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 (Heijtink et al., 2002; Heijtink 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 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 ≅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 (EC_{50} 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), EC_{50} values are color-coded: red, $\leq$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 IC_{50}s 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 (IC_{50}) 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 IC_{50} 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.

[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 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 chromotograms are shown in Figure 14. (J-L) Treatment of viremic huFNRG mice with combination of anti-HBs bNAb H006 + 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. 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 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 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 (Salisse and Sureau, 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 bNAb 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 bNAb H020, anti-HBs bNAb H007, combination of anti-HBs bNAb (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 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 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 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 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 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 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:

MGGWSSKPRQGMGTNLSVPNPLGFFPDHQLDPAFGANSNNPDWDFNPNKDHWPEANQVG
AGAFGPGFTPPHGGLLGWSPQAQGILTTVPVAPPPASTNRQSGRQPTPISPPLRDSHPQAMQ
WNSTTFHQALLDPRVRGLYFPAGGSSSGTVNPVPTTASPISSIFSRTGDPAPNMESTTSGFLGP
LLVLQAGFFLLTRILTIPQSLDSWWTSLNFLGGAPTCPGQNSQSPTSNHSPTSCPPICPGYRWM
CLRRFIIFLFILLLCLIFLLVLLDYQGMLPVCPLLPGTSTTSTGPCKTCTSPAQGTSMFPSCCCTKP
SDGNCTCIPIPSSWAFARFLWEWASVRFSWLSLLVPFVQWFVGLSPTVWLSVIWMMWYWG
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
CPPICPGYRWMCLRRFIIFLFILLLCLIFLLVLLDYHGMLPVCPLLPGTSTTSTGPCKTCTIPAQG
TSMFPSCCCTKPSDGNCTCIPIPSSWAFARFLWEWASVRFSWLSLLVPFVQWFVGLSPTVWLS
VIWMMWYWGPSLYNILSPFLPLLPIFFCLWVYI (SEQ ID NO: 3).

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

ATGGAGAACATCACATCAGGATTCCTAGGACCCCTGCTCGTGTTACAGGCGGGGTTTTTCTTG
TTGACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGACTTCTCTCAATTTTCTA
GGGGGATCTCCCGTGTGTCTTGGCCAAAATTCGCAGTCCCCAACCTCCAATCACTCACCAACC
TCCTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATATTCCTC
TTCATCCTGCTGCTATGCCTCATCTTCTTATTGGTTCTTCTGGATTATCAAGGTATGTTGCCC
GTTTGTCCTCTAATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACCTGCACGACT
CCTGCTCAAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAAACCTACGGATGGAAATTGC
ACCTGTATTCCCATCCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCCTCAGTC
CGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTCAGTGGTTCGTAGGGCTTTCCCCCACT
GTTTGGCTTTCAGCTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAGCATCGTGAG
TCCCTTTATACCGCTGTTACCAATTTTCTTTTGTCTCTGGGTATACATTTAA (SEQ ID NO:
4).

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

MENITSGFLGPLLVLQAGFFLLTRILTIPQSLDSWWTSLNFLGGSPVCLGQNSQSPTSNHSPTSC
PPICPGYRWMCLRRFIIFLFILLLCLIFLLVLLDYQGMLPVCPLIPGSTTTSTGPCKTCTTPAQGN
SMFPSCCCTKPTDGNCTCIPIPSSWAFAKYLWEWASVRFSWLSLLVPFVQWFVGLSPTVWLS
AIWMMWYWGPSLYSIVSPFIPLLPIFFCLWVYI (SEQ ID NO: 5).

[0042] In embodiments, antibodies of this disclosure bind to an epitope present in any 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 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 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 been 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 cysteinylation, 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 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 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 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 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 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 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 dextrins), 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 ($HBsAg^-$, $anti\text{-}HBs^-$, $anti\text{-}HBc^-$), 20 infected and spontaneously recovered ($HBsAg^-$, $anti\text{-}HBs^{+/-}$, $anti\text{-}HBc^+$), and 124 vaccinated ($HBsAg^-$, $anti\text{-}HBs^{+/-}$, $anti\text{-}HBc^-$) 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; Sankhyan 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 (EC_{50}) 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 EC_{50} 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 (IC_{50}) 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 IC_{50} values as low as 5 ng/ml (Figure 5C). By comparison, libivirumab had an IC_{50} 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 IC_{50} 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 $Å^2$; antibody-antigen buried surface of 600-900 $Å^2$ (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.

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 10^6-10^8 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 10^6-10^8 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 $\sim 10^{11}$ 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	(Robbiani et al., 2017)	N/A
Experimental Models: Mouse Strains		
Fah$^{-/-}$NOD*Rag*1$^{-/-}$*IL2rg*$^{-/-}$ 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
RNAsin Plus RNAse inhibitor	Promega	Cat#N2615
Random Primers	Thermo Fisher Scientific	Cat#48190011
Lipopolysaccharides from *E. coli* 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.

[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 was 81:78 (Figure 8D and 8E; Table S1).

[0111] **Animals**

[0112] *Fah*$^{-/-}$NOD*Rag1*$^{-/-}$*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 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 (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% CO_2. Human embryonic kidney HEK293-6E suspension cells were cultured at 37°C in 8% CO_2 with shaking at 120 rpm.

[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**

[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 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 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., 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 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 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 (EC_{50}) 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

[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 (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 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 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 FACSAriaII (Becton Dickinson) and stored at -80°C.

[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 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**

[0148] Six to eight week old *Fah*$^{-/-}$NOD*Rag1*$^{-/-}$*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 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 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 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 $1x10^4$ genome equivalent (GE) of mouse-passaged genotype C HBV viruses diluted in PBS. For prophylaxis experiments, 500 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 ($<10^8$ 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 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 (EC_{50}) values by ELISA assays (Figure 3A and 3C) and 50% inhibitory concentration (IC_{50}) 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; Heijtink et al., 2002; Heijtink 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 IC_{50}: 35 ng/ml, tuvirumab IC_{50}: ~100 ng/ml) (Galun et al., 2002; Heijtink 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.

Abou-Jaoude, G., and Sureau, C. (2007). Entry of hepatitis delta virus requires the conserved cysteine residues of the hepatitis B virus envelope protein antigenic loop and is blocked by inhibitors of thiol-disulfide exchange. J Virol. 81(23), 13057-13066. DOI: 10.1128/JVI.01495-07.

Adams, P.D., Afonine, P.V., Bunkoczi, G., Chen, V.B., Davis, I.W., Echols, N., Headd, J.J., Hung, L.W., Kapral, G.J., Grosse-Kunstleve, R.W., et al. (2010). PHENIX: a comprehensive Python-based system for macromolecular structure solution. Acta Crystallogr D Biol Crystallogr. 66(Pt 2), 213-221. DOI: 10.1107/S0907444909052925.

Bancroft, W.H., Mundon, F.K., and Russell, P.K. (1972). Detection of additional antigenic determinants of hepatitis B antigen. J Immunol. 109(4), 842-848.

Billerbeck, E., Mommersteeg, M.C., Shlomai, A., Xiao, J.W., Andrus, L., Bhatta, A., Vercauteren, K., Michailidis, E., Dorner, M., Krishnan, A., et al. (2016). Humanized mice efficiently engrafted with fetal hepatoblasts and syngeneic immune cells develop human monocytes and NK cells. J Hepatol. 65(2), 334-343. DOI: 10.1016/j.jhep.2016.04.022.

Blumberg, B.S. (1964). Polymorphisms of the Serum Proteins and the Development of Iso-Precipitins in Transfused Patients. Bull N Y Acad Med. 40, 377-386.

Braden, B.C., and Poljak, R.J. (1995). Structural features of the reactions between antibodies and protein antigens. FASEB J. 9(1), 9-16. DOI: 10.1096/fasebj.9.1.7821765.

Brochet, X., Lefranc, M.P., and Giudicelli, V. (2008). IMGT/V-QUEST: the highly customized and integrated system for IG and TR standardized V-J and V-D-J sequence analysis. Nucleic Acids Res. 36(Web Server issue), W503-508. DOI: 10.1093/nar/gkn316.

Cai, D., Mills, C., Yu, W., Yan, R., Aldrich, C.E., Saputelli, J.R., Mason, W.S., Xu, X., Guo, J.T., Block, T.M., et al. (2012). Identification of disubstituted sulfonamide compounds as specific inhibitors of hepatitis B virus covalently closed circular DNA formation. Antimicrob Agents Chemother. 56(8), 4277-4288. DOI: 10.1128/AAC.00473-12.

Celis, E., and Chang, T.W. (1984). Antibodies to hepatitis B surface antigen potentiate the response of human T lymphocyte clones to the same antigen. Science. 224(4646), 297-299. DOI: 10.1126/science.6231724.

Cerino, A., Bremer, C.M., Glebe, D., and Mondelli, M.U. (2015). A Human Monoclonal Antibody against Hepatitis B Surface Antigen with Potent Neutralizing Activity. PLoS One. 10(4), e0125704. DOI: 10.1371/journal.pone.0125704.

Chen, Y.C., Delbrook, K., Dealwis, C., Mimms, L., Mushahwar, I.K., and Mandecki, W. (1996). Discontinuous epitopes of hepatitis B surface antigen derived from a filamentous phage peptide library. Proc Natl Acad Sci U S A. 93(5), 1997-2001. DOI: 10.1073/pnas.93.5.1997.

Collaborative Computational Project, N. (1994). The CCP4 suite: programs for protein crystallography. Acta Crystallogr D Biol Crystallogr. 50(Pt 5), 760-763. DOI: 10.1107/S0907444994003112.

Colucci, G., Kohtz, D.S., and Waksal, S.D. (1986). Preparation and characterization of human monoclonal antibodies directed against the hepatitis B virus surface antigen. Liver. 6(3), 145-152.

Coursaget, P., Adamowicz, P., Bourdil, C., Yvonnet, B., Buisson, Y., Barres, J.L., Saliou, P., Chiron, J.P., and Mar, I.D. (1988). Anti-pre-S2 antibodies in natural hepatitis B virus infection and after immunization. Vaccine. 6(4), 357-361.

Dane, D.S., Cameron, C.H., and Briggs, M. (1970). Virus-like particles in serum of patients with Australia-antigen-associated hepatitis. Lancet. 1(7649), 695-698.

de Jong, Y.P., Dorner, M., Mommersteeg, M.C., Xiao, J.W., Balazs, A.B., Robbins, J.B., Winer, B.Y., Gerges, S., Vega, K., Labitt, R.N., et al. (2014). Broadly neutralizing antibodies abrogate established hepatitis C virus infection. Sci Transl Med. 6(254), 254ra129. DOI: 10.1126/scitranslmed.3009512.

Dienstag, J.L. (2008). Hepatitis B virus infection. N Engl J Med. 359(14), 1486-1500. DOI: 10.1056/NEJMra0801644.

Emsley, P., Lohkamp, B., Scott, W.G., and Cowtan, K. (2010). Features and development of Coot. Acta Crystallogr D Biol Crystallogr. 66(Pt 4), 486-501. DOI: 10.1107/S0907444910007493.

Eren, R., Ilan, E., Nussbaum, O., Lubin, I., Terkieltaub, D., Arazi, Y., Ben-Moshe, O., Kitchinzky, A., Berr, S., Gopher, J., et al. (2000). Preclinical evaluation of two human anti-hepatitis B virus (HBV) monoclonal antibodies in the HBV-trimera mouse model and in HBV chronic carrier chimpanzees. Hepatology. 32(3), 588-596. DOI: 10.1053/jhep.2000.9632.

