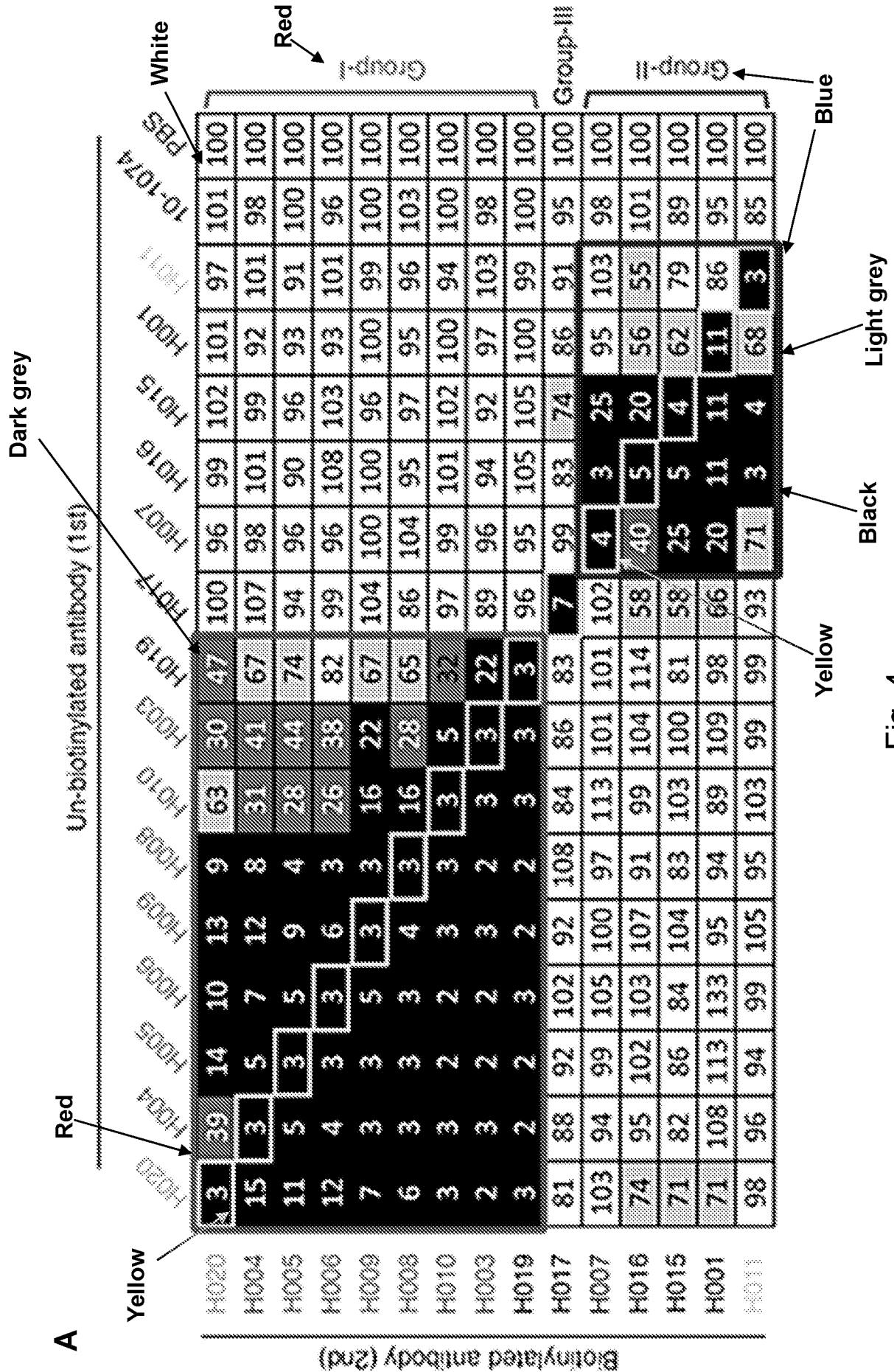


Fig. 4

B

SUBSTITUTE SHEET (RULE 26)

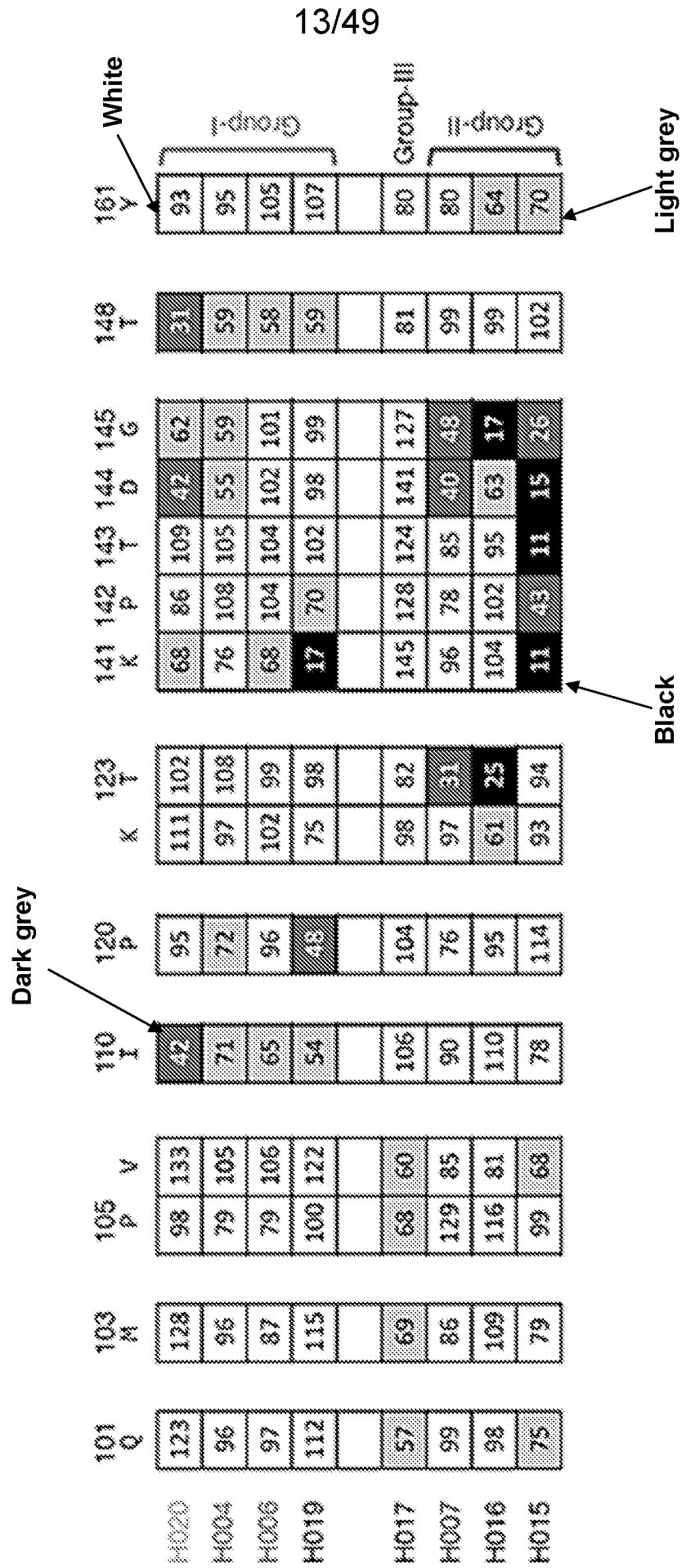


Fig. 4 (continued)

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Dark grey

White

Group-I

Group-III

Group-II

Light grey

Group-I

Group-III

Group-II

Fig. 4 (continued)

Black

	Q101R	Q101K	M103I	L109I	L109R	L110L	S113N	T114R	T115N	T116N	T118K	P120T	P120S	P120A	K122I	T123A	T123N	C124R	T125M	T126S	T126A	A128V	Q129H
H020	51	108	121	86	78	92	100	84	69	81	73	111	16	106	100	114	104	17	53	98	110	114	111
H036	45	145	157	123	92	93	126	108	87	94	85	89	29	97	96	95	103	47	86	98	96	106	114
H019	77	123	147	115	111	84	138	142	101	110	159	21	86	55	108	100	137	67	100	89	109	116	106
H017	21	108	120	122	73	97	93	82	90	76	86	124	11	129	93	111	80	94	76	100	113	74	122
H007	32	106	110	108	77	86	95	92	72	69	131	68	46	96	101	30	33	23	73	92	98	120	116
H016	41	122	119	110	80	103	96	89	82	77	109	81	41	96	51	27	27	29	82	92	103	111	113
H015	52	93	95	108	75	98	82	83	69	63	110	104	20	129	101	106	43	62	60	92	110	66	110

	G130R	G130N	M133T	F134L	C137Y	K141E	P142S	T143L	D144E	D144A	G145A	G145E	G145R	N146S	S154V	Y161F	K122R-G145R	T123N-T143S	C137Y-D144V	P142L-G145R	D144E-G145R	Wildtype H8Ag	Empty vector
H020	90	96	43	77	15	31	80	125	23	32	65	25	10	37	89	77	12	71	13	9	9	100	11
H036	90	99	59	91	26	55	105	119	83	78	83	27	24	65	100	89	30	77	14	20	15	100	13
H019	105	80	33	84	37	35	81	127	84	84	97	93	73	80	107	92	90	70	30	121	33	100	17
H017	78	108	76	82	103	78	98	126	97	108	104	68	79	57	94	77	77	65	83	126	73	100	11
H007	79	89	45	82	11	79	51	131	39	36	49	27	11	39	92	76	11	10	11	10	11	100	14
H016	82	92	53	86	23	85	80	114	71	55	12	23	10	70	98	83	34	12	12	11	11	100	13
H015	58	81	47	76	20	17	41	13	13	12	24	23	15	49	101	78	20	38	19	12	11	100	13

Fig. 4 (continued)

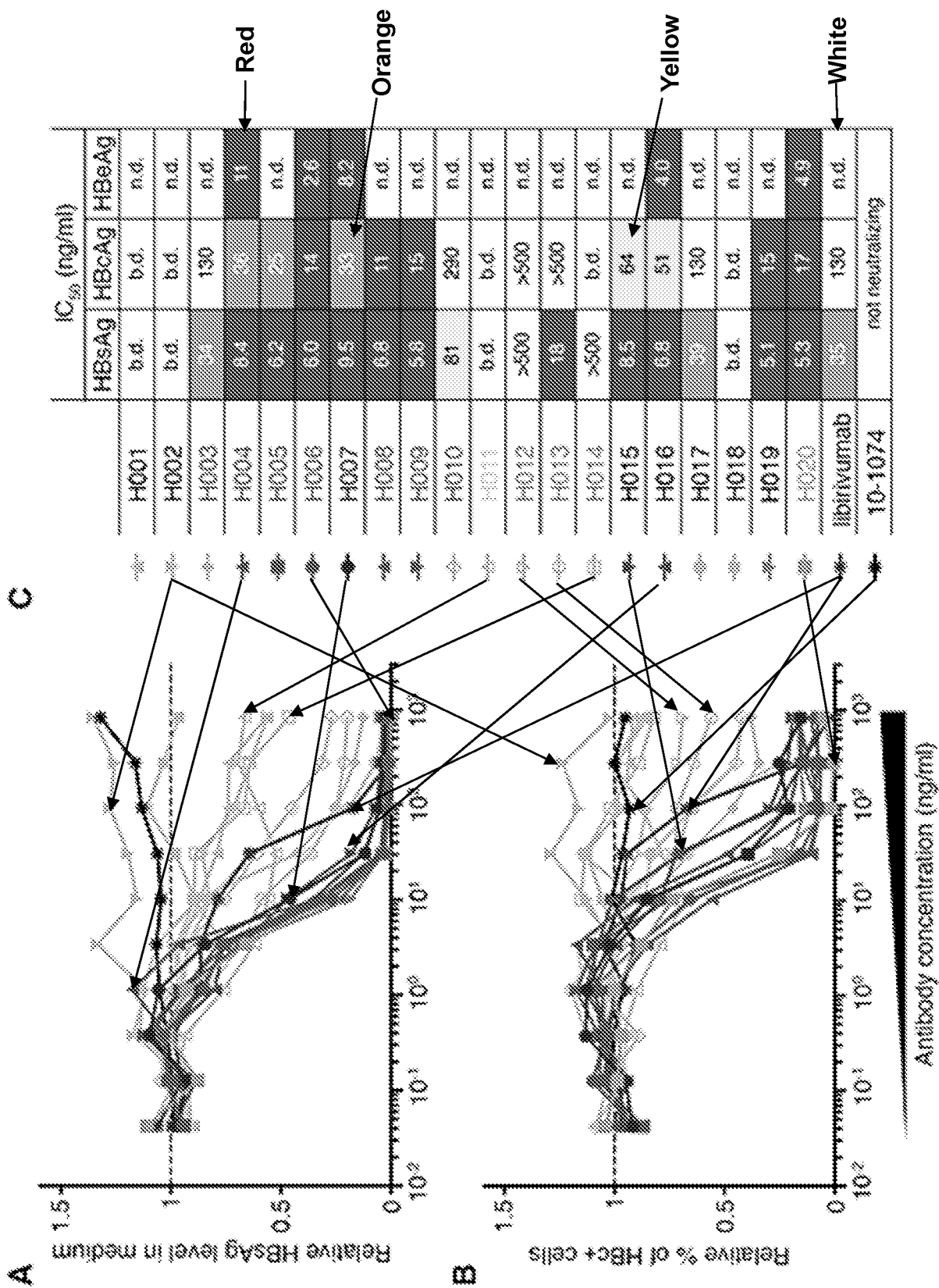


Fig. 5

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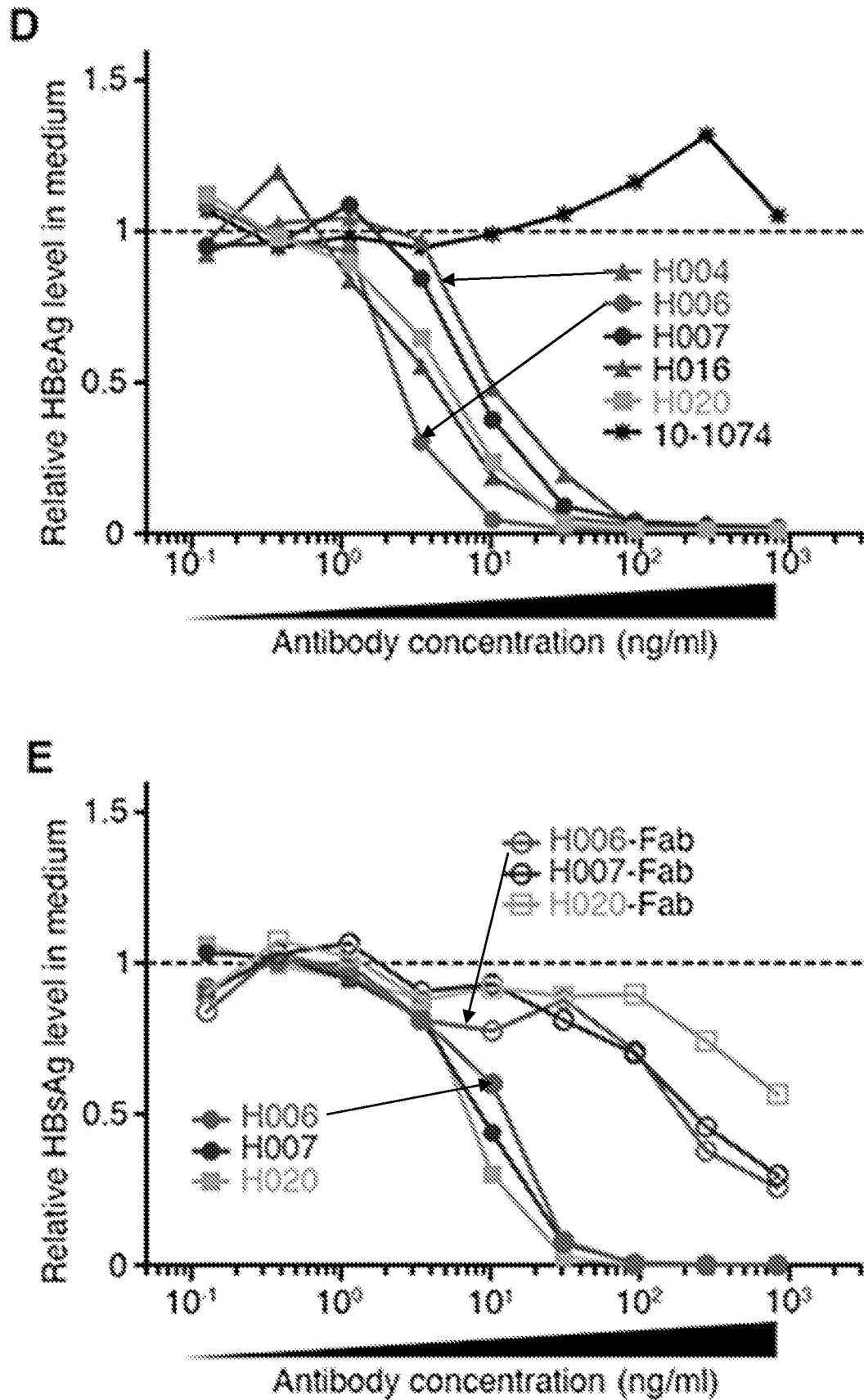


Fig. 5 (continued)

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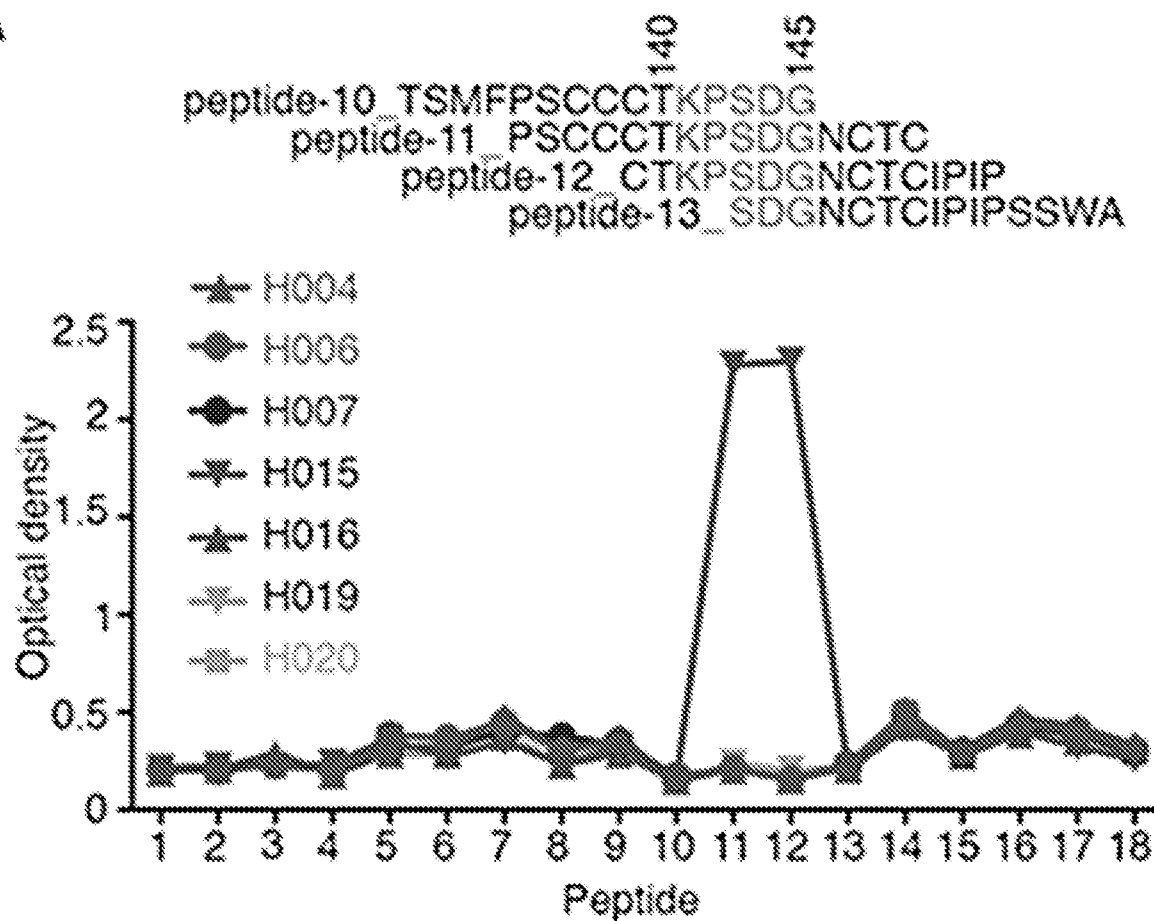
A

Fig. 6

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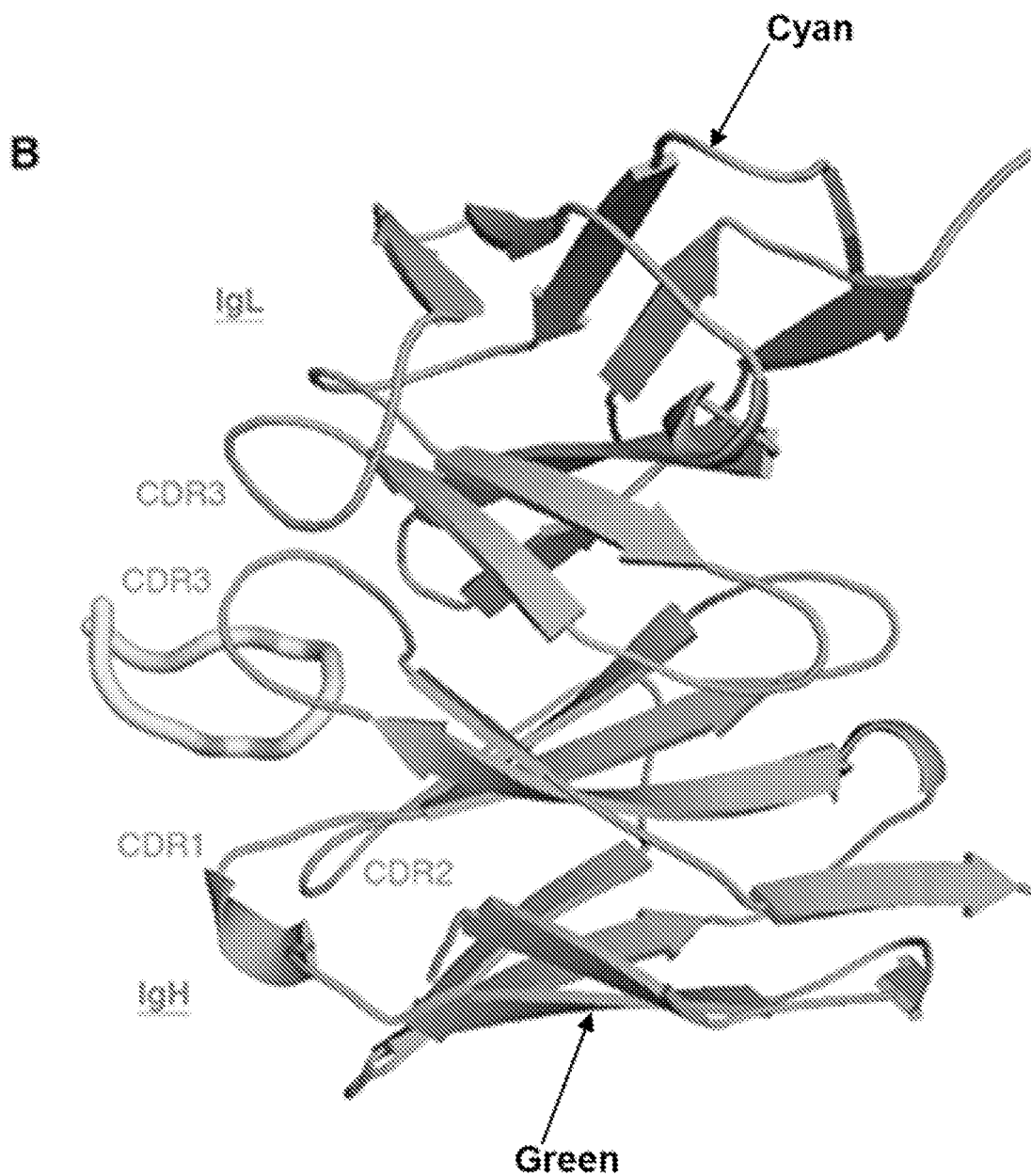


Fig. 6 (continued)

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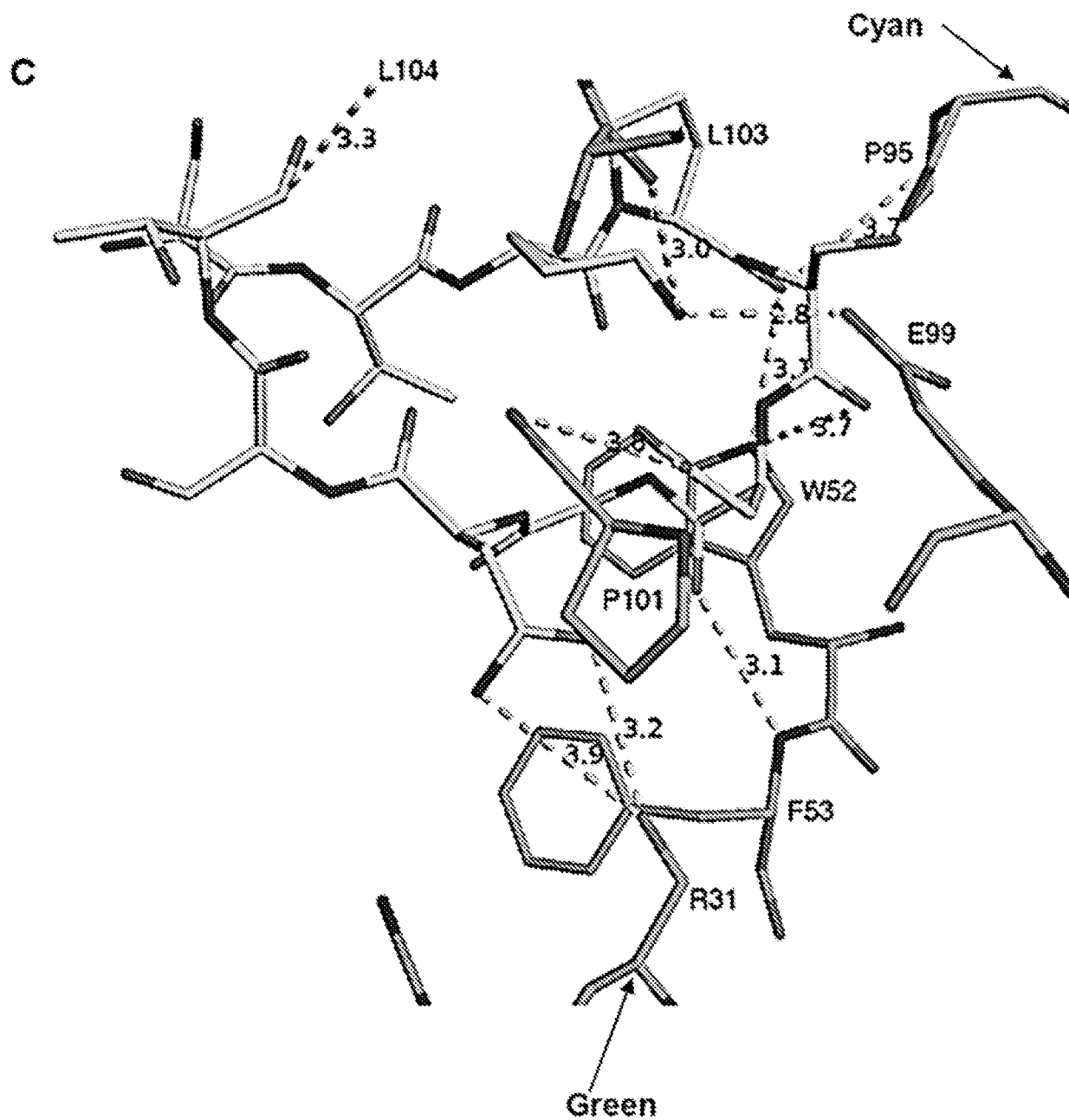


Fig. 6 (continued)

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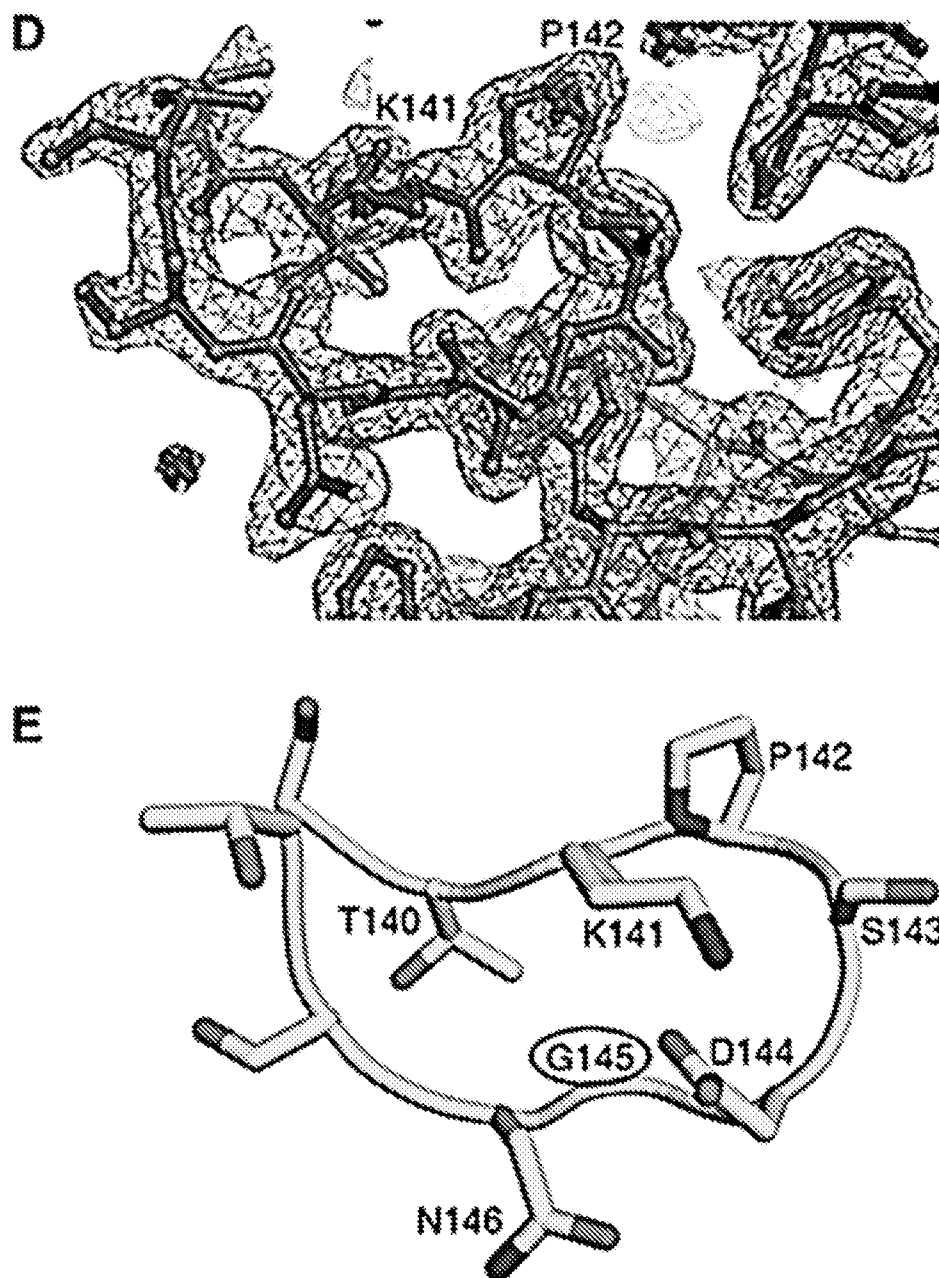