Eren, R., Lubin, I., Terkieltaub, D., Ben-Moshe, O., Zauberman, A., Uhlmann, R., Tzahor, T., Moss, S., Ilan, E., Shouval, D., et al. (1998). Human monoclonal antibodies specific to

hepatitis B virus generated in a human/mouse radiation chimera: the Trimera system. Immunology. 93(2), 154-161. DOI: 10.1046/j.1365-2567.1998.00426.x.

Escolano, A., Gristick, H.B., Abernathy, M.E., Merkenschlager, J., Gautam, R., Oliveira, T.Y., Pai, J., West, A.P., Jr., Barnes, C.O., Cohen, A.A., et al. (2019). Immunization expands B cells specific to HIV-1 V3 glycan in mice and macaques. Nature. 570(7762), 468-473. DOI: 10.1038/s41586-019-1250-z.

Galun, E., Eren, R., Safadi, R., Ashour, Y., Terrault, N., Keeffe, E.B., Matot, E., Mizrachi, S., Terkieltaub, D., Zohar, M., et al. (2002). Clinical evaluation (phase I) of a combination of two human monoclonal antibodies to HBV: safety and antiviral properties. Hepatology. 35(3), 673-679. DOI: 10.1053/jhep.2002.31867.

Ganem, D. (1982). Persistent infection of humans with hepatitis B virus: mechanisms and consequences. Rev Infect Dis. 4(5), 1026-1047.

Gao, Y., Zhang, T.Y., Yuan, Q., and Xia, N.S. (2017). Antibody-mediated immunotherapy against chronic hepatitis B virus infection. Hum Vaccin Immunother. 13(8), 1768-1773. DOI: 10.1080/21645515.2017.1319021.

Gilchuk, P., Kuzmina, N., Ilinykh, P.A., Huang, K., Gunn, B.M., Bryan, A., Davidson, E., Doranz, B.J., Turner, H.L., Fusco, M.L., et al. (2018). Multifunctional Pan-ebolavirus Antibody Recognizes a Site of Broad Vulnerability on the Ebolavirus Glycoprotein. Immunity. 49(2), 363-374 e310. DOI: 10.1016/j.immuni.2018.06.018.

Gitlin, A.D., von Boehmer, L., Gazumyan, A., Shulman, Z., Oliveira, T.Y., and Nussenzweig, M.C. (2016). Independent Roles of Switching and Hypermutation in the Development and Persistence of B Lymphocyte Memory. Immunity. 44(4), 769-781. DOI: 10.1016/j.immuni.2016.01.011.

Graber-Stiehl, I. (2018). The silent epidemic killing more people than HIV, malaria or TB. Nature. 564(7734), 24-26. DOI: 10.1038/d41586-018-07592-7.

Heijtink, R.A., Kruining, J., van Bergen, P., de Rave, S., van Hattum, J., Schutten, M., and Osterhaus, A.D. (2002). Characterization of a human monoclonal antibody obtained after immunization with plasma vaccine and a booster with recombinant-DNA hepatitis B vaccine. J Med Virol. 66(3), 304-311.

Heijtink, R.A., Kruining, J., Weber, Y.A., de Man, R.A., and Schalm, S.W. (1995). Anti-hepatitis B virus activity of a mixture of two monoclonal antibodies in an "inhibition in solution" assay. Hepatology. 22(4 Pt 1), 1078-1083.

Heijtink, R.A., van Nunen, A.B., van Bergen, P., Ostberg, L., Osterhaus, A.D., and de Man, R.A. (2001). Administration of a human monoclonal antibody (TUVIRUMAB) to chronic

hepatitis B patients pre-treated with lamivudine: monitoring of serum TUVIRUMAB in immune complexes. J Med Virol. 64(4), 427-434.

Hsu, H.Y., Chang, M.H., Ni, Y.H., Chiang, C.L., Wu, J.F., and Chen, H.L. (2015). Universal infant immunization and occult hepatitis B virus infection in children and adolescents: a population-based study. Hepatology. 61(4), 1183-1191. DOI: 10.1002/hep.27650.

Hu, J., and Liu, K. (2017). Complete and Incomplete Hepatitis B Virus Particles: Formation, Function, and Application. Viruses. 9(3), E56. DOI: 10.3390/v9030056.

Hyakumura, M., Walsh, R., Thaysen-Andersen, M., Kingston, N.J., La, M., Lu, L., Lovrecz, G., Packer, N.H., Locarnini, S., and Netter, H.J. (2015). Modification of Asparagine-Linked Glycan Density for the Design of Hepatitis B Virus Virus-Like Particles with Enhanced Immunogenicity. J Virol. 89(22), 11312-11322. DOI: 10.1128/JVI.01123-15.

Ijaz, S., Ferns, R.B., and Tedder, R.S. (2003). A 'first loop' linear epitope accessible on native hepatitis B surface antigen that persists in the face of 'second loop' immune escape. J Gen Virol. 84(Pt 2), 269-275. DOI: 10.1099/vir.0.18667-0.

Ijaz, S., Szypulska, R., Andrews, N., and Tedder, R.S. (2012). Investigating the impact of hepatitis B virus surface gene polymorphism on antigenicity using ex vivo phenotyping. J Gen Virol. 93(Pt 11), 2473-2479. DOI: 10.1099/vir.0.044305-0.

Ito, K., Qin, Y., Guarnieri, M., Garcia, T., Kwei, K., Mizokami, M., Zhang, J., Li, J., Wands, J.R., and Tong, S. (2010). Impairment of hepatitis B virus virion secretion by single-amino-acid substitutions in the small envelope protein and rescue by a novel glycosylation site. J Virol. 84(24), 12850-12861. DOI: 10.1128/JVI.01499-10.

Jeong, J.Y., Yim, H.S., Ryu, J.Y., Lee, H.S., Lee, J.H., Seen, D.S., and Kang, S.G. (2012). One-step sequence- and ligation-independent cloning as a rapid and versatile cloning method for functional genomics studies. Appl Environ Microbiol. 78(15), 5440-5443. DOI: 10.1128/AEM.00844-12.

Jin, A., Ozawa, T., Tajiri, K., Obata, T., Kondo, S., Kinoshita, K., Kadowaki, S., Takahashi, K., Sugiyama, T., Kishi, H., et al. (2009). A rapid and efficient single-cell manipulation method for screening antigen-specific antibody-secreting cells from human peripheral blood. Nat Med. 15(9), 1088-1092. DOI: 10.1038/nm.1966.

Julithe, R., Abou-Jaoude, G., and Sureau, C. (2014). Modification of the hepatitis B virus envelope protein glycosylation pattern interferes with secretion of viral particles, infectivity, and susceptibility to neutralizing antibodies. J Virol. 88(16), 9049-9059. DOI: 10.1128/JVI.01161-14.

Kabsch, W. (2010a). Integration, scaling, space-group assignment and post-refinement. Acta Crystallogr D Biol Crystallogr. 66(Pt 2), 133-144. DOI: 10.1107/S0907444909047374.

Kabsch, W. (2010b). Xds. Acta Crystallogr D Biol Crystallogr. 66(Pt 2), 125-132. DOI: 10.1107/S0907444909047337.

Kim, S.H., and Park, S.Y. (2002). Selection and characterization of human antibodies against hepatitis B virus surface antigen (HBsAg) by phage-display. Hybrid Hybridomics. 21(5), 385-392. DOI: 10.1089/153685902761022742.

Kramvis, A., Arakawa, K., Yu, M.C., Nogueira, R., Stram, D.O., and Kew, M.C. (2008). Relationship of serological subtype, basic core promoter and precore mutations to genotypes/subgenotypes of hepatitis B virus. J Med Virol. 80(1), 27-46. DOI: 10.1002/jmv.21049.

Laursen, N.S., and Wilson, I.A. (2013). Broadly neutralizing antibodies against influenza viruses. Antiviral Res. 98(3), 476-483. DOI: 10.1016/j.antiviral.2013.03.021.

Lazarus, J.V., Block, T., Brechot, C., Kramvis, A., Miller, V., Ninburg, M., Penicaud, C., Protzer, U., Razavi, H., Thomas, L.A., et al. (2018). The hepatitis B epidemic and the urgent need for cure preparedness. Nat Rev Gastroenterol Hepatol. 15(9), 517-518. DOI: 10.1038/s41575-018-0041-6.

Le Bouvier, G.L. (1971). The heterogeneity of Australia antigen. J Infect Dis. 123(6), 671-675. DOI: 10.1093/infdis/123.6.671.

Li, D., He, W., Liu, X., Zheng, S., Qi, Y., Li, H., Mao, F., Liu, J., Sun, Y., Pan, L., et al. (2017). A potent human neutralizing antibody Fc-dependently reduces established HBV infections. Elife. 6, e26738. DOI: 10.7554/eLife.26738.

Loomba, R., and Liang, T.J. (2017). Hepatitis B Reactivation Associated With Immune Suppressive and Biological Modifier Therapies: Current Concepts, Management Strategies, and Future Directions. Gastroenterology. 152(6), 1297-1309. DOI: 10.1053/j.gastro.2017.02.009.

Ma, Q., and Wang, Y. (2012). Comprehensive analysis of the prevalence of hepatitis B virus escape mutations in the major hydrophilic region of surface antigen. J Med Virol. 84(2), 198-206. DOI: 10.1002/jmv.23183.

Mayer, C.T., Gazumyan, A., Kara, E.E., Gitlin, A.D., Golijanin, J., Viant, C., Pai, J., Oliveira, T.Y., Wang, Q., Escolano, A., et al. (2017). The microanatomic segregation of selection by apoptosis in the germinal center. Science. 358(6360), eaao2602. DOI: 10.1126/science.aao2602.

McCoy, A.J., Grosse-Kunstleve, R.W., Adams, P.D., Winn, M.D., Storoni, L.C., and Read, R.J. (2007). Phaser crystallographic software. J Appl Crystallogr. 40(Pt 4), 658-674. DOI: 10.1107/S0021889807021206.

Michailidis, E., Pabon, J., Xiang, K., Park, P., Ramanan, V., Hoffmann, H.H., Schneider, W.M., Bhatia, S.N., de Jong, Y.P., Shlomai, A., et al. (2017). A robust cell culture system supporting the complete life cycle of hepatitis B virus. Sci Rep. 7(1), 16616. DOI: 10.1038/s41598-017-16882-5.

Michailidis, E., Vercauteren, K., Mancio-Silva, L., Andrus, L., Jahan, C., Ricardo-Lax, I., Zou, C., Kabbani, M., Park, P., Quirk, C., et al. (2020). Expansion, in vivo-ex vivo cycling, and genetic manipulation of primary human hepatocytes. Proc Natl Acad Sci U S A. 117(3), 1678-1688. DOI: 10.1073/pnas.1919035117.

Milner-White, E.J., and Poet, R. (1986). Four classes of beta-hairpins in proteins. Biochem J. 240(1), 289-292. DOI: 10.1042/bj2400289.

Mouquet, H., Scharf, L., Euler, Z., Liu, Y., Eden, C., Scheid, J.F., Halper-Stromberg, A., Gnanapragasam, P.N., Spencer, D.I., Seaman, M.S., et al. (2012). Complex-type N-glycan recognition by potent broadly neutralizing HIV antibodies. Proc Natl Acad Sci U S A. 109(47), E3268-3277. DOI: 10.1073/pnas.1217207109.

Norder, H., Courouce, A.M., Coursaget, P., Echevarria, J.M., Lee, S.D., Mushahwar, I.K., Robertson, B.H., Locarnini, S., and Magnius, L.O. (2004). Genetic diversity of hepatitis B virus strains derived worldwide: genotypes, subgenotypes, and HBsAg subtypes. Intervirology. 47(6), 289-309. DOI: 10.1159/000080872.