Fig. 6 (continued)

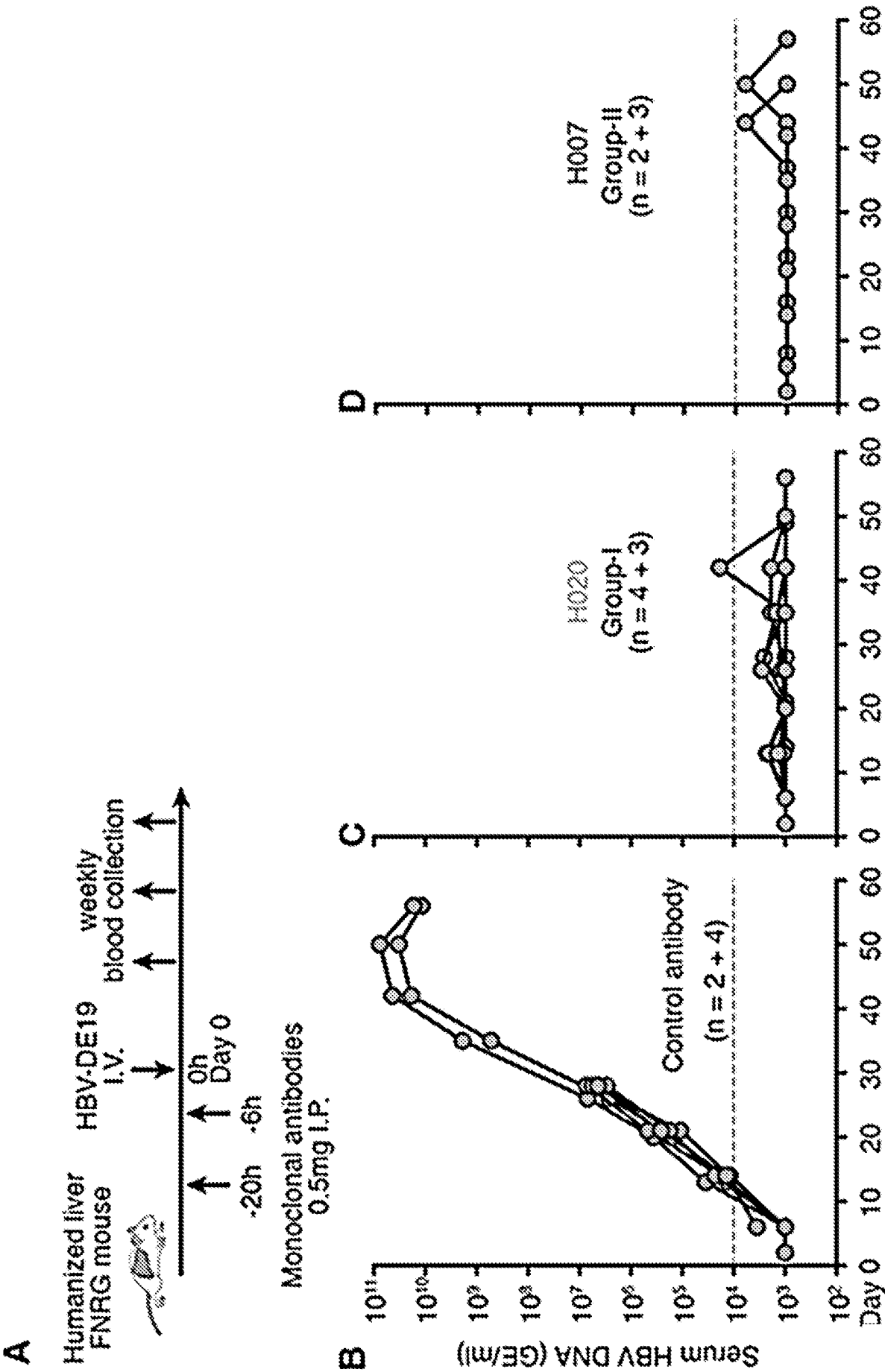
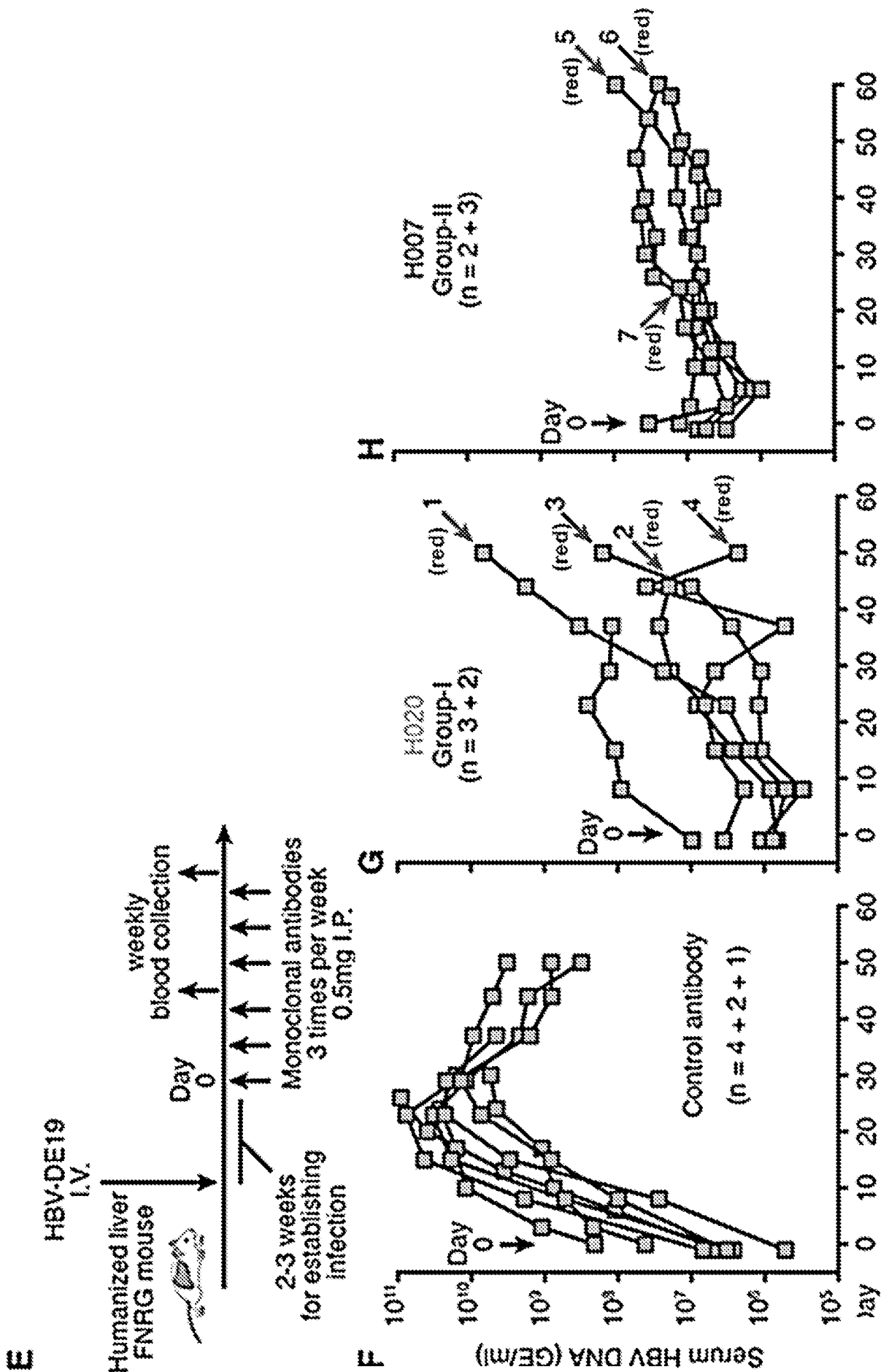


Fig. 7



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I	Red arrow	Escape mutation
	1	G145R
	2	G145R
	3	G145R
	4	G145E
	5	G145R
	6	G145R
	7	G145R
	8	K122R / G145R
	9	C137Y
	10	C137Y / D144V

Fig. 7 (continued)

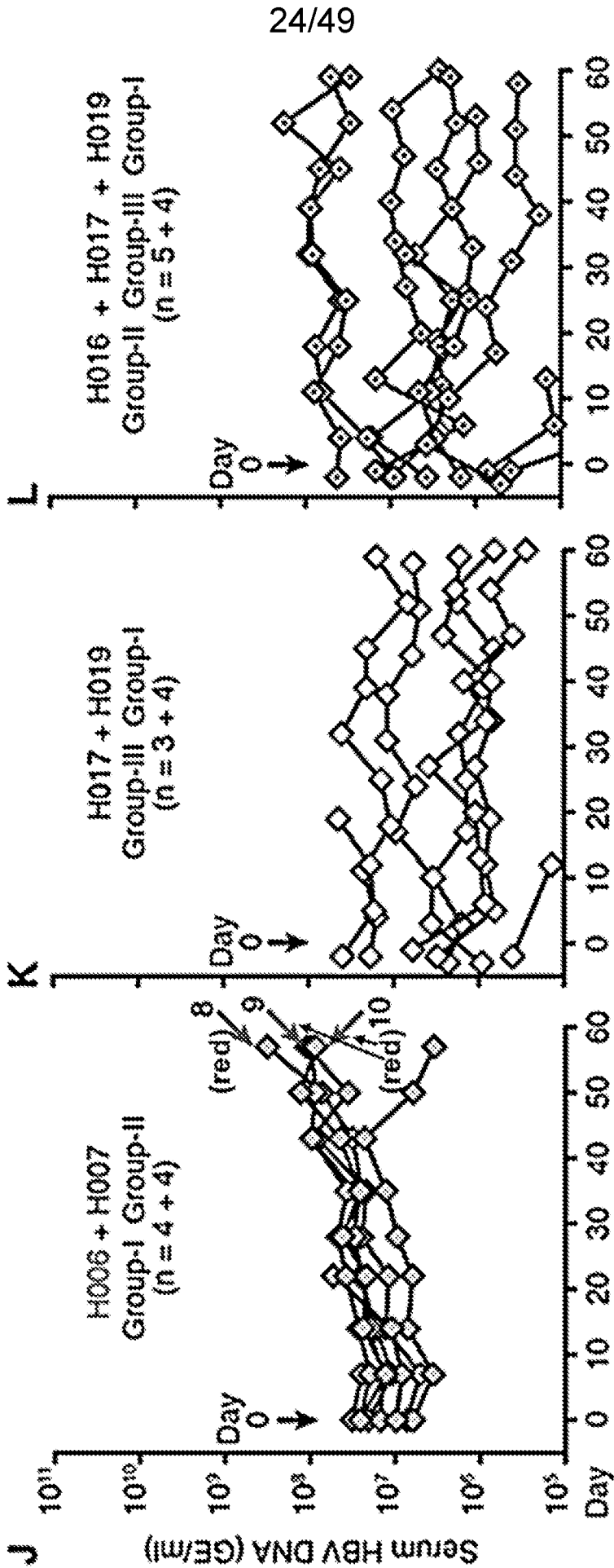


Fig. 7 (continued)