Pappas, L., Foglierini, M., Piccoli, L., Kallewaard, N.L., Turrini, F., Silacci, C., Fernandez-Rodriguez, B., Agatic, G., Giacchetto-Sasselli, I., Pellicciotta, G., et al. (2014). Rapid development of broadly influenza neutralizing antibodies through redundant mutations. Nature. 516(7531), 418-422. DOI: 10.1038/nature13764.

Paulij, W.P., de Wit, P.L., Sunnen, C.M., van Roosmalen, M.H., Petersen-van Ettekoven, A., Cooreman, M.P., and Heijtink, R.A. (1999). Localization of a unique hepatitis B virus epitope sheds new light on the structure of hepatitis B virus surface antigen. J Gen Virol. 80 (Pt 8), 2121-2126. DOI: 10.1099/0022-1317-80-8-2121.

Revill, P., Testoni, B., Locarnini, S., and Zoulim, F. (2016). Global strategies are required to cure and eliminate HBV infection. Nat Rev Gastroenterol Hepatol. 13(4), 239-248. DOI: 10.1038/nrgastro.2016.7.

Robbiani, D.F., Bozzacco, L., Keeffe, J.R., Khouri, R., Olsen, P.C., Gazumyan, A., Schaefer-Babajew, D., Avila-Rios, S., Nogueira, L., Patel, R., et al. (2017). Recurrent Potent Human

Neutralizing Antibodies to Zika Virus in Brazil and Mexico. Cell. 169(4), 597-609 e511. DOI: 10.1016/j.cell.2017.04.024.

Rouers, A., Klingler, J., Su, B., Samri, A., Laumond, G., Even, S., Avettand-Fenoel, V., Richetta, C., Paul, N., Boufassa, F., et al. (2017). HIV-Specific B Cell Frequency Correlates with Neutralization Breadth in Patients Naturally Controlling HIV-Infection. EBioMedicine. 21, 158-169. DOI: 10.1016/j.ebiom.2017.05.029.

Sa'adu, A., Locniskar, M., Bidwell, D., Howard, C., McAdam, K.P., and Voller, A. (1992). Development and characterization of human anti-HBs antibodies. J Virol Methods. 36(1), 25-34.

Salisse, J., and Sureau, C. (2009). A function essential to viral entry underlies the hepatitis B virus "a" determinant. J Virol. 83(18), 9321-9328. DOI: 10.1128/JVI.00678-09.

Salpini, R., Colagrossi, L., Bellocchi, M.C., Surdo, M., Becker, C., Alteri, C., Aragri, M., Ricciardi, A., Armenia, D., Pollicita, M., et al. (2015). Hepatitis B surface antigen genetic elements critical for immune escape correlate with hepatitis B virus reactivation upon immunosuppression. Hepatology. 61(3), 823-833. DOI: 10.1002/hep.27604.

Sankhyan, A., Sharma, C., Dutta, D., Sharma, T., Chosdol, K., Wakita, T., Watashi, K., Awasthi, A., Acharya, S.K., Khanna, N., et al. (2016). Inhibition of preS1-hepatocyte interaction by an array of recombinant human antibodies from naturally recovered individuals. Sci Rep. 6, 21240. DOI: 10.1038/srep21240.

Scheid, J.F., Mouquet, H., Feldhahn, N., Seaman, M.S., Velinzon, K., Pietzsch, J., Ott, R.G., Anthony, R.M., Zebroski, H., Hurley, A., et al. (2009a). Broad diversity of neutralizing antibodies isolated from memory B cells in HIV-infected individuals. Nature. 458(7238), 636-640. DOI: 10.1038/nature07930.

Scheid, J.F., Mouquet, H., Feldhahn, N., Walker, B.D., Pereyra, F., Cutrell, E., Seaman, M.S., Mascola, J.R., Wyatt, R.T., Wardemann, H., et al. (2009b). A method for identification of HIV gp140 binding memory B cells in human blood. J Immunol Methods. 343(2), 65-67. DOI: 10.1016/j.jim.2008.11.012.

Scheid, J.F., Mouquet, H., Ueberheide, B., Diskin, R., Klein, F., Oliveira, T.Y., Pietzsch, J., Fenyo, D., Abadir, A., Velinzon, K., et al. (2011). Sequence and structural convergence of broad and potent HIV antibodies that mimic CD4 binding. Science. 333(6049), 1633-1637. DOI: 10.1126/science.1207227.

Schommers, P., Gruell, H., Abernathy, M.E., Tran, M.K., Dingens, A.S., Gristick, H.B., Barnes, C.O., Schoofs, T., Schlotz, M., Vanshylla, K., et al. (2020). Restriction of HIV-1

Escape by a Highly Broad and Potent Neutralizing Antibody. Cell. 180(3), 471-489 e422. DOI: 10.1016/j.cell.2020.01.010.

Sheu, S.Y., Yang, D.Y., Selzle, H.L., and Schlag, E.W. (2003). Energetics of hydrogen bonds in peptides. Proc Natl Acad Sci U S A. 100(22), 12683-12687. DOI: 10.1073/pnas.2133366100.

Sun, S., and Li, J. (2017). Humanized chimeric mouse models of hepatitis B virus infection. Int J Infect Dis. 59, 131-136. DOI: 10.1016/j.ijid.2017.04.002.

Sureau, C., and Salisse, J. (2013). A conformational heparan sulfate binding site essential to infectivity overlaps with the conserved hepatitis B virus a-determinant. Hepatology. 57(3), 985-994. DOI: 10.1002/hep.26125.

Tajiri, K., Kishi, H., Tokimitsu, Y., Kondo, S., Ozawa, T., Kinoshita, K., Jin, A., Kadowaki, S., Sugiyama, T., and Muraguchi, A. (2007). Cell-microarray analysis of antigen-specific B-cells: single cell analysis of antigen receptor expression and specificity. Cytometry A. 71(11), 961-967. DOI: 10.1002/cyto.a.20471.

Tajiri, K., Ozawa, T., Jin, A., Tokimitsu, Y., Minemura, M., Kishi, H., Sugiyama, T., and Muraguchi, A. (2010). Analysis of the epitope and neutralizing capacity of human monoclonal antibodies induced by hepatitis B vaccine. Antiviral Res. 87(1), 40-49. DOI: 10.1016/j.antiviral.2010.04.006.

Tan, J., Pieper, K., Piccoli, L., Abdi, A., Perez, M.F., Geiger, R., Tully, C.M., Jarrossay, D., Maina Ndungu, F., Wambua, J., et al. (2016). A LAIR1 insertion generates broadly reactive antibodies against malaria variant antigens. Nature. 529(7584), 105-109. DOI: 10.1038/nature16450.

Tan, J., Sack, B.K., Oyen, D., Zenklusen, I., Piccoli, L., Barbieri, S., Foglierini, M., Fregni, C.S., Marcandalli, J., Jongo, S., et al. (2018). A public antibody lineage that potently inhibits malaria infection through dual binding to the circumsporozoite protein. Nat Med. 24(4), 401-407. DOI: 10.1038/nm.4513.

Thomas, D.L. (2019). Global Elimination of Chronic Hepatitis. N Engl J Med. 380(21), 2041-2050. DOI: 10.1056/NEJMra1810477.

Tiller, T., Meffre, E., Yurasov, S., Tsuiji, M., Nussenzweig, M.C., and Wardemann, H. (2008). Efficient generation of monoclonal antibodies from single human B cells by single cell RT-PCR and expression vector cloning. J Immunol Methods. 329(1-2), 112-124. DOI: 10.1016/j.jim.2007.09.017.

Tokimitsu, Y., Kishi, H., Kondo, S., Honda, R., Tajiri, K., Motoki, K., Ozawa, T., Kadowaki, S., Obata, T., Fujiki, S., et al. (2007). Single lymphocyte analysis with a microwell array chip. Cytometry A. 71(12), 1003-1010. DOI: 10.1002/cyto.a.20478.

Tong, S., Li, J., Wands, J.R., and Wen, Y.M. (2013). Hepatitis B virus genetic variants: biological properties and clinical implications. Emerg Microbes Infect. 2(3), e10. DOI: 10.1038/emi.2013.10.

Trepo, C., Chan, H.L., and Lok, A. (2014). Hepatitis B virus infection. Lancet. 384(9959), 2053-2063. DOI: 10.1016/S0140-6736(14)60220-8.

van Nunen, A.B., Baumann, M., Manns, M.P., Reichen, J., Spengler, U., Marschner, J.P., de Man, R.A., and International Study, G. (2001). Efficacy and safety of an intravenous monoclonal anti-HBs in chronic hepatitis B patients. Liver. 21(3), 207-212.

Venkatakrishnan, B., and Zlotnick, A. (2016). The Structural Biology of Hepatitis B Virus: Form and Function. Annu Rev Virol. 3(1), 429-451. DOI: 10.1146/annurev-virology-110615-042238.

von Boehmer, L., Liu, C., Ackerman, S., Gitlin, A.D., Wang, Q., Gazumyan, A., and Nussenzweig, M.C. (2016). Sequencing and cloning of antigen-specific antibodies from mouse memory B cells. Nat Protoc. 11(10), 1908-1923. DOI: 10.1038/nprot.2016.102.

Walker, L.M., Huber, M., Doores, K.J., Falkowska, E., Pejchal, R., Julien, J.P., Wang, S.K., Ramos, A., Chan-Hui, P.Y., Moyle, M., et al. (2011). Broad neutralization coverage of HIV by multiple highly potent antibodies. Nature. 477(7365), 466-470. DOI: 10.1038/nature10373.

Wang, W., Sun, L., Li, T., Ma, Y., Li, J., Liu, Y., Li, M., Wang, L., Li, C., Xie, Y., et al. (2016). A human monoclonal antibody against small envelope protein of hepatitis B virus with potent neutralization effect. MAbs. 8(3), 468-477. DOI: 10.1080/19420862.2015.1134409.

Wardemann, H., Yurasov, S., Schaefer, A., Young, J.W., Meffre, E., and Nussenzweig, M.C. (2003). Predominant autoantibody production by early human B cell precursors. Science. 301(5638), 1374-1377. DOI: 10.1126/science.1086907.

West, A.P., Jr., Diskin, R., Nussenzweig, M.C., and Bjorkman, P.J. (2012). Structural basis for germ-line gene usage of a potent class of antibodies targeting the CD4-binding site of HIV-1 gp120. Proc Natl Acad Sci U S A. 109(30), E2083-2090. DOI: 10.1073/pnas.1208984109.

White, A.D., Keefe, A.J., Ella-Menye, J.R., Nowinski, A.K., Shao, Q., Pfaendtner, J., and Jiang, S. (2013). Free energy of solvated salt bridges: a simulation and experimental study. J Phys Chem B. 117(24), 7254-7259. DOI: 10.1021/jp4024469.

Wrammert, J., Koutsonanos, D., Li, G.M., Edupuganti, S., Sui, J., Morrissey, M., McCausland, M., Skountzou, I., Hornig, M., Lipkin, W.I., et al. (2011). Broadly cross-reactive antibodies dominate the human B cell response against 2009 pandemic H1N1 influenza virus infection. J Exp Med. 208(1), 181-193. DOI: 10.1084/jem.20101352.

Wu, X., Yang, Z.Y., Li, Y., Hogerkorp, C.M., Schief, W.R., Seaman, M.S., Zhou, T., Schmidt, S.D., Wu, L., Xu, L., et al. (2010). Rational design of envelope identifies broadly neutralizing human monoclonal antibodies to HIV-1. Science. 329(5993), 856-861. DOI: 10.1126/science.1187659.

Yan, H., Zhong, G., Xu, G., He, W., Jing, Z., Gao, Z., Huang, Y., Qi, Y., Peng, B., Wang, H., et al. (2012). Sodium taurocholate cotransporting polypeptide is a functional receptor for human hepatitis B and D virus. Elife. 1, e00049. DOI: 10.7554/eLife.00049.

Ye, B., Liu, X., Li, X., Kong, H., Tian, L., and Chen, Y. (2015). T-cell exhaustion in chronic hepatitis B infection: current knowledge and clinical significance. Cell Death Dis. 6, e1694. DOI: 10.1038/cddis.2015.42.

Ye, J., Ma, N., Madden, T.L., and Ostell, J.M. (2013). IgBLAST: an immunoglobulin variable domain sequence analysis tool. Nucleic Acids Res. 41(Web Server issue), W34-40. DOI: 10.1093/nar/gkt382.

Yurasov, S., Wardemann, H., Hammersen, J., Tsuiji, M., Meffre, E., Pascual, V., and Nussenzweig, M.C. (2005). Defective B cell tolerance checkpoints in systemic lupus erythematosus. J Exp Med. 201(5), 703-711. DOI: 10.1084/jem.20042251.

Zanetti, A.R., Tanzi, E., Manzillo, G., Maio, G., Sbreglia, C., Caporaso, N., Thomas, H., and Zuckerman, A.J. (1988). Hepatitis B variant in Europe. Lancet. 2(8620), 1132-1133. DOI: 10.1016/s0140-6736(88)90541-7.

Zhang, T.Y., Guo, X.R., Wu, Y.T., Kang, X.Z., Zheng, Q.B., Qi, R.Y., Chen, B.B., Lan, Y., Wei, M., Wang, S.J., et al. (2019). A unique B cell epitope-based particulate vaccine shows effective suppression of hepatitis B surface antigen in mice. Gut. 69(2), 343-354. DOI: 10.1136/gutjnl-2018-317725.

Zhang, T.Y., Yuan, Q., Zhao, J.H., Zhang, Y.L., Yuan, L.Z., Lan, Y., Lo, Y.C., Sun, C.P., Wu, C.R., Zhang, J.F., et al. (2016). Prolonged suppression of HBV in mice by a novel antibody that targets a unique epitope on hepatitis B surface antigen. Gut. 65(4), 658-671. DOI: 10.1136/gutjnl-2014-308964.

Zhu, D., Liu, L., Yang, D., Fu, S., Bian, Y., Sun, Z., He, J., Su, L., Zhang, L., Peng, H., et al. (2016). Clearing Persistent Extracellular Antigen of Hepatitis B Virus: An Immunomodulatory Strategy To Reverse Tolerance for an Effective Therapeutic Vaccination. J Immunol. 196(7), 3079-3087. DOI: 10.4049/jimmunol.1502061.

[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.

DONOR ID	ANTI-HBs ELISA TITER	STATUE	BIG BLOOD DRAW	INFECTION RATE (1:5 SERUM) PERCENTAGE OF HBcAg+ CELLS			AVERAGE	NEUTRALIZATION CAPACITY		INFECTION RATE (1:50 SERUM) PERCENTAGE OF HBcAg+ CELLS			AVERAGE	NEUTRALIZATION CAPACITY
QWA-0947-001	9.08	Vaccinated		114.00	127.12	133.64	124.92	0.80		118.06	128.90	122.19	123.05	0.81
QWA-0947-002	516.12	Vaccinated		65.28	77.58	75.13	72.66	1.38		131.60	137.04	133.44	134.03	0.75
QWA-0947-003	0	Vaccinated		108.59	118.31	118.53	115.14	0.87		132.81	136.65	132.22	133.89	0.75
QWA-0947-004	267.1	Vaccinated		113.39	121.91	121.67	118.99	0.84		142.69	146.69	153.24	147.54	0.68
QWA-0947-005	113.01	Vaccinated		82.91	87.48	95.39	88.59	1.13		148.24	149.36	146.75	148.12	0.68
QWA-0947-006	325.77	Vaccinated		81.19	85.97	96.43	87.86	1.14		117.48	116.83	119.74	118.02	0.85
QWA-0947-007	63.54	Vaccinated		100.37	105.53	110.73	105.54	0.95		134.11	135.15	138.51	135.92	0.74
QWA-0947-008	21.8	Vaccinated		40.86	35.60	42.82	39.76	2.52		78.64	84.09	84.79	82.51	1.21
QWA-0947-009	>1000	Vaccinated	BIG BLOOD DRAW	12.84	14.39	17.20	14.81	6.75		34.66	38.81	33.48	35.65	2.81
QWA-0947-010	0.33	Vaccinated		93.33	93.42	104.91	97.22	1.03		105.41	116.72	115.58	112.57	0.89
QWA-0947-011	1.29	Vaccinated	BIG BLOOD DRAW	109.40	113.87	94.10	105.79	0.95		95.79	93.25	81.95	90.33	1.11

QWA-0947-012	12.87	Vaccinated		102.04	102.94	108.81	104.60	0.96		142.95	137.95	125.12	135.34	0.74
QWA-0947-013	>1000	Vaccinated	BIG BLOOD DRAW	9.24	8.31	8.33	8.63	11.59		19.95	20.81	17.29	19.35	5.17
QWA-0947-014	248.31	Vaccinated		80.90	80.65	79.88	80.48	1.24		117.58	120.17	115.37	117.71	0.85
QWA-0947-015	76.1	Vaccinated		97.26	91.48	86.95	91.90	1.09		112.79	109.82	101.19	107.93	0.93
QWA-0947-016	0.36	Non-Vaccinated		100.22	96.77	95.84	97.61	1.02		118.04	120.05	117.34	118.48	0.84
QWA-0947-017	0.63	Vaccinated		100.30	102.98	101.55	101.61	0.98		122.27	119.42	110.93	117.54	0.85
QWA-0947-018	3.24	Vaccinated		101.65	113.38	96.98	104.00	0.96		118.18	121.26	107.05	115.50	0.87
QWA-0947-019	>1000	Vaccinated		47.62	43.35	40.11	43.69	2.29		105.86	100.46	89.54	98.62	1.01
QWA-0947-020	1.21	Non-Vaccinated		77.13	75.25	60.04	70.81	1.41		116.28	113.72	108.65	112.88	0.89
QWA-0947-021	15.81	Vaccinated		33.85	41.39	34.98	36.74	2.72		89.74	89.87	88.60	89.40	1.12
QWA-0947-022	2.17	Vaccinated		83.52	94.22	93.88	90.54	1.10		100.08	119.88	110.19	110.05	0.91
QWA-0947-023	183.37	Vaccinated		93.15	119.57	116.08	109.60	0.91		113.43	117.91	103.45	111.60	0.90
QWA-0947-024	256.85	Vaccinated		55.70	60.03	49.13	54.95	1.82		104.68	116.21	105.17	108.69	0.92
QWA-0947-025	709.29	Vaccinated		76.18	77.38	75.01	76.19	1.31		100.58	105.57	116.82	107.66	0.93
QWA-0947-026	0.49	Non-Vaccinated		83.02	102.42	96.98	94.14	1.06		104.24	117.09	105.73	109.02	0.92
QWA-0947-027	0.3	Non-Vaccinated	BIG BLOOD DRAW	103.51	128.79	114.82	115.71	0.86		105.91	126.68	117.03	116.54	0.86
QWA-0947-028	6.51	Non-Vaccinated		84.03	90.88	87.77	87.56	1.14		107.23	117.89	108.21	111.11	0.90
QWA-0947-029	1.67	Non-Vaccinated		103.72	98.68	83.74	95.38	1.05		96.06	102.25	100.20	99.50	1.00
QWA-0947-030	0.09	Vaccinated	BIG BLOOD DRAW	86.06	84.44	91.73	87.41	1.14		111.74	115.73	102.26	109.91	0.91

QWA-0947-031	488.3	Core Ab +		71.30	66.21	56.71	64.74	1.54		94.99	102.87	94.27	97.38	1.03
QWA-0947-032	>1000	Vaccinated		71.12	67.87	56.53	65.17	1.53		97.45	107.81	106.59	103.95	0.96
QWA-0947-033	330.93	Vaccinated		99.61	93.60	87.25	93.49	1.07		106.28	116.65	108.45	110.46	0.91
QWA-0947-034	588.26	Core Ab +		40.92	41.19	35.30	39.14	2.56		99.54	111.16	105.28	105.32	0.95
QWA-0947-035	365.7	Vaccinated		101.52	113.83	94.76	103.37	0.97		129.77	131.60	121.19	127.52	0.78
QWA-0947-036	108.83	Vaccinated		87.55	85.69	77.65	83.63	1.20		122.28	122.03	107.69	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		119.79	125.09	115.27	120.05	0.83
QWA-0947-039	230.99	Vaccinated		102.08	99.23	91.54	97.62	1.02		113.01	115.04	98.95	109.00	0.92
QWA-0947-040	0.26	Vaccinated		54.12	57.38	45.32	52.27	1.91		102.43	107.89	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	101.25	101.19	96.68	1.03
QWA-0947-042	128.75	Core Ab +		97.03	106.51	110.26	104.60	0.96		114.07	149.01	121.98	128.35	0.78
QWA-0947-043	229.75	Core Ab +		78.56	94.35	95.71	89.54	1.12		95.18	144.23	123.82	121.08	0.83
QWA-0947-044	222.48	Core Ab +		45.85	56.61	65.34	55.93	1.79		94.00	133.96	109.86	112.60	0.89
QWA-0947-045	>1000	Core Ab +		51.82	66.02	61.55	59.80	1.67		104.36	122.03	120.96	115.78	0.86
QWA-0947-046	350.93	Vaccinated		89.57	99.40	111.55	100.17	1.00		100.98	129.50	111.79	114.09	0.88
QWA-0947-047	0.33	Vaccinated		126.88	138.30	142.37	135.85	0.74		112.35	156.77	127.72	132.28	0.76
QWA-0947-048	>1000	Vaccinated	BIG BLOOD DRAW	35.94	44.44	46.02	42.14	2.37		83.08	109.89	94.60	95.86	1.04
QWA-0947-049	>1000	Core Ab +	BIG BLOOD DRAW	94.21	120.65	119.57	111.48	0.90		113.33	139.10	126.42	126.28	0.79

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	133.23	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

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

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

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		151.82	146.04	144.65	147.50	0.68		112.36	109.15	124.29	115.26	0.87
QWA-0947-119	91.47	Vaccinated		114.36	109.63	108.87	110.96	0.90		108.91	112.79	104.89	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