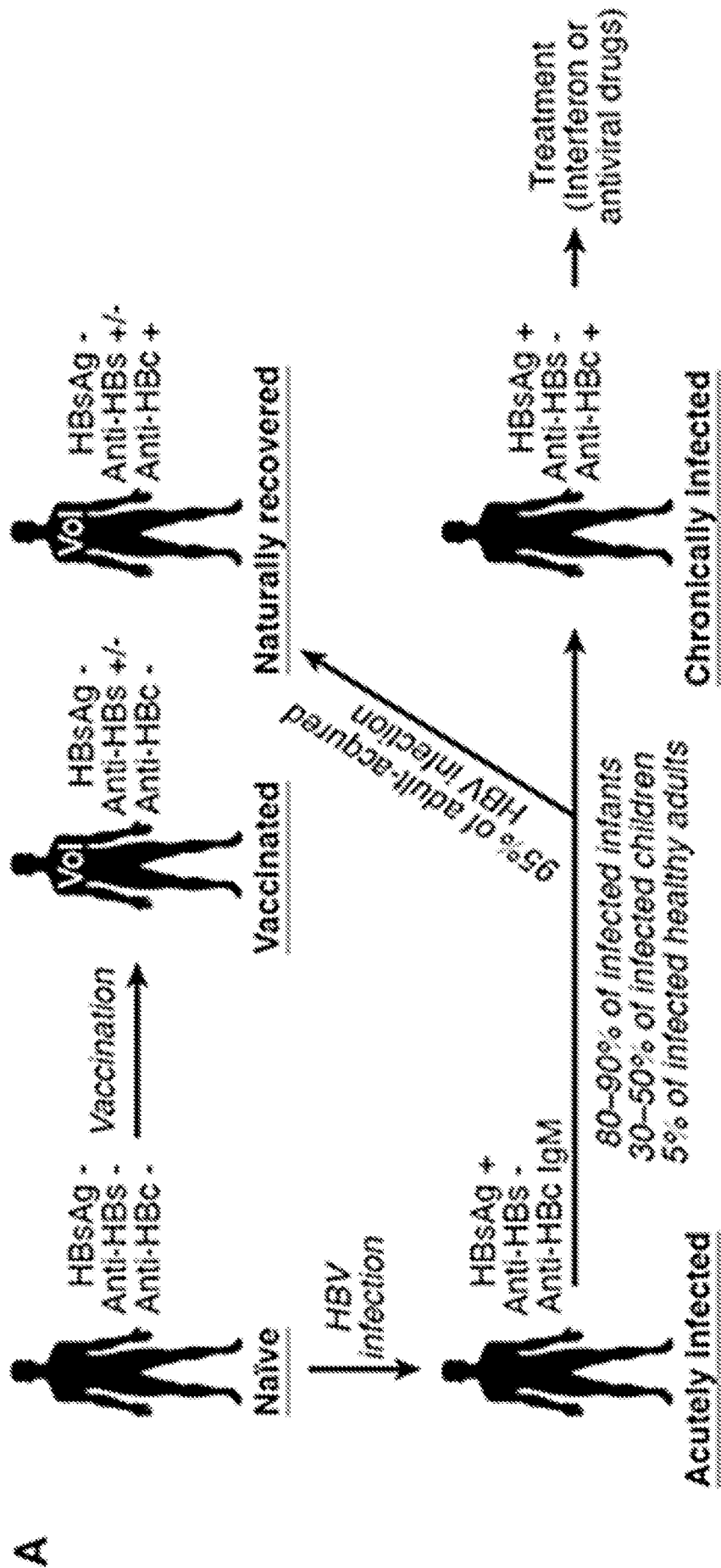


Fig. 8

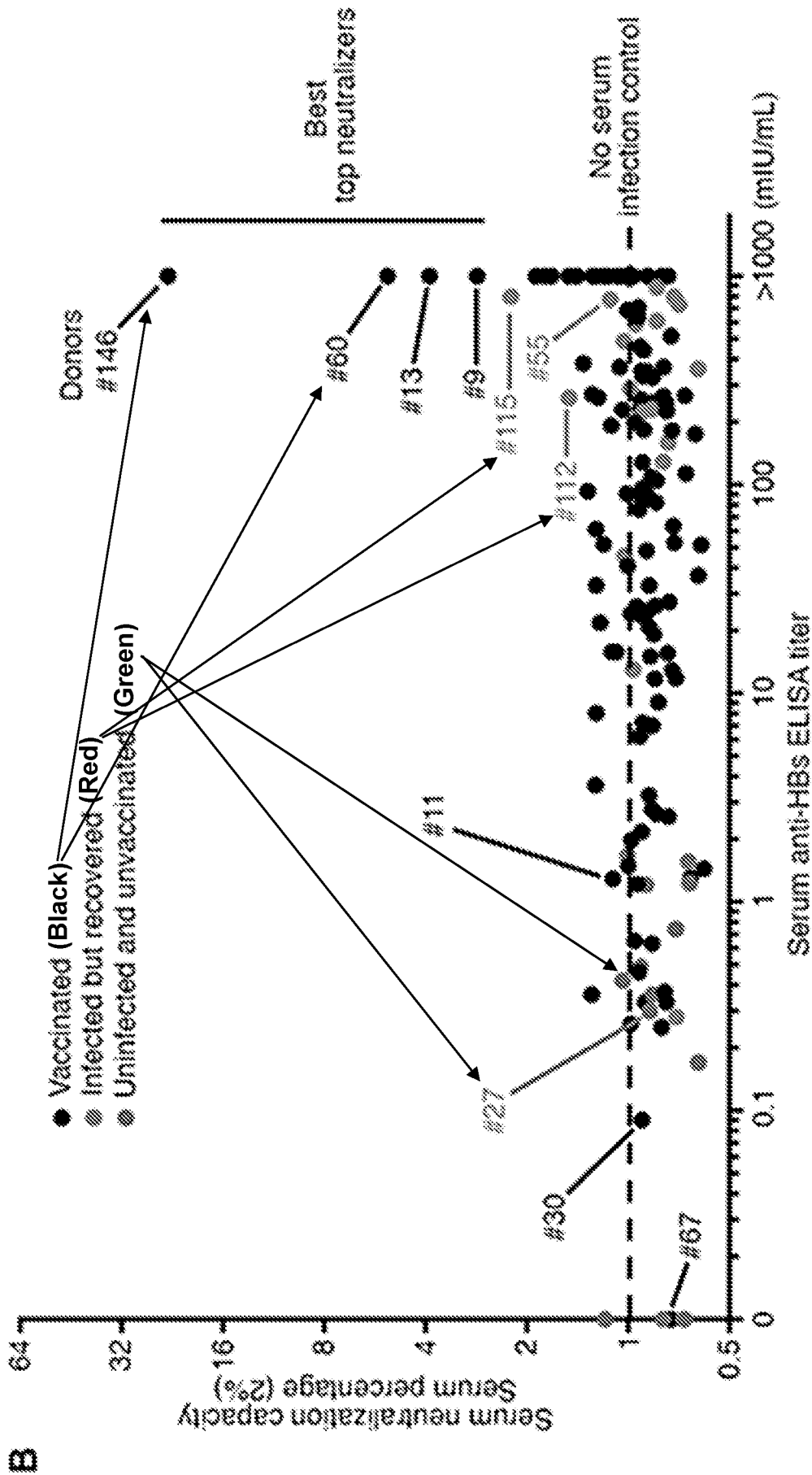


Fig. 8 (continued)

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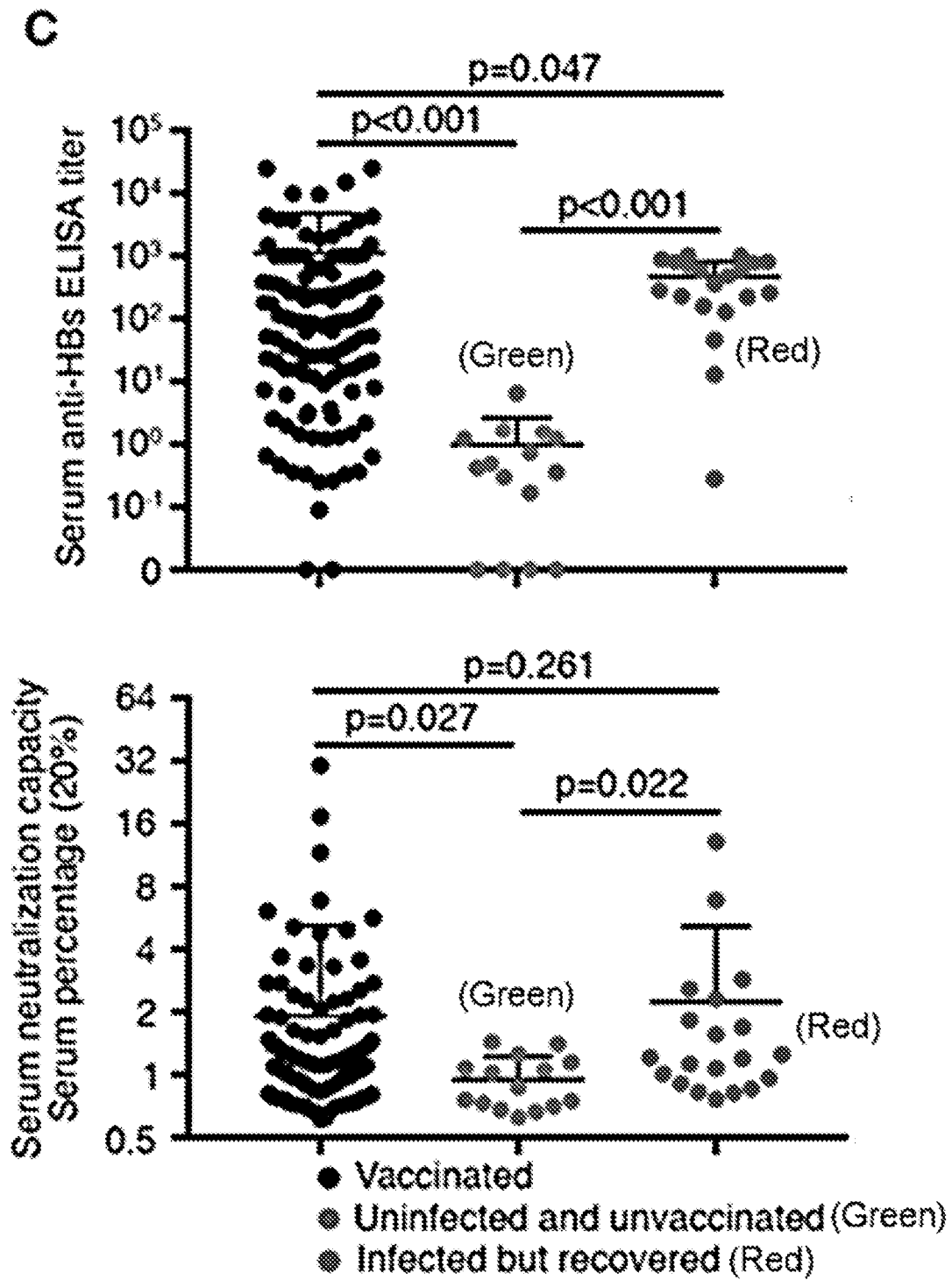


Fig. 8 (continued)

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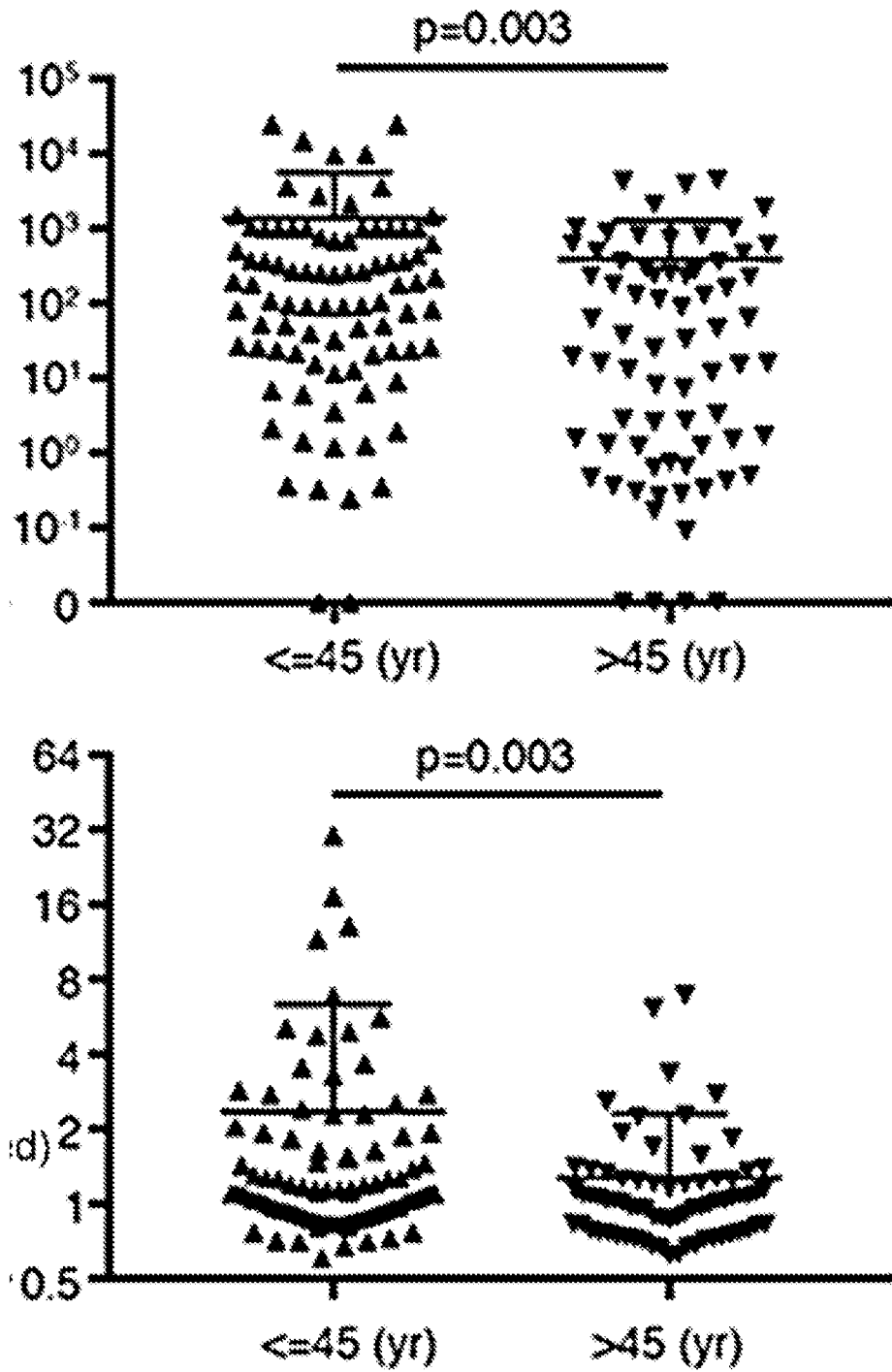
D

Fig. 8 (continued)

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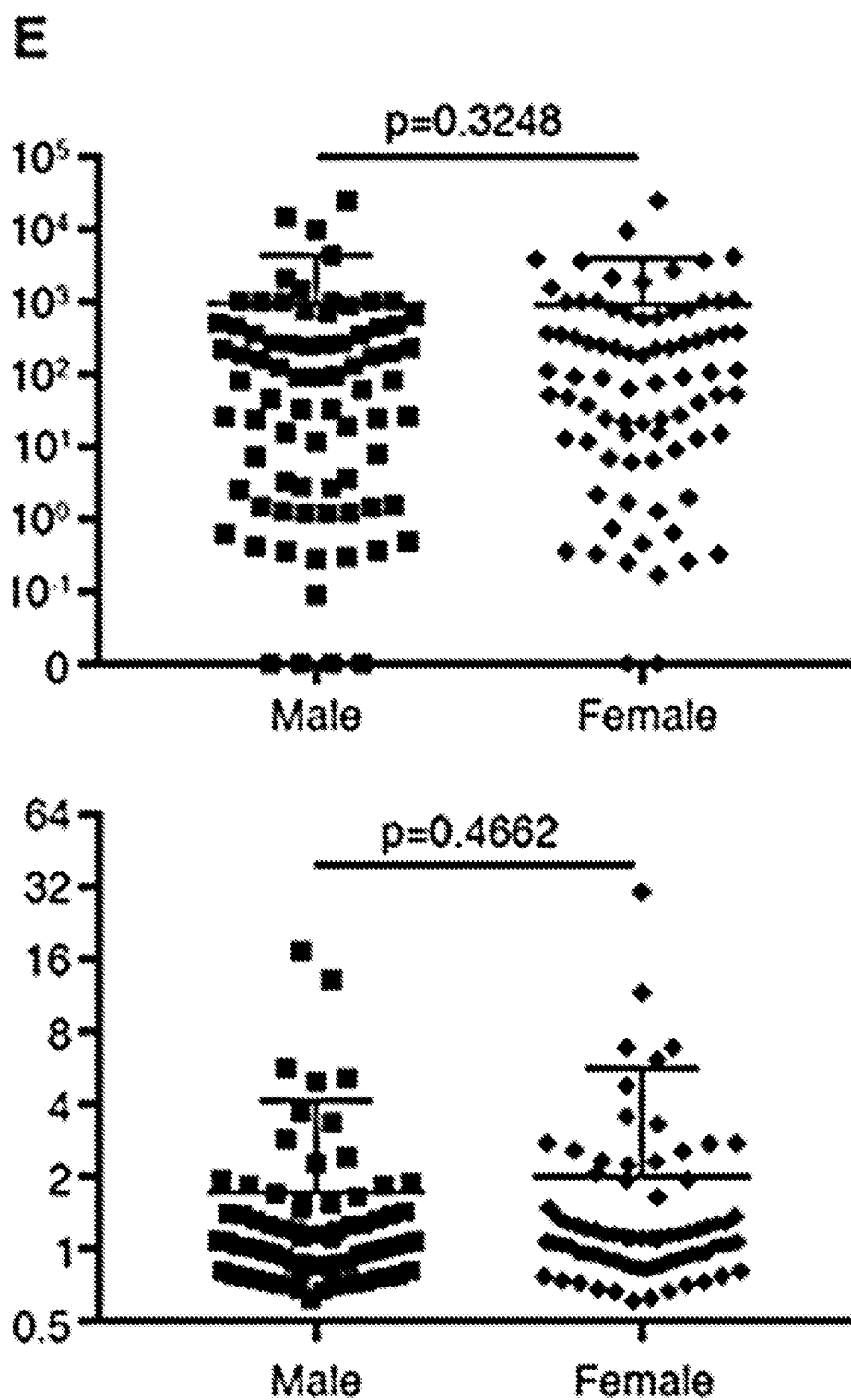