QWA-0947-127	1.23	Non-Vaccinated		128.75	125.40	143.54	132.56	0.75		162.01	157.22	139.08	152.77	0.65
QWA-0947-128	>1000	Vaccinated		30.63	25.86	36.31	30.94	3.23		69.73	82.09	84.44	78.76	1.27
QWA-0947-129	0.17	Non-Vaccinated		166.56	156.86	157.89	160.44	0.62		162.24	168.18	154.52	161.65	0.62
QWA-0947-131	11.81	Vaccinated		143.14	129.67	114.98	129.26	0.77		156.94	144.37	119.26	140.19	0.71
QWA-0947-132	0	Non-Vaccinated		143.37	148.51	134.41	142.09	0.70		170.72	146.03	126.56	147.77	0.68
QWA-0947-133	731.27	Core Ab +		86.48	85.37	78.16	83.34	1.20		157.64	137.87	131.07	142.20	0.70
QWA-0947-134	>1000	Vaccinated		31.62	30.52	27.60	29.92	3.34		144.36	137.82	115.14	132.44	0.76
QWA-0947-135	796.93	Core Ab +		81.56	81.84	88.25	83.88	1.19		157.58	142.42	116.84	138.95	0.72
QWA-0947-136	0	Non-Vaccinated		128.19	132.95	139.91	133.68	0.75		165.85	140.56	137.58	148.00	0.68
QWA-0947-137	1.56	Non-Vaccinated		155.09	151.93	137.05	148.02	0.68		175.51	155.22	128.75	153.16	0.65
QWA-0947-138	0.74	Non-Vaccinated		160.76	159.87	135.61	152.08	0.66		165.30	137.96	119.52	140.93	0.71
QWA-0947-139	0	Non-Vaccinated		143.96	145.71	123.98	137.88	0.73		143.82	125.60	114.22	127.88	0.78
QWA-0947-140	609.46	Core Ab +		93.61	96.21	89.99	93.27	1.07		125.42	135.92	106.58	122.64	0.82
QWA-0947-141	>1000	Vaccinated		35.14	37.74	36.31	36.40	2.75		90.32	87.71	83.80	87.28	1.15
QWA-0947-142	0.01	Non-Vaccinated		72.39	72.79	69.24	71.47	1.40		85.86	89.49	80.98	85.44	1.17
QWA-0947-143	51.9	Vaccinated		83.85	74.96	78.42	79.07	1.26		89.70	83.02	81.24	84.65	1.18
QWA-0947-144	192.41	Vaccinated		99.03	103.75	104.69	102.49	0.98		88.00	80.96	100.21	89.73	1.11
QWA-0947-145	>1000	Vaccinated		35.23	36.75	36.99	36.32	2.75		91.40	83.04	84.37	86.27	1.16
QWA-0947-146	>1000	Vaccinated	BIG BLOOD DRAW	3.21	3.17	3.47	3.28	30.45		4.66	4.45	3.82	4.31	23.18

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							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	9	IGHV1-18*01	IGHD6-13*01	IGHJ6*02	GYTFTTYG	26	ISTYNRNT	27	ARNGYSSWHGGTHYYYALDF	28	IGKV1-5*03	IGKJ1*01	QSITNW	29	KAS	QQYYSYPWT	30								
	55	IGHV1-18*01	IGHD2-15*01	IGHJ4*02	GYSFNTYG	31	ISTYNGKT	32	ARDSVSWWNLLFKSLEKLTLDY	33								IGLV2-23*01	IGLJ3*02	SSDVGSYDL	34	EAS		CSYSGSTTCV	35
	55	IGHV1-18	IGHD2-15*01	IGHJ4*02	GYSFNTYG	36	ISTYNGKT	37	ARDSVSWWNLLFKS	38	IGKV3-20*01	IGKJ4*01	QSVSNSY	39	GAS	QQFGSSPLT	40	IGLV2-8*01	IGLJ1*01	SSDIGGYNY	41	EVN		NSYAGNNNFV	42

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01							LEKLTLDY															
	55	IGHV1-18*01	IGHD2-15*01	IGHJ4*02	GYSFNTYG	43	ISTYNGKT	44	ARDSVSWWNLLFKSLEKLTLDY	45	IGKV3-11*01	IGKJ1*01	QSVSSY	46	DAS	QHRSNSWT	47								
	55	IGHV1-18*01	IGHD4-17*01	IGHJ4*02	GYTFSSYG	48	ISAHSGNT	49	ARDPDFGDYGSDIVDY	50								IGLV3-25*02	IGLJ3*02	ALPVQF	51	KDS		QSADSTATYWV	52
	99	IGHV1-18*01	IGHD3-16*01	IGHJ6*03	GYSFSSYG	53	ISAYNGDT	54	ARWGVGMTFSYHYHYMDV	55								IGLV3-19*01	IGLJ3*02	SLRTYY	56	GKN		GSRDNSGYS	57
	99	IGHV1-18*01	IGHD6-13*01	IGHJ4*02	GYTFGSFG	58	ISGYSGKT	59	ARGRGDSSTWYSLY	60	IGKV3-11*01	IGKJ4*01	QSVGSY	61	DAS	QQYNDWLT	62								
	146	IGHV1	IGHD1-	IGHJ1*01	DYRSINSG	63	ISPFNGNT	64	AGDTTS	65	IGKV4-	IGKJ3*01	ESVFFS	66	WAS	QQYY	67								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-18*01	1*01						SAALTF		1*01		PHNRNY			TTPS									
	146	IGHV1-18*01	IGHD1-26*01	IGHJ6*02	GYNFISYA	68	ISPYNGKK	69	ARFFGGATMTVYFYGLDV	70	IGKV1-5*01	IGKJ1*01	QSIKTW	71	DAS	QQYNSYSGWT	72								
	146	IGHV1-18*01	IGHD6-19*01	IGHJ4*02	GYKFTNYG	73	INAYNGHT	74	TRSEQWRSRGEY	75								IGLV1-44*01	IGLJ3*02	NSNVGNNV	76	ANS		ASWDDSLSGSWV	77
	146	IGHV1-18*01	IGHD1-26*01	IGHJ5*02	GYTFSNYG	78	ISASSGNT	79	GRDDSGSYPMSP	80	IGKV3-20*01	IGKJ4*01	QSVSGSSY	81	GAS	QQYXSSPLA	82								
	146	IGHV1-18*01	IGHD1-20*01	IGHJ4*02	GYTFRNYG	83	INAHNGDT	84	VRDINFIFDY	85								IGLV7-43*01	IGLJ3*02	TGAVTSSYY	86	RTN		LLYXWSSSALG	87
	69	IGHV1	IGHD3-	IGHJ6*03	GYSFTSYG	88	INVYNANT	89	AREGWFGEF	90	IGKV3-	IGKJ1*01	LSVSSN	91	DAS	QQYHEW	92								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-18*04	10*01						RRNYNYYMDV		15*01					PRT									
	49	IGHV1-24*01	IGHD4-11*01	IGHJ3*01	GYTLTELS	93	FDPDEGEV	94	TLVTRVDAFDV	95	IGKV1-39*01	IGKJ2*01	QSVRTY	96	AAS	QQSYFAPYT	97								
	49	IGHV1-24*01	IGHD4-11*01	IGHJ3*01	GYSHTELP	98	FDPDEGET	99	TLVTRVDAFEV	100	IGKV1-39*01	IGKJ2*01	QNIRNY	101	AAS	QQSYFAPYT	102								
	49	IGHV1-24*01	IGHD2-21*02	IGHJ3*01	GYTLTELP	103	FDPDEGET	104	TLVTGVDAFAV	105	IGKV1-39*01	IGKJ2*01	QNIRTY	106	TAS	QQSYFAPYT	107								
	49	IGHV1-24*01	IGHD3-16*01	IGHJ3*01	GYIFSELS	108	FDPDEGET	109	TSVIKADAFEV	110	IGKV1-39*01	IGKJ2*01	QNIRTY	111	VAS	QQSYFAPYT	112								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	13	IGHV1-3*01	IGHD2-21*01	IGHJ6*02	GYTFTHYA	113	LNGGNDR	114	ARGGWIIQNGGARYYHGMDV	115	IGKV3-20*01	IGKJ4*01	QSVSSSQ	116	GAS	QHYNNPVA	117	IGLV3-21*02	IGLJ2*01	NIRNKN	118	ADS		QVWDGGSYHVI	119
	13	IGHV1-3*01	IGHD3-10*01	IGHJ4*02	GYTFTRYP	120	INAANGDT	121	ARKDYYGSGSYEFDN	122								IGLV2-11*01	IGLJ2*01	SSDVGGYNY	123	DVN		CSYAGNYILV	124
	69	IGHV1-3*01	IGHD2-2*01	IGHJ3*01	GYNFQRSA	125	INVGNGNT	126	AKGRSSHDLYDPFDF	127	IGKV1-5*03	IGKJ2*01	ENIGGW	128	KAS	QQYNSYSRYT	129								
	99	IGHV1-3*01	IGHD3-10*01	IGHJ4*02	GYTFTSYP	130	INPANGDT	131	ARKNYYASGSYHFDL	132								IGLV2-11*01	IGLJ3*02	NSDVGGYNY	133	DVT		SSYAGKYTLV	134
	146	IGHV1-3*01	IGHD1-1*01	IGHJ3*02	GYTLTSYA	135	INAGSGLT	136	ARVGIPLRGAGGSPFDI	137	IGKV1-39*01	IGKJ4*01	QSVSTY	138	TAS	QQSSSVPLT	139								
H0	146	IGHV1	IGHD3-	IGHJ3*02	GYTFTTYA	140	INAGNGIT	141	ARVGILVRG	142	IGKV1-	IGKJ4*01	QSISTY	143	SAS	QQSYS	144								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
01		-3*01	16*01						AGGSPFDI		39*01					TPLT									
	146	IGHV1-3*01	IGHD3-16*01	IGHJ3*02	GYTFTTYA	145	INAGNGIT	146	ARVGILVRGAGGSPFDI	147	IGKV1-39*01	IGKJ4*01	QSISTY	148	TAS	QQSYSTPLT	149								
	146	IGHV1-3*01	IGHD4-11*01	IGHJ3*01	GYTFSRHA	150	INIGNGNT	151	AREDYTGNYYDAFDF	152	IGKV1-5*03	IGKJ4*01	QSVSTW	153	KAS	QLYNSYSGTT	154								
	146	IGHV1-3*01	IGHD6-13*01	IGHJ6*02	GYSFSNYA	155	INAAYGNT	156	ARDGVKEQLVYYYFGMDV	157								IGLV1-40*01	IGLJ2*01	SSNIGKNYD	158	GDT		QSYDSNLSGSVV	159
	146	IGHV1-3*01	IGHD3-10*01	IGHJ4*02	TYVFTAYA	160	INAGNGDT	161	ARGALLWFRDDFDF	162	IGKV1-27*01	IGKJ3*01	QGISNY	163	AAS	QKYDSAPYT	164	IGLV1-51*01	IGLJ1*01	SSNIGNTY	165	DNN		GSWDSSLYSFYV	166
	99	IGHV1-46*01	IGHD2-2*01	IGHJ1*01	GYTFSNYH	167	INPSGDST	168	ASRLDAIPFQV	169	IGKV3-20*01	IGKJ2*01	PNASGS	170	GAS	QQYGGLPFT	171								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	99	IGHV1-46*01	IGHD4-23*01	IGHJ6*04	GYIVTSYR	172	IDPSDTYT	173	ARKGNYGSRYDWYFDV	174								IGLV2-14*01	IGLJ3*02	SSDVGDYSY	175	DVN		SSYTSSSTGV	176
	55	IGHV1-46*03	IGHD3-9*01	IGHJ3*01	GYTFTNFN	177	INPGAGTT	178	TRDPILRYFDWQSRDAFDV	179	IGKV1-17*01	IGKJ3*01	QGIRND	180	AAS	LQHNGYPIT	181								
	60	IGHV1-69*01	IGHD3-10*01	IGHJ6*01	GGTFSSYS	182	IVPIFGIP	183	ARVPSVATCNFGCYSAMDV	184	IGKV1-39*01	IGKJ3*01	QSISNY	185	GAS	QQSYSTLFS	186	IGLV2-14*01	IGLJ1*01	SSDVGGYKY	187	EVT		SSYTGSSTRYV	188
	146	IGHV1-69*06	IGHD3-3*01	IGHJ4*02	GGKFIAYG	189	TIPIYGTA	190	ARASFGDLWSGYPNQFFDH	191	IGKV1-17*03	IGKJ1*01	QGISNS	192	GAS	LQHNTYPWT	193								
	13	IGHV2-5*02	IGHD3-9*01	IGHJ5*02	GFSFSTGGVG	194	IYGDGDE	195	AHRLLTAYYDH	196	IGKV1-5*03	IGKJ1*01	QSISRW	197	KAS	QQYNSYSWA	198								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	55	IGHV2-5*02	IGHD6-13*01	IGHJ5*02	GFSLSTFGVG	199	IYWDDDK	200	AHTVAAAATFWFDP	201								IGLV1-44*01	IGLJ2*01	SSNIGSNT	202	STN		ATWDDSLNGLV	203
	69	IGHV2-5*02	IGHD2-21*02	IGHJ3*02	GFSLSTTAVG	204	IYGDDDK	205	AHSSYFDCGGDCSDVAFDI	206								IGLV3-10*01	IGLJ3*02	ALPRKY	207	EDN		YSTDSSGDPV	208
	146	IGHV2-5*02	IGHD2-15*01	IGHJ3*01	GFSLTTNGMG	209	IYWDDDK	210	ARSYCRGGNCYSTAFNV	211								IGLV2-11*01	IGLJ2*01	SSDVGGYDY	212	GVN		CSYAGAYTYVA	213
H002	146	IGHV2-70D*04	IGHD7-27*01	IGHJ4*02	GFSLSTNTMR	214	IDWDDEK	215	ARSNHWGSHFDY	216								IGLV3-21*02	IGLJ1*01	NIGGKT	217	DNS		QVWDTSGDHLYV	218
	55	IGHV3-11*01	IGHD2-21*01	IGHJ3*01	GFTFSDYY	219	IRGSHSSV	220	ARDLPGDEYLDAFDL	221	IGKV4-1*01	IGKJ4*01	QSLLYSSNNKNY	222	WAS	QQFYTAPLT	223								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	60	IGHV3-11*01	IGHD6-13*01	IGHJ6*02	GLTLSDYY	224	ISHDGSTI	225	ASGAAVPYFYYGVDV	226								IGLV3-1*01	IGLJ2*01	KLGDAY	227	QDT		QAWGSSPAKV	228
	99	IGHV3-13*01	IGHD3-22*01	IGHJ4*02	GFTFSSYD	229	IGAATDT	230	ARAVHYYDSSGHYSGYYFDY	231								IGLV1-44*01	IGLJ2*01	SSNIGSNT	232	SNN		ATWDASLKGVV	233
	55	IGHV3-15*01	IGHD1-1*01	IGHJ4*02	GFTFSNAW	234	IRSKTDGGTA	235	TTQNAFES	236								IGLV3-21*01	IGLJ1*01	NIGSKS	237	YDS		QVWDSSSDHYV	238
	55	IGHV3-15*01	IGHD2/OR15-2a*01	IGHJ6*02	GFTFSNAY	239	IKSITDGGTI	240	HTLSTTHYYGMDV	241	IGKV3-20*01	IGKJ4*01	QSVTSNY	242	GAS	QQYINSPLT	243								
	146	IGHV3-15*01	IGHD6-25*01	IGHJ4*02	GFTFSNTY	244	IQRKTDGGTA	245	AAHNRAAY	246	IGKV1-5*01	IGKJ2*01	QSISNW	247	DAS	QQYYSYPLT	248								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	9	IGHV3-21*01	IGHD3-3*02	IGHJ4*02	GLTFSTHS	249	ISGSSDYI	250	ARARPPGTAFGFDH	251								IGLV1-40*01	IGLJ2*01	SSNIGAGYD	252	DNN		QSYDSSLSGAL	253
	13	IGHV3-21*01	IGHD3-16*01	IGHJ4*02	GFTFSSYV	254	VSSSSYSI	255	VRTFYFDY	256	IGKV3-15*01	IGKJ1*01	QSVRTN	257	SAS	QQYDIWPPRT	258								
	55	IGHV3-21*01	IGHD4-17*01	IGHJ1*01	GFTFSSFS	259	ISSSSRYI	260	VRDMTTVTTCXXQH	261								IGLV1-44*01	IGLJ2*01	SSNIGSHT	262	TNS		AAWDDSLNGLV	263
	55	IGHV3-21*01	IGHD4-17*01	IGHJ1*01	GFTFSSFS	264	ISSSSRYI	265	VRDMTTVTTCYLQH	266								IGLV1-44*01	IGLJ2*01	SSNIGSHT	267	TNS		AAWDDSLNGLV	268
	146	IGHV3-21*01	IGHD4-17*01	IGHJ4*02	GFSFSIYS	269	IGNRGNPK	270	ARGRTYGDSN	271	IGKV3-15*01	IGKJ1*01	RSISSN	272	RAS	QQYDNWHT	273								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	146	IGHV3-21*01	IGHD3-3*01	IGHJ4*02	GFSFNAYS	274	ISSSSSYI	275	ARVPILLAQGVPTFDL	276	IGKV3-15*01	IGKJ2*01	QSVNSN	277	SAS	QQYSDWPRYT	278								
	9	IGHV3-23*01	IGHD2-2*02	IGHJ6*03	GFTFTRYT	279	VSGSGSST	280	AKAAILGNYNYYMDV	281								IGLV3-21*02	IGLJ2*01	NIASKS	282	DDN		QVWDSSADHLVV	283
	13	IGHV3-23*01	IGHD1-1*01	IGHJ4*01	EFRFGSYA	284	IIATGAKT	285	VKDAIYMSNWPWYFDY	286								IGLV3-21*02	IGLJ2*01	NIGSKS	287	DDN			
	13	IGHV3-23*01	IGHD6-13*01	IGHJ4*02	GFTFTNYA	288	ISGSGGST	289	AKDPIYSSWPYYFDY	290								IGLV3-21*02	IGLJ2*01	NIGSRG	291	EDS		QVWDSSSDHPEVV	292
H021	13	IGHV3-23*01	IGHD6-13*01	IGHJ4*02	GFRFSSYA	293	ISGSGGST	294	AKDPIYTSRWPYYFDY	295	IGKV1-39*01	IGKJ2*03	QSISSY	296	AAS	QQSYSLYS	297	IGLV3-21*02	IGLJ2*01	NIGSKS	298	DDS		QVWHSSSDHSEVI	299