Fig. 8 (continued)

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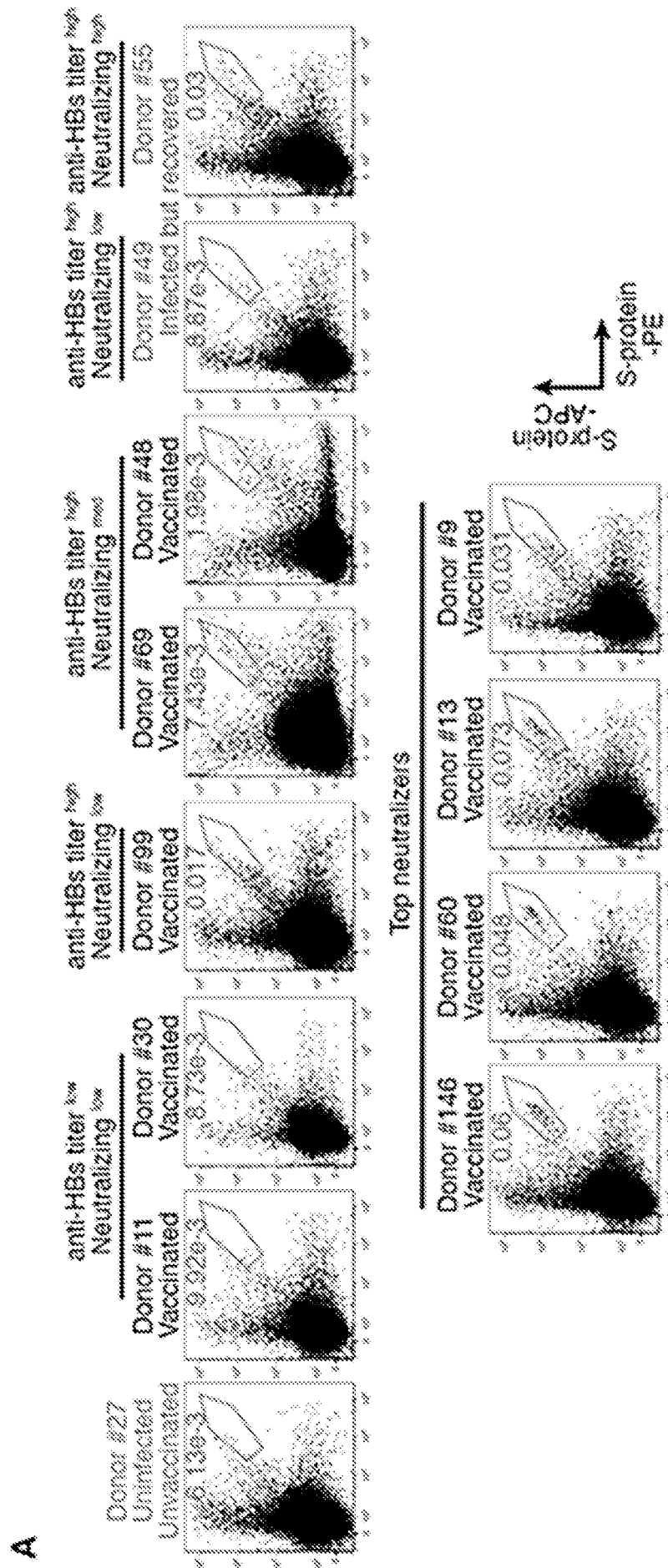


Fig. 9

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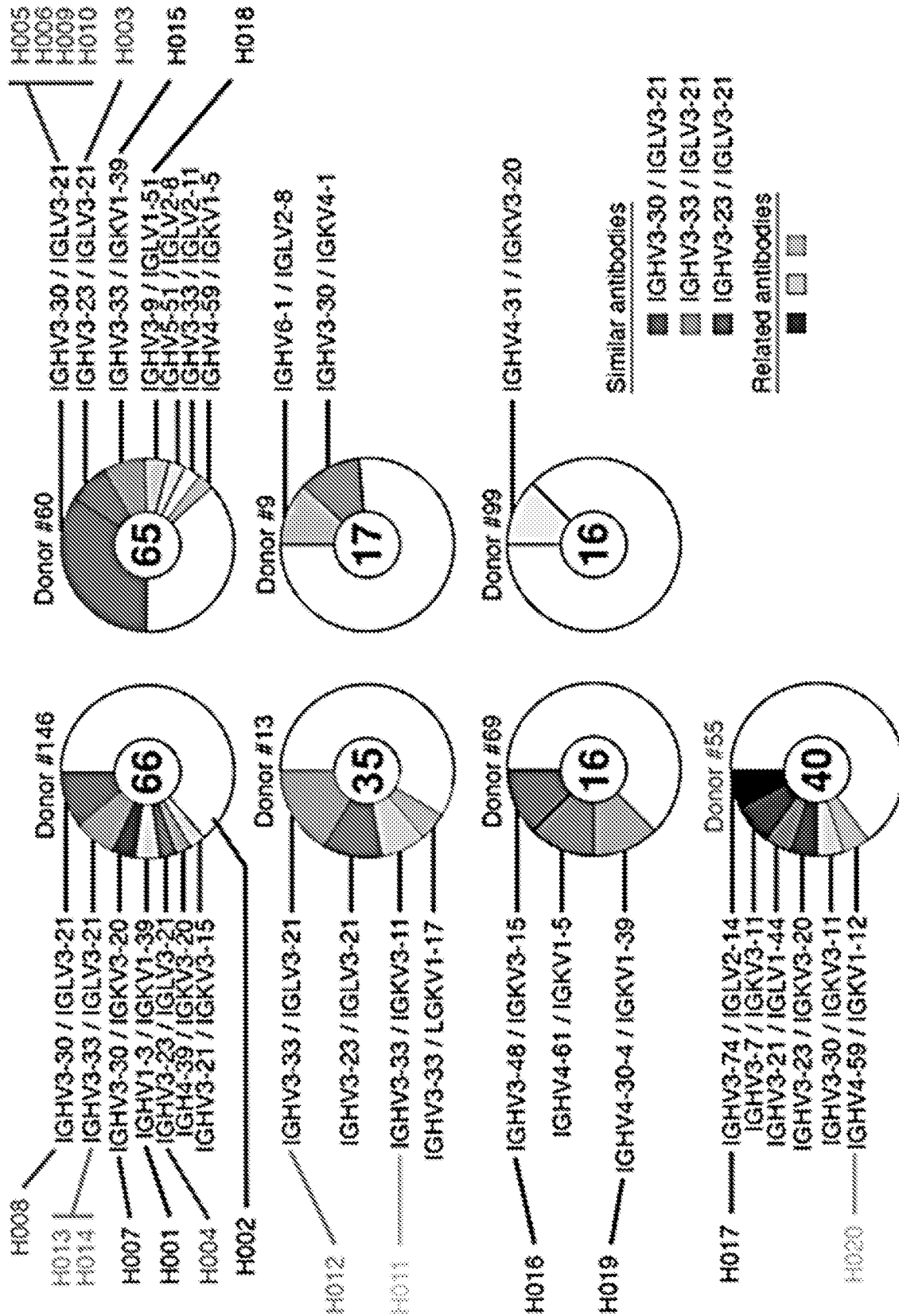


Fig. 9 (continued)

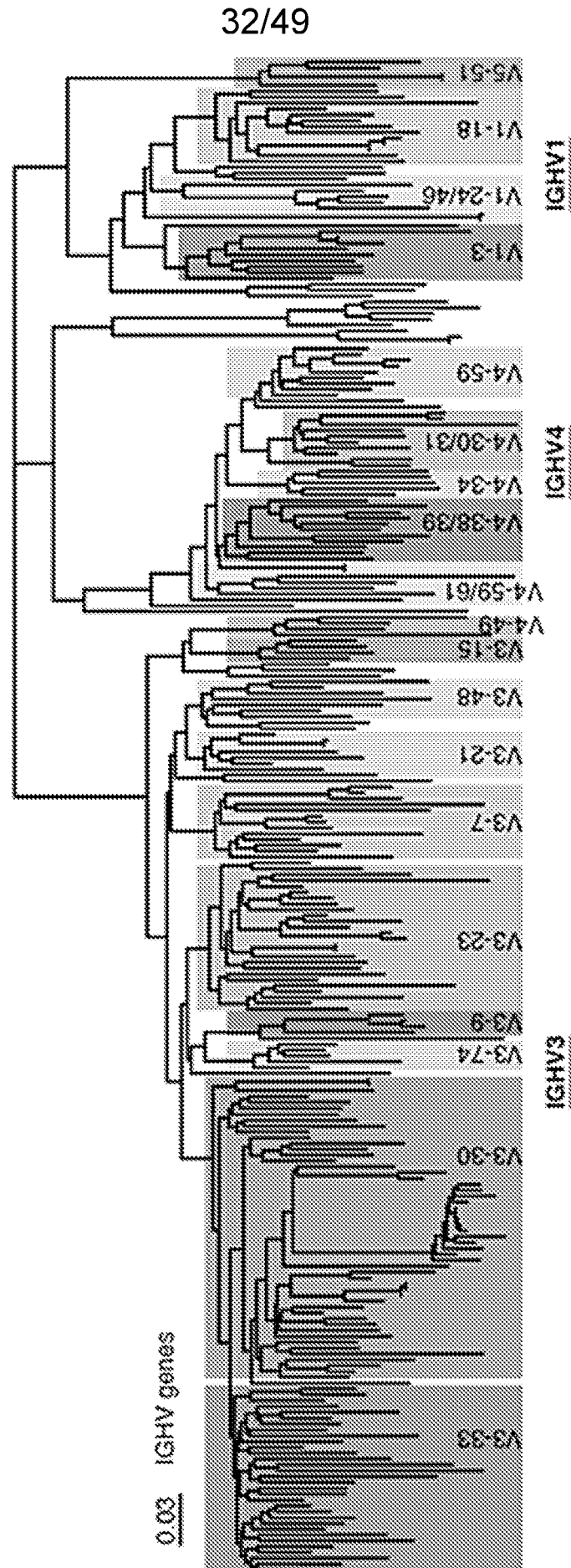


Fig. 9 (continued)

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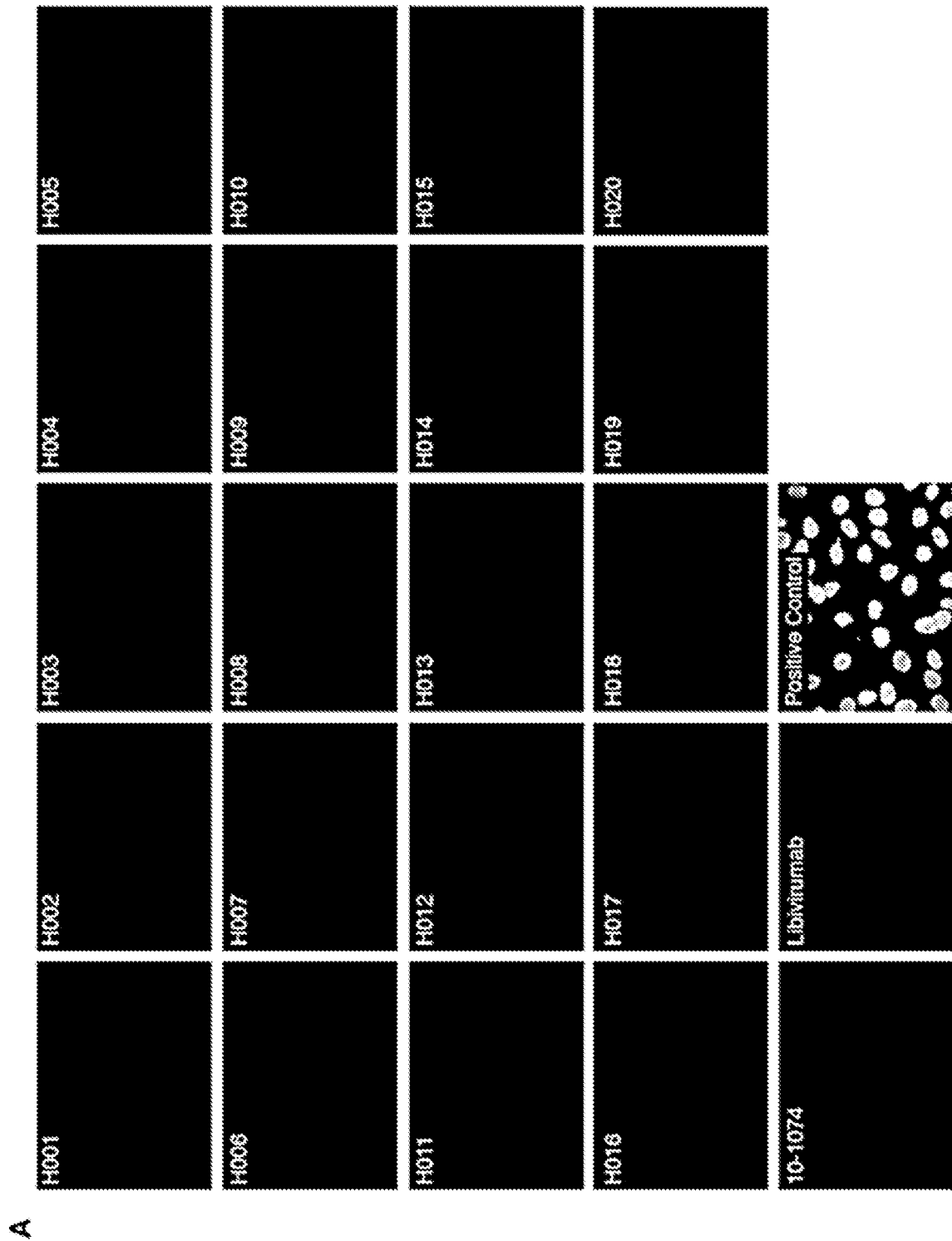
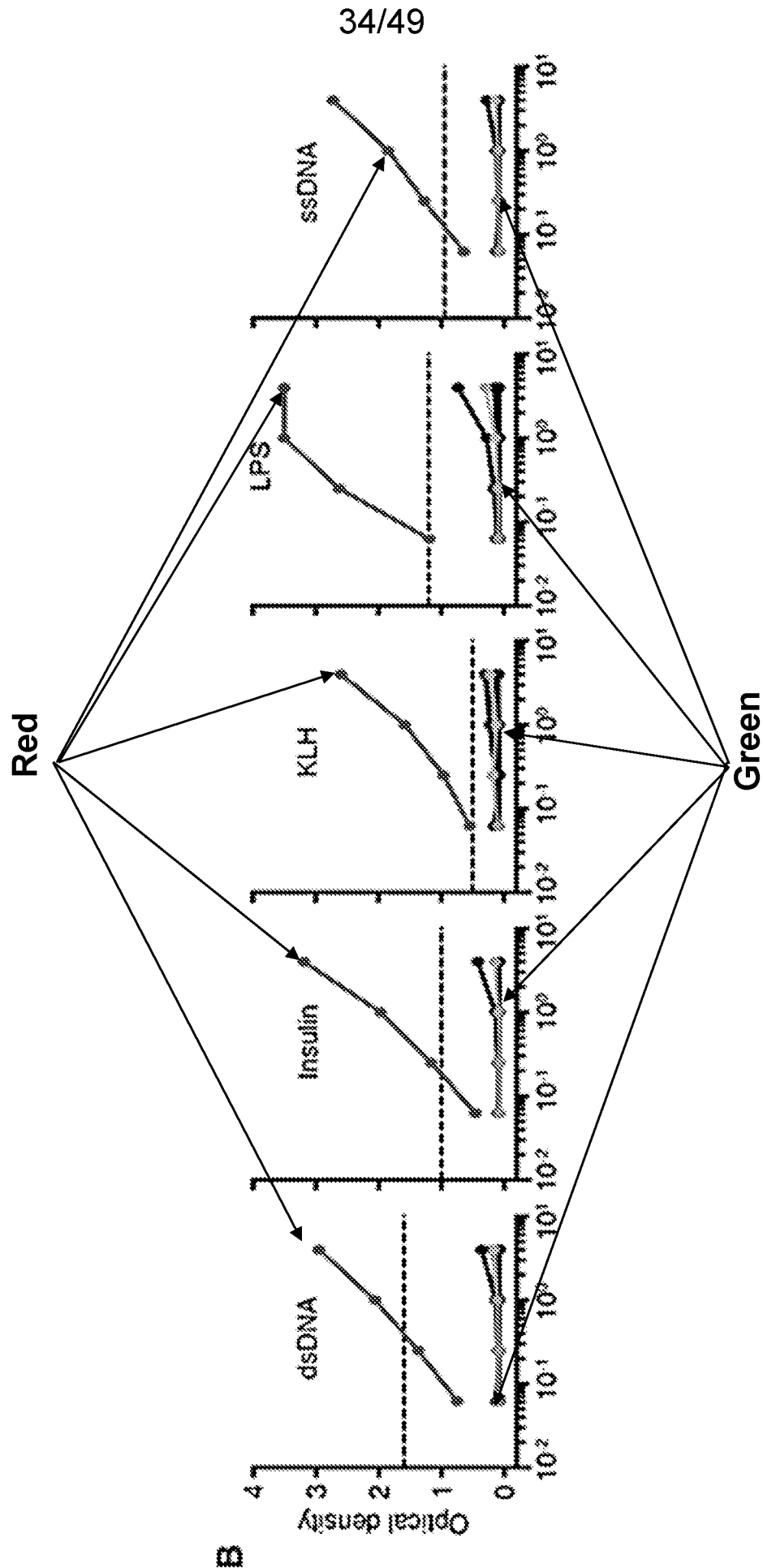


Fig. 10



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A

	Q	G	M	L	P	V	C	P	L	I	P	G	S	T	T	T	S	T	G	P	C	K	T	C	T
101	123		128		98	133		121	107	95	110	108	106	98	105	102	93	93	93	95		111	102		103
H020																									
H004	96		96		79	105		100	96	71	113	101	103	103	101	100	100	101	92	72		97	108		112
H006	97		87		79	106		92	110	65	114	102	97	97	98	96	98	95	92	96		102	99		103
H019	112		115		100	122		105	106	54	112	99	92	92	99	91	99	95	114	45		75	98		83
H017	57		69		68	60		87	85	106	100	80	91	90	91	88	98	89	84	104		98	82		78
H007	99		86		129	85		108	85	90	99	105	103	104	107	105	99	107	102	76		97	51		97
H016	98		109		116	81		94	96	110	86	97	103	102	104	103	106	109	113	95		61	25		95
H015	75		79		99	68		80	100	78	80	85	94	95	94	100	96	100	94	114		93	94		108

Group-I

Group-II

Group-III

White

Dark grey

Black

Light grey

Fig. 11

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A (continued)

	T	P	A	Q	G	N	S	M	F	P	S	C	C	C	T	K	P	T	D	G	N	C	T	C	I
H020	96	94		96	106	89	91	95	97	94	101				102	68	86	109	37	62	93				95
H004	110	107		101	102	95	99	102	108	101	100				109	76	108	105	55	59	92				112
H006	101	108		100	101	93	97	101	103	101	98				100	68	104	104	102	101	92				108
H019	102	91		94	88	81	91	89	84	89	103				101	17	70	102	98	99	102				86
H017	99	101		92	102	103	94	99	95	108	120				133	145	128	124	141	127	105				91
H007	98	104		103	102	111	104	107	105	104	98				97	96	78	85	40	45	106				99
H016	95	97		102	100	120	110	99	95	109	98				86	104	102	95	63	17	108				106
H015	97	99		105	101	111	108	106	109	103	101				105	11	33	11	15	26	107				94

Dark grey

Light grey

White

Black

Group-I

Group-II

Fig. 11 (continued)

A (continued)

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	151	P	I	P	S	S	S	W	A	F	A	K	Y	161	L	W	E	W	A	S	V	R	F	S	W	Emp	WT	
H020	103		104	98	115					99		99	93	110	107	100	99			104	105		96	93	100	19	100	Group-I
H004	103		108	97	108					103		99	95	102	96	91	99			97	96		94	100	99	27	100	Group-I
H006	100		108	102	111					109		106	105	102	94	93	99			98	102		106	101	105	17	100	Group-I
H019	98		100	93	101					99		94	107	110	100	105	104			99	96		99	103	89	25	100	Group-I
H017	109		145	113	117					117		106	80	94	101	99	92			110	104		106	102	96	16	100	Group-III
H007	99		100	108	93					98		107	80	97	101	102	101			99	100		100	99	101	21	100	Group-III
H016	98		90	99	85					95		97	64	94	102	104	103			104	101		107	106	105	20	100	Group-III
H015	99		91	103	87					97		97	70	85	100	105	95			99	99		97	97	100	17	100	Group-III

Dark grey

White

Light grey

Black

Fig. 11 (continued)

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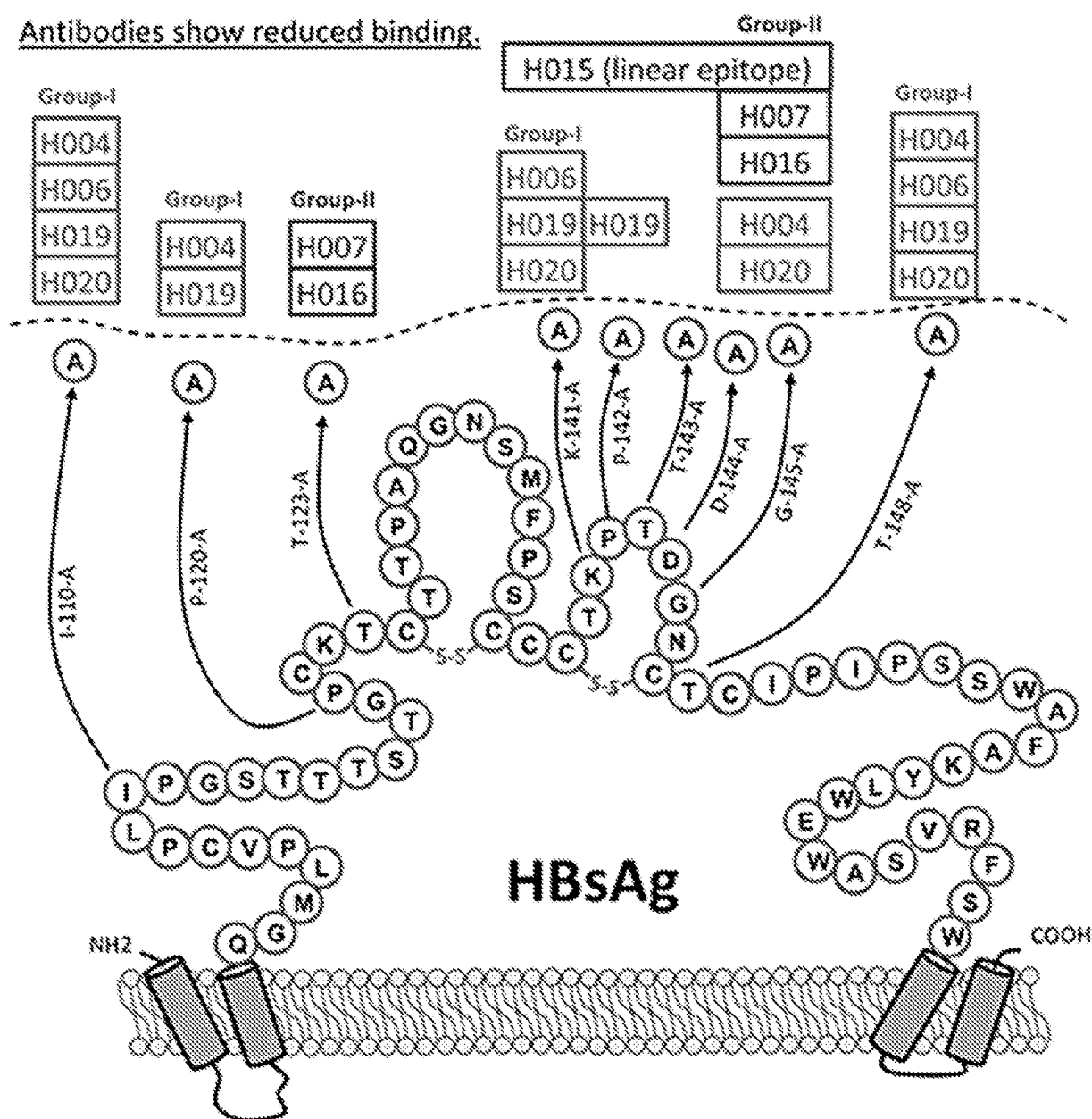
BAntibodies show reduced binding.

Fig. 11 (continued)

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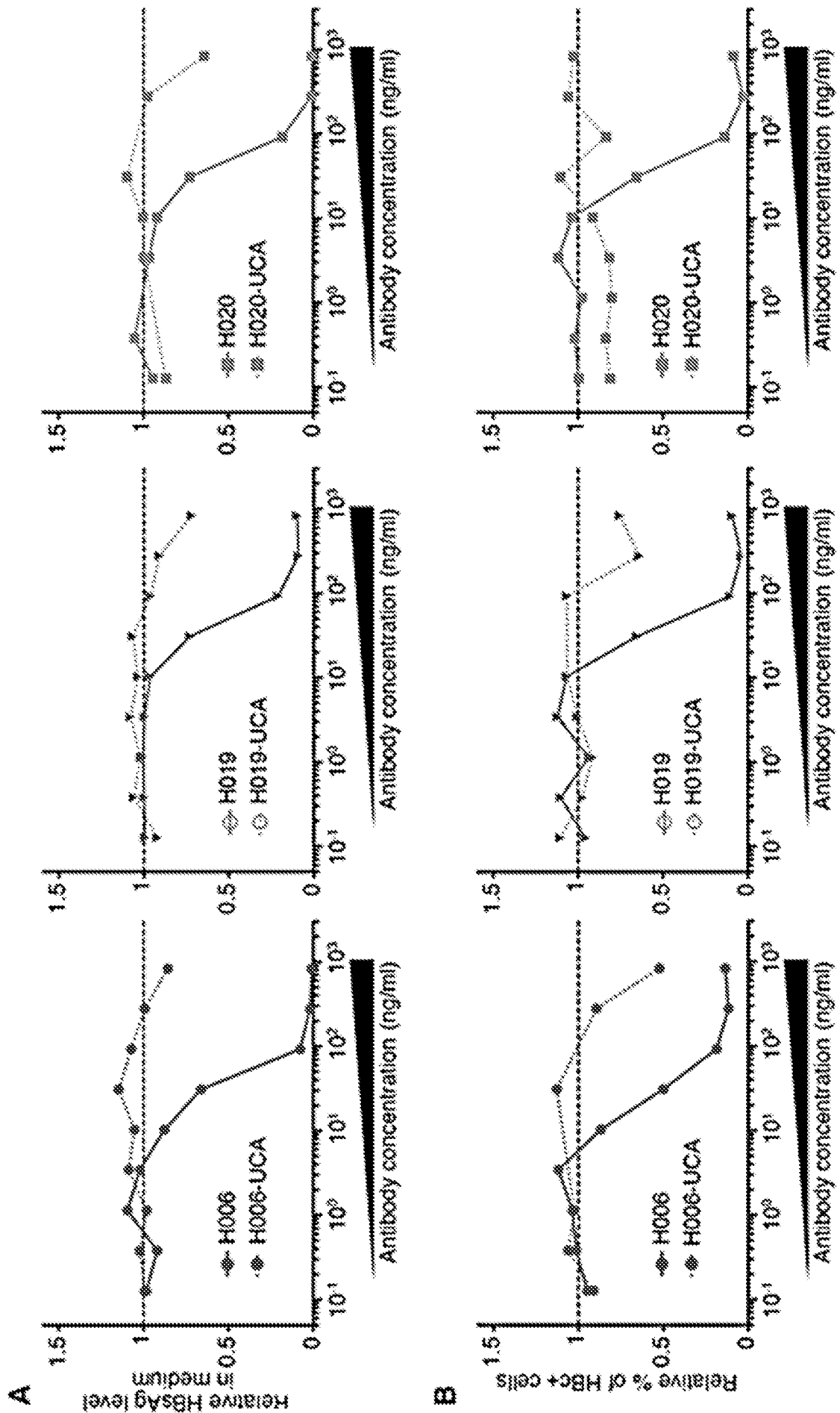