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	13	IGHV3-23*01	IGHD3-10*01	IGHJ4*02	GFRFSSYA	300	ISGRDAST	301	AKDGVLGSYHQYYFQY	302								IGLV3-21*02	IGLJ2*01	NIGSKS	303	DDT		QVWDNSSDHPGVV	304
	13	IGHV3-23*01	IGHD5-12*01	IGHJ4*02	GFTFSSYA	305	ISGSGGST	306	AKGSRNGPYIVATLHFDY	307	IGKV3-15*01	IGKJ4*01	QSVSSN	308	GAF	QHYNHWSLT	309								
	55	IGHV3-23*01	IGHD6-13*01	IGHJ4*02	GFTFNNYA	310	VSGNGGST	311	VLSSSWMDNPFDF	312								IGLV5-45*02	IGLJ3*02	SGINVGTYR	313	YKSDSDK	314	MIWHSSAWV	315
	55	IGHV3-23*01	IGHD1-26*01	IGHJ4*02	GFTFSSYA	316	ASASGRNT	317	AGFPSGTHFFDY	318	IGKV3-11*01	IGKJ1*01	QSVSNH	319	DAS	QQRSNWWT	320								
	55	IGHV3-23*01	IGHD1-26*01	IGHJ4*02	GFTFSSYA	321	ASASGRNT	322	AGFPSGTHFFDY	323	IGKV3-20*01	IGKJ4*01	QSVSNSY	324	GAS	QQFGSSPLT	325	IGLV2-8*01	IGLJ1*01	SSDIGGYNY	326	EVN		NSYAGNNNFV	327

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	55	IGHV3-23*01	IGHD2-2*01	IGHJ6*02	EFTFSSYA	328	ISGSGDTT	329	ARPDALHCSSITSCSLYGLAYYYGMDV	330								IGLV1-44*01	IGLJ3*02	SSNIGTNT	331	SNN		AAWDDRLIGWV	332
	55	IGHV3-23*01	IGHD1-26*01	IGHJ4*02	GFTFSSHG	333	ISGNGGFT	334	AKRMVEATNRYFDY	335	IGKV3-20*01	IGKJ2*01	QSVSNSY	336	GVS	QQYGSSPYT	337								
	55	IGHV3-23*01	IGHD1-26*01	IGHJ4*02	GFTFINYA	338	ISANGIYT	339	ARDSSEWVLGIDF	340								IGLV2-11*01	IGLJ2*01	SSDVGGYNY	341	DVN		CSYAGSYTVV	342
	60	IGHV3-23*01	IGHD4/OR15-4a*01	IGHJ2*01	GFTFSSYA	343	ITGSGGST	344	AKDAVRSANHAWYFDF	345								IGLV3-21*02	IGLJ2*01	NIGIKS	346	DDT		QVWDSNSDHPKVV	347
	60	IGHV3-23	IGHD5-12*01	IGHJ4*02	GFTFSSTA	348	ISSNGAGT	349	AKGYGLFDS	350	IGKV3-15*01	IGKJ1*01	QSLVTN	351	GAS	QQYINWPPWS	352								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01																							
H003	60	IGHV3-23*01	IGHD2-21*01	IGHJ2*01	GFTFSSYA	353	LTATGGNT	354	AKDAIRNSNHAWYFDV	355								IGLV3-21*02	IGLJ2*01	NIGSKS	356	DDN		QVWDPTSDQV	357
	60	IGHV3-23*01	IGHD2-8*01	IGHJ4*02	GFTFSSYG	358	ISGRGDET	359	AKSRVTNSGSIDH	360	IGKV1-39*01	IGKJ5*01	QTIGTY	361	AAS	QQSYSTSIT	362								
	60	IGHV3-23*01	IGHD4/OR15-4a*01	IGHJ2*01	GFRFNNYA	363	ISGGDGYT	364	AKDAILSANHPWYFDF	365	IGKV4-1*01	IGKJ4*01	QSVLYSSNNKNY	366	WAS	QQYYSTPLT	367	IGLV3-21*02	IGLJ3*02	NIGTNS	368	EDS		QVWDSSSDHPKVV	369
	60	IGHV3-23*01	IGHD2-21*01	IGHJ2*01	GFTFSSYA	370	IVNSGGST	371	AKDAIRSSNHPWYFHV	372								IGLV3-21*02	IGLJ2*01	NIGSES	373	DDS		QVWDGSSDHPKVL	374
	60	IGHV3-23	IGHD4/OR15-	IGHJ2*01	GFRFNNYA	375	ITGGEGYT	376	AKDAILSANHPWYFDF	377								IGLV3-21*02	IGLJ3*02	NIGTNS	378	EDS		QVWDRSSDQSKVV	379

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01	4a*01																					
	146	IGHV3-23*01	IGHD3/OR15-3a*01	IGHJ4*02	GFTFSTHA	380	ISGGSEWS	381	AKGYGLFDF	382	IGKV3-15*01	IGKJ1*01	QSVSSN	383	GPS	QQYINRPPWT	384								
	9	IGHV3-23*03	IGHD1-1*01	IGHJ4*02	GFTFSNYA	385	IYTGGSKT	386	AKVLLGGWNGVFDH	387	IGKV3-11*01	IGKJ4*01	QSVDSY	388	DAS	QQRSTWPPS	389								
H004	146	IGHV3-23*04	IGHD3-10*01	IGHJ6*02	GFRFNNYG	390	FSGSGSNI	391	AKDGYFGSGSLYGIDV	392								IGLV3-21*02	IGLJ2*01	NIGSKS	393	EDS		QVWDSNHDHPGVV	394
	146	IGHV3-23*04	IGHD3-10*01	IGHJ6*02	GFTFTSYA	395	ISGSGGST	396	AKDGYYGSGSLYGMDV	397								IGLV3-21*02	IGLJ2*01	NIGSKS	398	DDS		QVWDSTSDHPGVV	399
	146	IGHV3-23	IGHD3-9*01	IGHJ6*02	GFTFSSYA	400	FSGSGST	401	AKVIQYPRGFWF	402								IGLV1-51*01	IGLJ3*02	SSNIGNNY	403	DNN		GTWDSSLNNCV	404

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*04							YGMDV															
	60	IGHV3-30-3*01	IGHD3-10*01	IGHJ6*02	GFTFTSYA	405	ISYDGSTH	406	ARDPGVPYYHYAMDV	407								IGLV2-8*01	IGLJ2*01	SSDVGGYHY	408	EVS		SSYAGSNNYIL	409
	146	IGHV3-30-3*01	IGHD3-3*01	IGHJ4*02	EFTFSTYA	410	ISADGNNR	411	VRDETDWEIGVVVATPEFDY	412	IGKV1-17*01	IGKJ2*01	QGIRND	413	AAS	LQHNSYPRT	414	IGLV1-44*01	IGLJ2*01	GSNVGGNT	415	SND		STWDDSLNGVV	416
	146	IGHV3-30-3*02	IGHD4-23*01	IGHJ4*02	GFPFSSHA	417	LSFNGDYI	418	VTGIRARDYGGSTFDL	419								IGLV10-54*01	IGLJ2*01	NKNVGNEG	420	RND		AAWDSSLSAMI	421
	9	IGHV3-30*02	IGHD3-10*01	IGHJ3*01	GFRFTNYG	422	IRYDGSKK	423	AKDGRWFGESGGFDV	424								IGLV3-21*02	IGLJ2*01	NIGNTV	425	DDN		QVWESTDPVV	426

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	9	IGHV3-30*03	IGHD2-2*01	IGHJ2*01	GFTFTSYS	427	MSYDGSYE	428	ARDYCSRTNCINWIFDL	429	IGKV3-20*01	IGKJ4*01	PSVSSSY	430	GVS	QQYGSSPLT	431								
	60	IGHV3-30*03	IGHD2-8*02	IGHJ6*02	GFRFTGYG	432	ISNDGSKK	433	AKDGYLSAARGYGMDV	434								IGLV3-21*02	IGLJ2*01	NIGGKS	435	DDR		QVWETTSDQLV	436
	146	IGHV3-30*03	IGHD4-17*01	IGHJ4*02	GFTFSNYD	437	ISYDGSNK	438	ARDTFGDYYFDY	439								IGLV1-40*01	IGLJ1*01	NSNIGAGYD	440	GNH		QSYDSRLSVPYV	441
	9	IGHV3-30*04	IGHD5-18*01	IGHJ6*02	KFTFSKYA	442	TSYNGGSK	443	ARGGYTYGSYYYSMDV	444	IGKV4-1*01	IGKJ3*01	QSVLYSSNNKNY	445	WAS	QQYYSTPFT	446								
	9	IGHV3-30*04	IGHD5-18*01	IGHJ6*02	RFTFSKYA	447	ISYDGSSK	448	ARGGYTYGSYYYAMDV	449	IGKV4-1*01	IGKJ3*01	QSLLYSSNNKNY	450	WAS	QQYYSTPFT	451								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	55	IGHV3-30*04	IGHD1-26*01	IGHJ4*02	GFTFSSYS	452	MSNTGSTK	453	ARALLSVVGSKSYYFDF	454	IGKV3-11*01	IGKJ1*01	QSVSSY	455	DAS	QHRSNSWT	456								
	55	IGHV3-30*04	IGHD1-26*01	IGHJ4*02	GFTFSSYS	457	MSNTGSTK	458	ARALLSVVGSKSYYFDF	459	IGKV3-11*01	IGKJ1*01	QSVSSY	460	DAS	QHRSNSWT	461								
	55	IGHV3-30*04	IGHD1-26*01	IGHJ6*02	GFNFNVYA	462	ISYDGSKK	463	ARDEKYSGLYSGRTGDYYYGMDV	464								IGLV1-51*01	IGLJ2*01	NSNIGNNF	465	NSD		GTWDSSLSLGV	466
	55	IGHV3-30*04	IGHD3-22*01	IGHJ6*02	GFTFSAYS	467	ISYDGSNR	468	ARDGKLGRTYHDSRQSYFYIMDV	469								IGLV2-14*01	IGLJ2*01	SSDVGGYNY	470	DVN		SSYTSSTSLV	471
	13	IGHV3-30	IGHD3-10*01	IGHJ6*02	GFRFSSYG	472	TSFDGSKT	473	AKDAYYFASGSF	474								IGLV3-21*02	IGLJ2*01	NIGSKS	475	DDN		QVWGSGGVI	476

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*18							FGMDV															
	13	IGHV3-30*18	IGHD3-10*01	IGHJ6*02	GFTFSRYG	477	ISYDGSNK	478	AKDAYYYGSGYGMDV	479	IGKV1-5*03	IGKJ4*01	QSISVW	480	KAS	QQYTSFST	481	IGLV1-47*01	IGLJ1*01	SSNIGSDY	482	RNN		AAWDDRLSGYV	483
	60	IGHV3-30*18	IGHD3-10*01	IGHJ6*02	GFTFRSYG	484	ISSDGSKK	485	AKDGYVVSGSGYGMDV	486								IGLV3-21*02	IGLJ2*01	NIGSKS	487	DDS		QVWDSSSDHVV	488
H009	60	IGHV3-30*18	IGHD1-26*01	IGHJ6*02	RFSFNTYG	489	ISYDGSHE	490	AKTDIKWGATNYGMDV	491								IGLV3-21*02	IGLJ2*01	NIGRKS	492	DDN		QVWDGTRDHLVV	493
	60	IGHV3-30*18	IGHD5-12*01	IGHJ4*02	GFTFSNYA	494	TLYDGSHS	495	AKDSAGYGLHY	496	IGKV1-17*01	IGKJ1*01	QGIRTD	497	AAS	LQHNSYPWT	498	IGLV3-19*01	IGLJ2*01	SLRSFY	499	NKD		NSRDSIGNHVV	500
	60	IGHV3-30	IGHD3-22*01	IGHJ6*02	GFRFTGYG	501	ISNDGSKK	502	AKDGYLSAARGY	503								IGLV3-21*02	IGLJ2*01	NVGSKS	504	DDS		QVWDTTTDQLV	505

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*18							GMDV																
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	506	ISNDGSKT	507	AKDGYLSAARGYGMDV	508								IGLV3-21*02	IGLJ2*01	NIGGKS	509	DDS		QVWDTTSDQLV	510
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	511	ISNDGSKK	512	AKDGYLSAARGYGMDV	513								IGLV3-21*02	IGLJ2*01	NIGALS	514	DDN		QVWDTSSDQLV	515
H005	60	IGHV3-30*18	IGHD3-16*01	IGHJ6*02	GFRFTGYG	516	ISNDGSKK	517	AKDAYLSAARGYGMHV	518								IGLV3-21*02	IGLJ2*01	NIGGKS	519	DDS		QVWDTASDQLV	520
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	521	ISNDGSKK	522	AKDGYLSAARGYGMDV	523								IGLV3-21*02	IGLJ2*01	NIGGKS	524	DDR		QVWDTTSDQLV	525
	60	IGHV3-30	IGHD3-22*01	IGHJ6*02	GFRFTGYG	526	ISNDGSKK	527	AKDGYLSAARGY	528								IGLV3-21*02	IGLJ2*01	NIGGKS	529	DDT		QVWDTTSDQLV	530

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*18							GMDV															
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	531	ISNDGSKK	532	AKDGYLSAARGYGMDV	533								IGLV3-21*02	IGLJ2*01	NIGGKS	534	DDS		QVWDTTSDQLV	535
	60	IGHV3-30*18	IGHD1-26*01	IGHJ6*02	GFTFNTYA	536	ISYDGSNK	537	AKTDIRWGATNYGMDV	538								IGLV3-21*02	IGLJ2*01	NIGSKS	539	DDN		QVWDGSSDHLVV	540
H0100	60	IGHV3-30*18	IGHD3-3*01	IGHJ4*02	GFSFSTYG	541	ISYDGMIK	542	AKGPLFGLFSFDQ	543								IGLV3-21*03	IGLJ2*01	NIGDMS	544	DDS		QVWDNSRNRGI	545
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	546	ISNDGSKK	547	AKDGYLSAARGYGMDV	548								IGLV3-21*02	IGLJ2*01	NIGGKS	549	DDR		QVWDTTSDQLV	550
	60	IGHV3-30	IGHD3-22*01	IGHJ6*02	GFRFTGYS	551	ISNDGSKR	552	AKDGYLSAARGY	553	IGKV2-30*01	IGKJ1*01	QSLVYSDGNTY	554	KVS	TQVTLWPPWT	555								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*18							GMDV																
H006	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	556	ISNDGSKK	557	AKDGYLSAARGYGMDV	558								IGLV3-21*02	IGLJ2*01	NIGGKS	559	DDN		QVWDTTSDQLV	560
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	561	ISNDGSKK	562	AKDGYLSAARGYGMDV	563								IGLV2-18*02	IGLJ2*01	SSDVGSYNR	564	EVS		SSYTSSSTLV	565
	60	IGHV3-30*18	IGHD2-21*02	IGHJ4*02	GFTFRSYG	566	ISSDGSKK	567	AKDPIKVSANGWGFDY	568								IGLV3-21*03	IGLJ2*01	NIGSKS	569	DDT		QVWDSNSDHVV	570
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	571	ISNDGSRK	572	AKDGYLSAARGFGMDV	573								IGLV3-21*02	IGLJ2*01	NIGGKS	574	DDS		QVWDTTSDQLV	575
	60	IGHV3-30	IGHD2-15*01	IGHJ6*02	RFSFSTYG	576	ISYDGSEK	577	AKTDIMWRAVN	578								IGLV3-21*02	IGLJ2*01	NIGSKS	579	DDN		QVWDDSRDHLVI	580

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*18							YGMDV															
	60	IGHV3-30*18	IGHD2-15*01	IGHJ6*02	RFSFSTYG	581	ISYDGSEK	582	AKTDIMWRAVNYGMDV	583								IGLV3-21*02	IGLJ2*01	NIGSKS	584	DDN		QVWDDSRDHLVI	585
	60	IGHV3-30*18	IGHD2-21*01	IGHJ6*02	GFSFSTYG	586	ISYDGSSK	587	AKTDIMWQAVNYGMDV	588								IGLV3-21*02	IGLJ2*01	NIGSKS	589	DDN		QVWDDSRDHLVI	590
	60	IGHV3-30*18	IGHD3-22*01	IGHJ6*02	GFRFTGYG	591	ISNDGSKK	592	AKDGYLSAARGYGMDV	593								IGLV3-21*02	IGLJ2*01	NIGGKS	594	DDR		QVWDTTSDQLV	595
	60	IGHV3-30*18	IGHD2-15*01	IGHJ6*02	RFSFSTYG	596	ISYDGSEK	597	AKTDIMWRAVNYGMDV	598								IGLV3-21*02	IGLJ2*01	NIGSKS	599	DDN		QVWDESRDHLVI	600
	60	IGHV3-30	IGHD3-22*01	IGHJ6*02	GFRFTGYG	601	ISNDGSKK	602	AKDGYLSAARGY	603								IGLV3-21*02	IGLJ2*01	NIGGKS	604	DDR		QVWDTTSDQLV	605