Fig. 12

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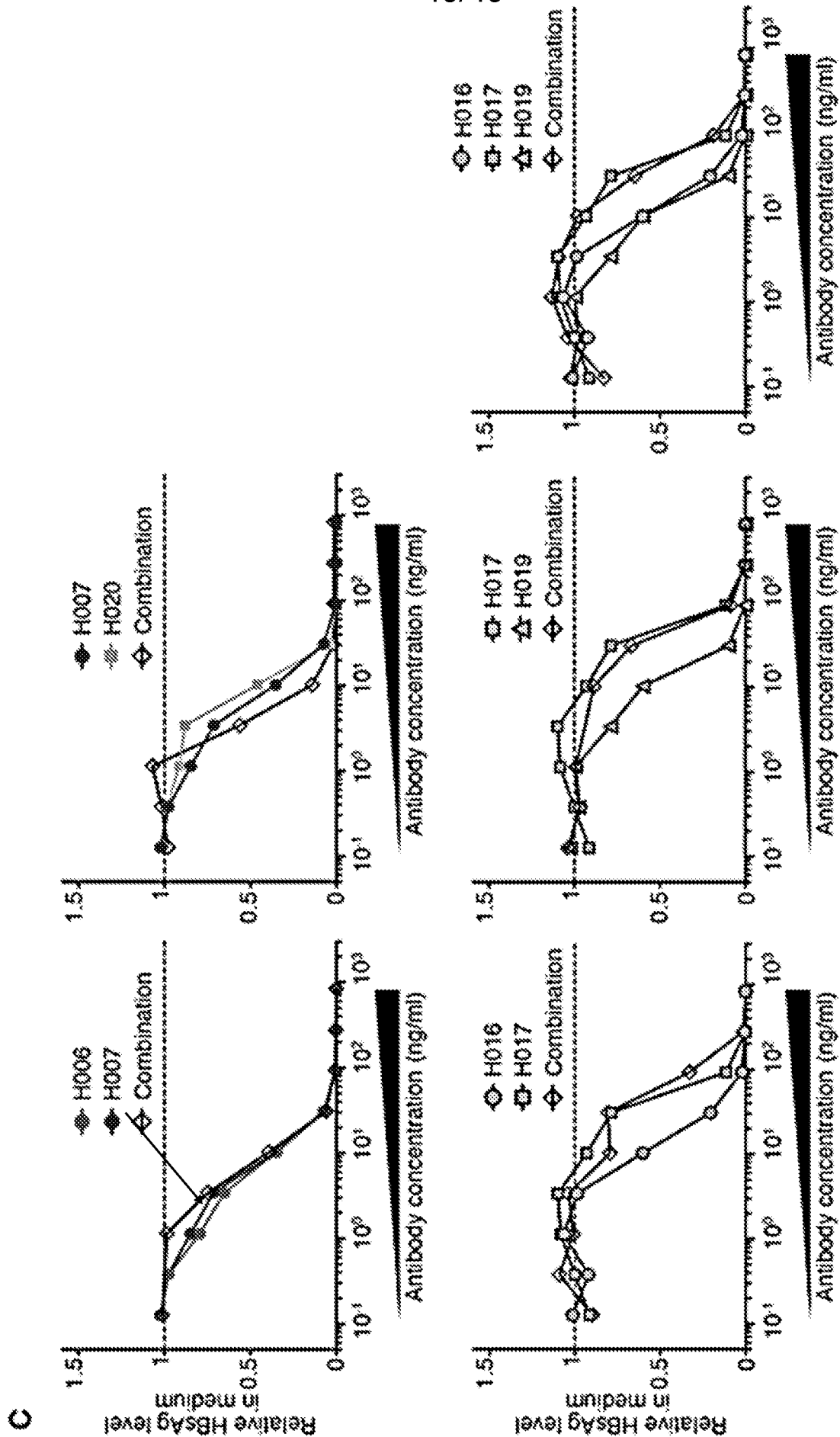


Fig. 12 (continued)

Fig. 13

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B

Wavelength (Å)	0.979
Resolution range	67.35-1.78 (1.82-1.78)
Space group	P2 ₁ 2 ₁ 2 ₁
Unit cell	49.9 71.2 134.7
Total reflections	615,285 (56,022)
Unique reflections	46,432 (4,386)
Multiplicity	12.9 (12.1)
Completeness (%)	99.5 (91.0)
Mean I/sigma (I)	17.2 (1.26)
Wilson B-factor	33
Anisotropy	0.449
R-merge	0.084 (1.26)
R-meas	0.090 (1.309)
R-pim	0.034 (0.505)
CC _{1/2}	0.999 (0.793)
Reflections used in refinement	46432 (4380)
Reflections used for R-free	1999 (188)
R-work	0.182 (0.276)
R-free	0.227 (0.293)

Number of non-hydrogen atoms	3752
Macromolecules	3391
Solvent	361
Protein residues	451
RMSZ (bonds)	0.37
RMSZ (angles)	0.55
Ramachandran favored (%)	98
Ramachandran allowed (%)	2
Ramachandran outliers (%)	0.00
Rotamer outliers (%)	0.00
Clashscore	1.00
Average B-factor	39
Average B of H/L	39
Average B of the peptide	49
Macromolecules	38
Solvent	43
Fo,Fc correlation	0.97
Bulk solvent k _{iso} (e/Å ³), B _{iso} (Å ²)	0.32, 42.8

Fig. 13 (continued)

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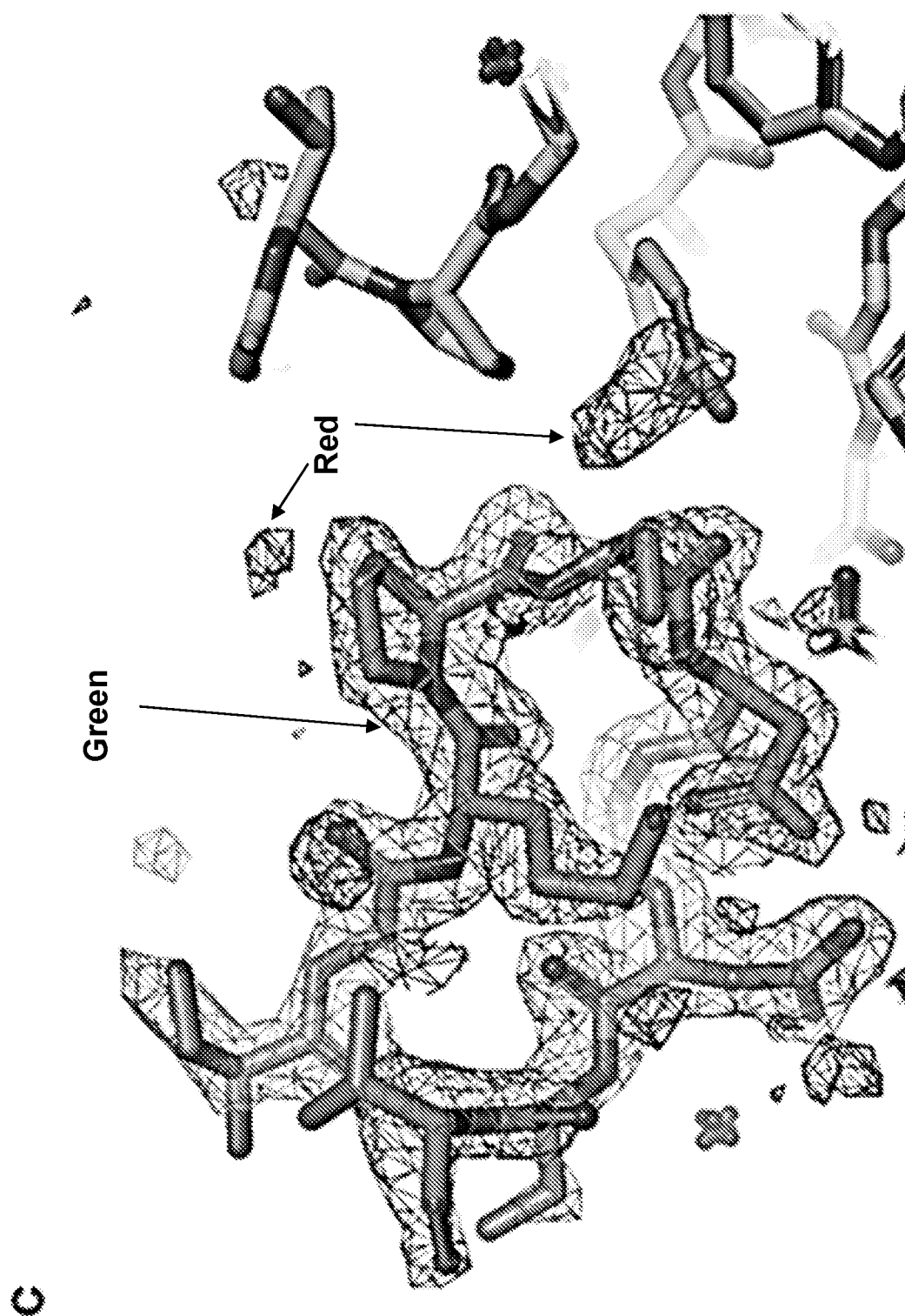


Fig. 13 (continued)

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D

H-bonds within the peptide
Ser139(O) – Thr 148(N, OG1)
Lys141(N) – ASN146(O)
Lys141(O) – Gly145(N)
Asp144(OD2) – Asp146(N, ND2)
Asp144(OD1) – Asp146(N)
Salt bridge within the peptide
Lys141(NZ) – Asp144(OD2)
H-bonds between Fab and peptide
Lys141(NZ) – Asp H100(O)
Lys141(NZ) – Leu103(O)
Pro142(O) – Trp H52(NE1)
Ser143(O) – Tyr H59(OH)
Ser143(OG) – Glu H99(OE2)
Asp144(O) – Phe H53(N)
Salt Bridge between Fab and peptide
Lys141(NZ) – Glu H99(OE2)
Hydrophobic between Fab and peptide
Pro142 – Leu L29
Gly145 – Trp H52

Fig. 13 (continued)

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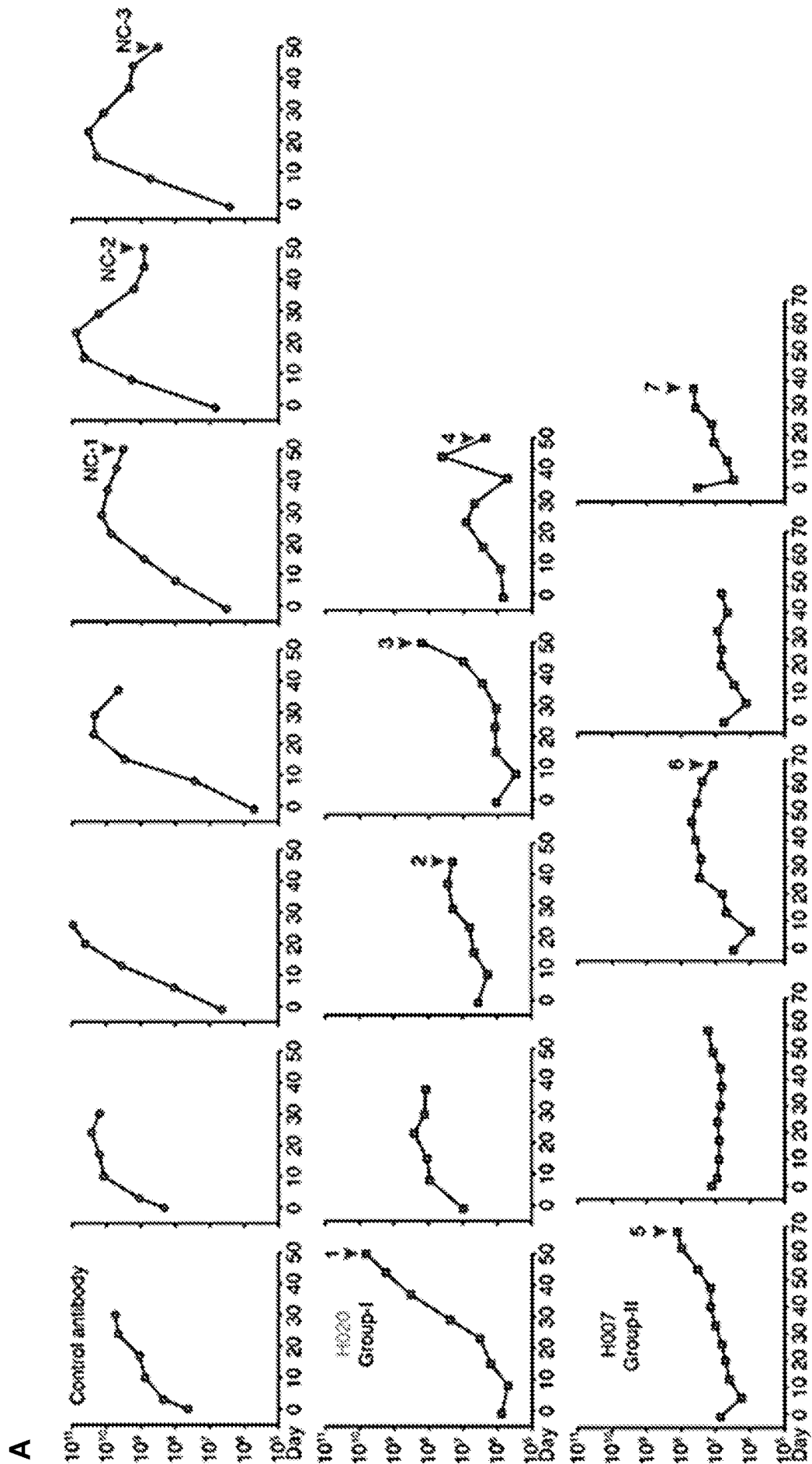


Fig. 14

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A (continued)

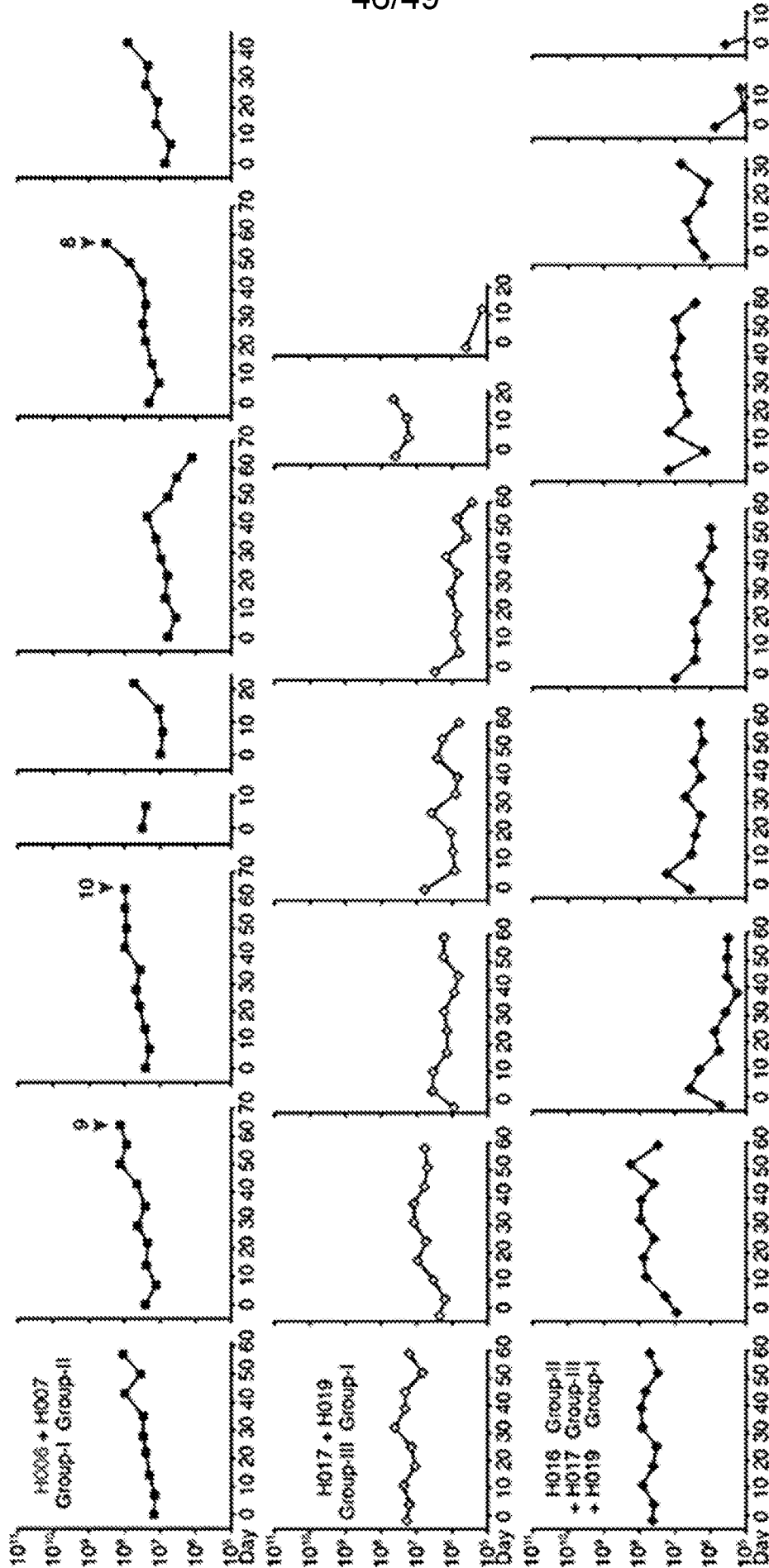


Fig. 14 (continued)

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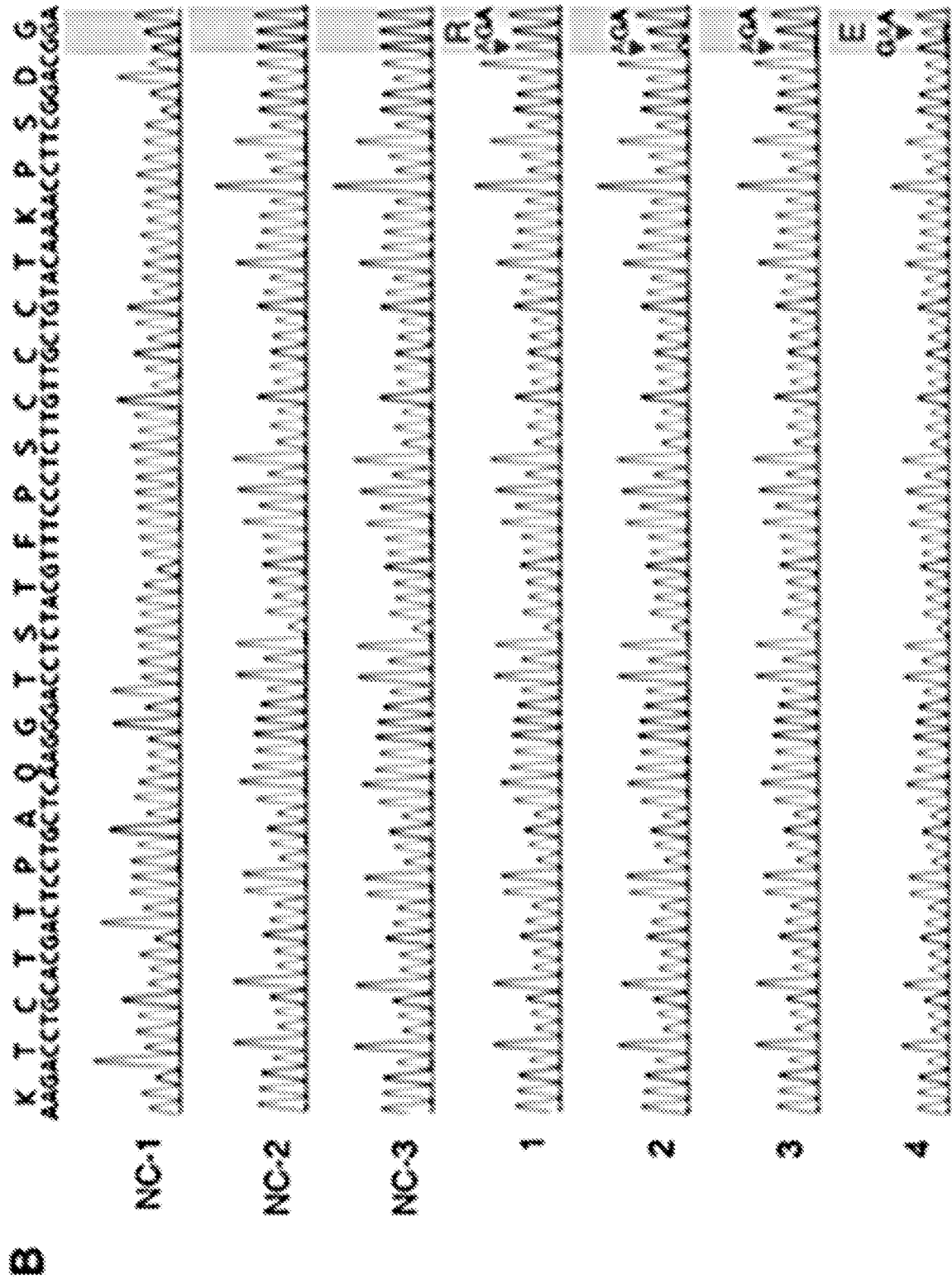


Fig. 14 (continued)

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B (continued)

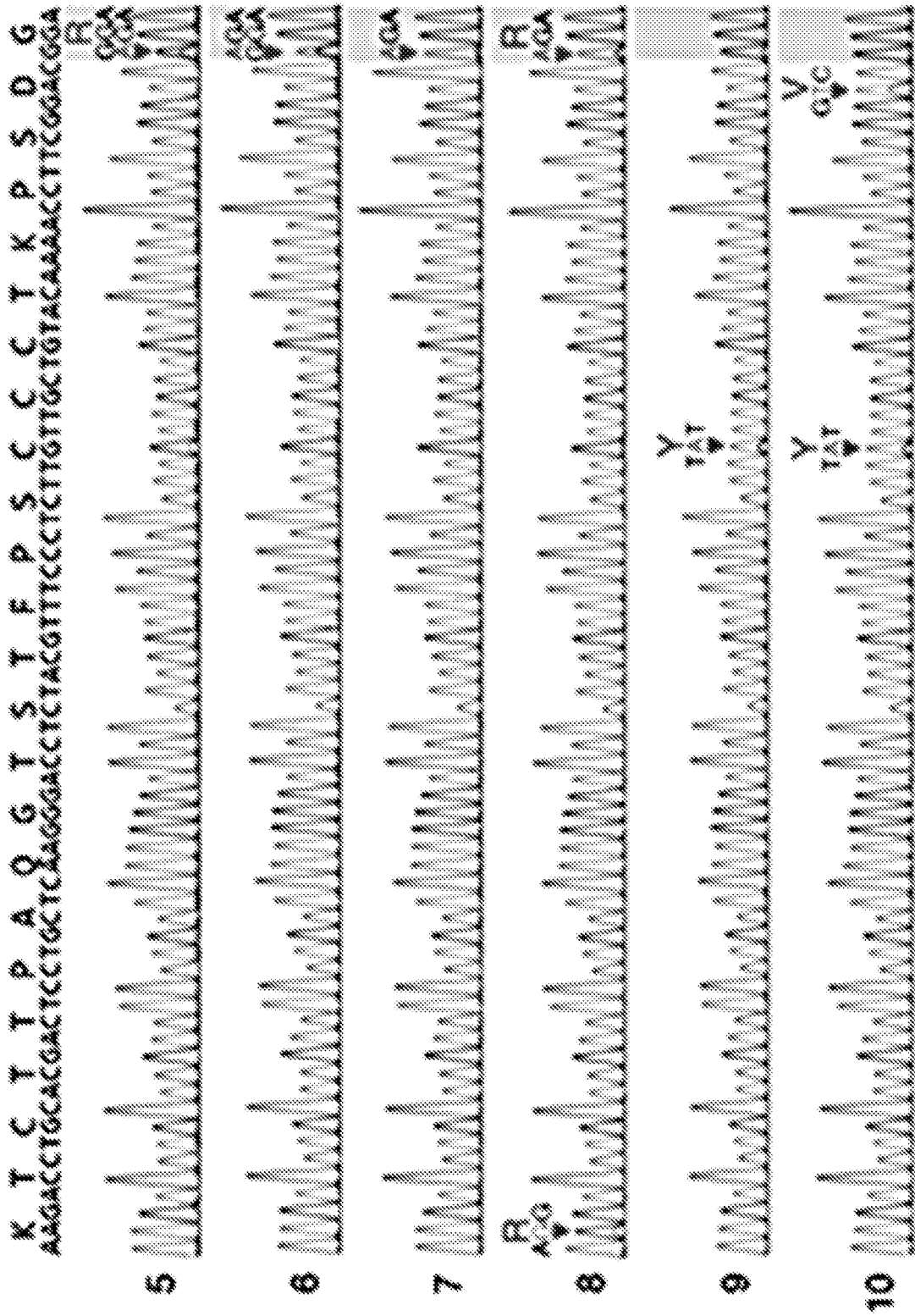


Fig. 14 (continued)

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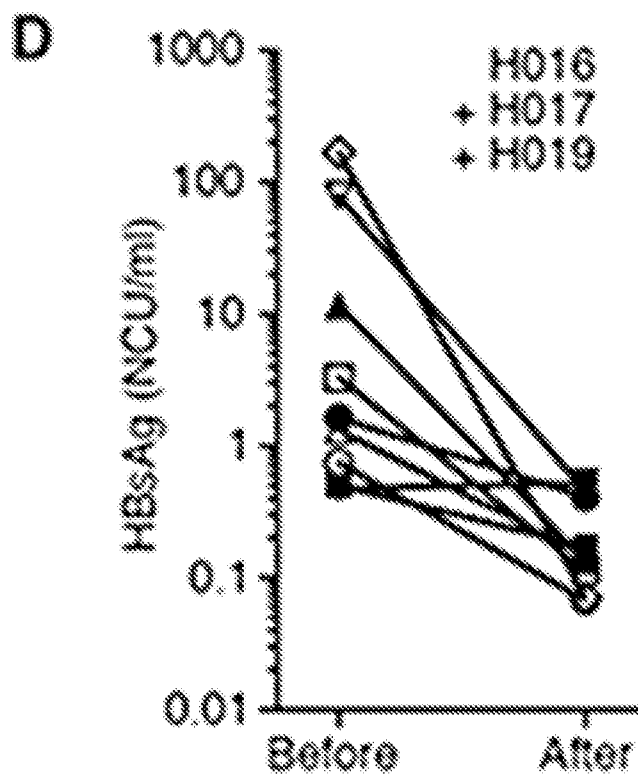
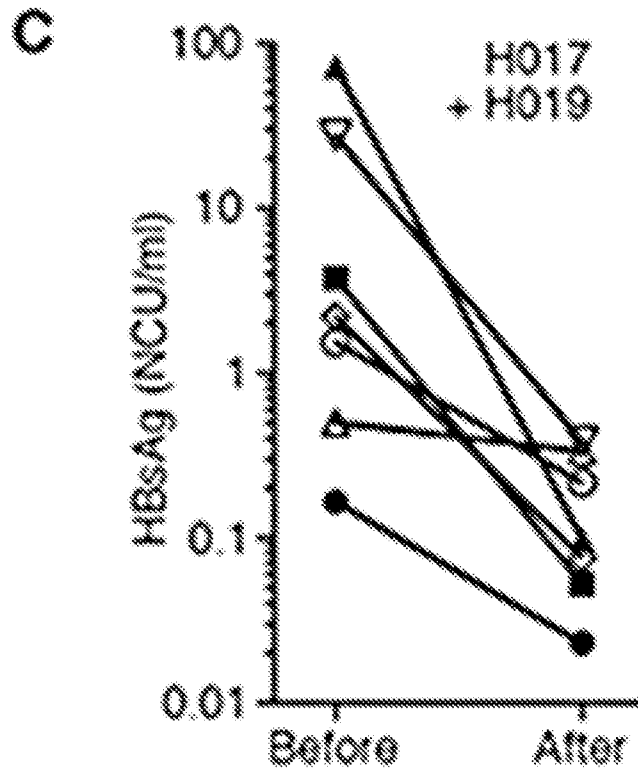


Fig. 14 (continued)

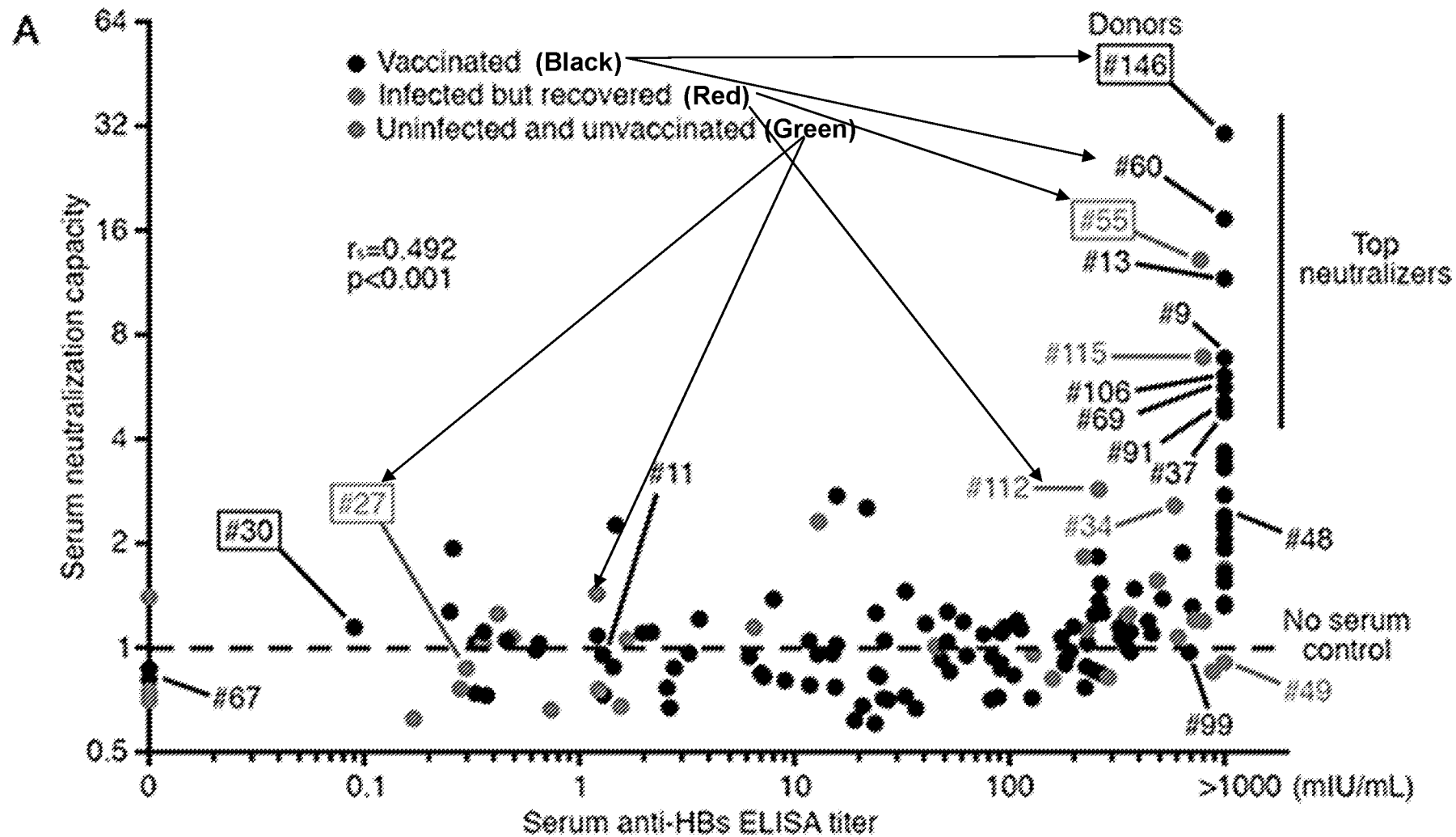


Fig. 1