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*18							GMDV																
H008	146	IGHV3-30*18	IGHD1-26*01	IGHJ6*02	GFRFTMYG	606	IPFDGRTQ	607	AKDGILGARGLYGIDV	608								IGLV3-21*02	IGLJ2*01	DVGSKS	609	DDT		QVWDSSSDHVV	610
H007	146	IGHV3-30*18	IGHD3-3*01	IGHJ6*02	GFTFNNYA	611	ISYDGSNK	612	AKEIGGFDFRSGSQRSYYYGVDV	613	IGKV3-20*01	IGKJ2*01	QTIYTTY	614	GAS	QQYSSSPPGYT	615								
	146	IGHV3-30*18	IGHD3-3*01	IGHJ6*02	GFTFSRHG	616	ISYDGGNK	617	AKEIGGFDFRSGDQLTYYYGMDV	618	IGKV3-20*01	IGKJ2*01	QSVYSTY	619	GAS	HQYVTSPPGYT	620								
	146	IGHV3-30*18	IGHD5-18*01	IGHJ6*02	GFSFSNYG	621	ISYDGSNK	622	AKDAYIYARGSYYGMDV	623								IGLV3-21*02	IGLJ2*01	NIASKS	624	DDT		QVWDSSSNDPVV	625

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	146	IGHV3-30*18	IGHD1-26*01	IGHJ6*02	GFRFTKYG	626	ISFDGSTQ	627	AKDGILGARGRGXYGIDV	628								IGLV3-21*02	IGLJ2*01	NIRSKN	629	DDN		QVWDSYSDHVV	630
	146	IGHV3-30*18	IGHD3-3*01	IGHJ6*02	GFTFSNYA	631	ISFDGSNK	632	AKEIGGFDFRSGKQRSYYYGVDV	633	IGKV3-20*01	IGKJ2*01	QTVYNTY	634	GAS	QQYGNSPPGYT	635								
	146	IGHV3-30*18	IGHD3-10*01	IGHJ4*02	GFRFTIYG	636	VSYDGSKQ	637	AKDAYYYGSGSHNNPDY	638								IGLV3-21*02	IGLJ3*02	NIGSQS	639	DDS		QVWDSSSMGV	640
	146	IGHV3-30*18	IGHD3-16*02	IGHJ4*02	GFTFSNYG	641	ISYDGRDK	642	AKGYDYIWGTYRPRPDLDS	643								IGLV1-44*01	IGLJ3*02	NSNVGNNV	644	ANS		ASWDDSLSGSWV	645
	146	IGHV3-30	IGHD6-13*01	IGHJ4*02	GFTFSDYG	646	VSYDGTSE	647	AKDPVQRSNWYYFDY	648								IGLV3-21*02	IGLJ2*01	NIGSKT	649	DDR		QVWHSTTEPVV	650

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*18																							
	146	IGHV3-30*18	IGHD1-20*01	IGHJ4*02	GFTFSNYG	651	TSYDGINK	652	AKDPVHRSNWFYFDH	653								IGLV3-21*02	IGLJ2*01	YIGSKT	654	DDR		QVWYSNSEPVV	655
	146	IGHV3-30*18	IGHD3-3*01	IGHJ6*02	GTSFSTSG	656	ISPNAFDK	657	AKGSPIIRFLMMDV	658	IGKV1-5*03	IGKJ1*01	QSIDTW	659	KAS	QYSVYST	660	IGLV3-21*02	IGLJ3*02	NIGSKN	661	DDN		QVWDNNSDHVV	662
	13	IGHV3-33*01	IGHD6-13*01	IGHJ4*02	GFTFSSYG	663	IWSDGSNK	664	AREAGIAAPASLDF	665								IGLV3-21*02	IGLJ2*01	NIRGKS	666	ADS		QVWDSSSDHVV	667
	13	IGHV3-33*01	IGHD6-13*01	IGHJ4*02	GFTFSNYG	668	IWSDGTNK	669	TREAGIAAPAALDY	670								IGLV3-21*02	IGLJ2*01	NIGNKN	671	DDN		QVWDSSSYHVV	672
H011	13	IGHV3-33	IGHD1-7*01	IGHJ3*01	GFTFSNYG	673	VWYDGSYK	674	VRDNWSYNAFDV	675	IGKV3-11*01	IGKJ2*03	QSISSY	676	GTS	QHRNSWPYS	677								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01																							
	13	IGHV3-33*01	IGHD6-19*01	IGHJ4*02	GFIFSDYG	678	IWKDGSNK	679	VRENSGWYYFDY	680	IGKV1-17*01	IGKJ4*01	QGIRNN	681	TAS	LQHDSYPFT	682								
H012	13	IGHV3-33*01	IGHD6-13*01	IGHJ4*02	GFAFRSYG	683	IWHDGSNK	684	AREGAIAAPASLDV	685								IGLV3-21*02	IGLJ2*01	NIRSRN	686	ADS		QVWDSGTDHVI	687
	13	IGHV3-33*01	IGHD6-13*01	IGHJ4*02	GFTFSSFG	688	IWSDGSNQ	689	AREGGIAAPAALDF	690								IGLV3-21*02	IGLJ2*01	NIRNKN	691	ADS		QVWDGGSYHVI	692
	13	IGHV3-33*01		IGHJ4*02	GVTFNSYG	693	IWYDGTNK	694	ARESKAYPYYFDY	695	IGKV1-39*01	IGKJ2*03	QNISIF	696	DAS	QHSSFPPQDS	697								
	13	IGHV3-33	IGHD1-1*01	IGHJ4*02	GFTFSNYA	698	IWYDGTYK	699	ARESNGFGSDF	700	IGKV1-17*01	IGKJ1*01	QGIRNN	701	AAS	LQHNSFPRT	702								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01																							
	13	IGHV3-33*01	IGHD3-10*01	IGHJ3*02	GFVFSSYG	703	VWYDGSYK	704	VRDNWSYNAFDI	705	IGKV3-11*01	IGKJ2*03	QSISSY	706	ATS	QHRNSWPYS	707								
	13	IGHV3-33*01	IGHD1-20*01	IGHJ3*02	GFTFSNYG	708	IWYDGSYK	709	ARDNWKYNAFDI	710	IGKV3-11*01	IGKJ2*03	QSVSSY	711	DAS	QHRSNWPYS	712								
	13	IGHV3-33*01	IGHD6-19*01	IGHJ4*02	GFTFSRYG	713	IWSDGSNQ	714	ARESSGWYYFDY	715								IGLV2-23*01	IGLJ1*01	SSDVGNYNF	716	EGS		CLYAGSSISYV	717
	13	IGHV3-33*01	IGHD6-13*01	IGHJ5*02	GFTFSSFG	718	IWYDGSNE	719	AREERIAAPASLDL	720								IGLV3-21*02	IGLJ2*01	NIGRKN	721	ADS		QVWDSSTYHVV	722
	13	IGHV3-33	IGHD6-25*01	IGHJ4*02	GFTFSSYG	723	IWHDGTNQ	724	ARELRIAAPAALDY	725								IGLV3-21*02	IGLJ2*01	NIANKN	726	ADS		QVWDSGSDHVL	727

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01																							
	49	IGHV3-33*01	IGHD3-16*01	IGHJ4*02	GFTFSSFN	728	IWYDGSHK	729	ARQMFTGHFDY	730	IGKV3-15*01	IGKJ1*01	QGVSSN	731	DAS	QHYNNWPRT	732								
	60	IGHV3-33*01	IGHD2-2*01	IGHJ6*02	GFTFSGYG	733	IWNDGSFK	734	AREGRGQLLFHGMDV	735	IGKV3-20*01	IGKJ3*01	QSVSSSY	736	GAS	QQYGRSQGFT	737								
	60	IGHV3-33*01	IGHD2-21*02	IGHJ4*02	GFTFSGHG	738	IWSSGSKT	739	ARDGHCDGGCYSALYDY	740								IGLV2-23*01	IGLJ3*02	SSDVGNYNL	741	EGT		CSFAGSRWV	742
H015	60	IGHV3-33*01	IGHD6-6*01	IGHJ4*02	GFSFSRHG	743	IWFDGTND	744	AREDPHLLIATLDL	745	IGKV1-39*01	IGKJ4*01	QGLTSF	746	SAS	QQSYGTPALA	747								
	60	IGHV3-33	IGHD4-11*01	IGHJ2*01	GFTFRSYG	748	IWADGTKQ	749	ARETTIFNWYFDL	750	IGKV1-39*01	IGKJ4*01	QSINKY	751	TAS	QQSFSIPPT	752								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01																							
	60	IGHV3-33*01	IGHD5-18*01	IGHJ4*02	GFTFSDYG	753	IWSDGSNK	754	ARERRGFSYGLDDN	755								IGLV2-11*01	IGLJ2*01	SSDVGGYNS	756	DVS		CSYAGRYTFVV	757
	60	IGHV3-33*01	IGHD6-19*01	IGHJ3*01	GFTFSRYG	758	IWKDGTND	759	ARERQAEIAVASFDF	760	IGKV1-39*01	IGKJ4*01	QRIGDF	761	AAS	QQAYNAPPLT	762								
	60	IGHV3-33*01	IGHD6-19*01	IGHJ4*02	GFTFSNYG	763	IWKDGTNK	764	ARESHYSAWYVLDY	765								IGLV1-51*01	IGLJ3*02	RSNIGSNY	766	GND		GSWDGSLSVGV	767
	60	IGHV3-33*01	IGHD2-8*01	IGHJ4*02	GFTFSRHG	768	IWYDGSNK	769	ARERDPNVFIATLDL	770	IGKV1-39*01	IGKJ4*01	QTITRS	771	ATS	QQSDSTPALA	772								
	60	IGHV3-33	IGHD3-16*01	IGHJ4*02	GFTFSRYG	773	IWNDGSTK	774	ARERDPYVFMATLDS	775								IGLV2-11*01	IGLJ3*02	SSDVGGYNY	776	DVS		CSYAGSYTWV	777

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01																							
	60	IGHV3-33*01	IGHD2-21*01	IGHJ2*01	GFTFRNYG	778	IWADGTNQ	779	ARETTIFQWYFDL	780	IGKV1-39*01	IGKJ4*01	QSINNY	781	GAS	QQSFSIPPT	782								
	69	IGHV3-33*01	IGHD2-15*01	IGHJ6*02	GFTFSSYG	783	IWYDGSLK	784	ARETTFGRFCSGGSCYSDYYYGMDV	785	IGKV2-24*01	IGKJ1*01	QSLVHSDGNTY	786	QIS	MQAAQFPWT	787								
	69	IGHV3-33*01	IGHD6-13*01	IGHJ4*02	GFVFSNYG	788	IWADGTNS	789	AREGGIVAADK	790								IGLV1-51*01	IGLJ1*01	SSNIGNNY	791	DNN			
H014	146	IGHV3-33*01	IGHD4/OR15-4a*01	IGHJ4*02	GFSFSDYG	792	IWRDGSNS	793	AREARVAAPASYDY	794								IGLV3-21*02	IGLJ3*02	KIVNKN	795	DDD		QVWDNGSNHVV	796
	146	IGHV3	IGHD6-	IGHJ4*02	GFTFSSCG	797	IWADGTNK	798	AREALIAAP	799								IGLV3-	IGLJ	NIRSKN	800	DDD		QVWDNNS	801

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-33*01	13*01						ATFDY									21*02	2*01					RHVV	
	146	IGHV3-33*01	IGHD6-13*01	IGHJ5*02	GFTFRNYG	802	IWADGSNK	803	AREGHIAAPAALDL	804								IGLV3-21*02	IGLJ2*01	NIRNKN	805	DDD		QVWDSSSEHVV	806
H013	146	IGHV3-33*01	IGHD6-13*01	IGHJ4*02	GFTFSGNG	807	IWSDGSNK	808	AREANIAAPAIYDH	809								IGLV3-21*02	IGLJ2*01	NIRSKN	810	DDN		QVWDSYSDHVV	811
	146	IGHV3-33*01	IGHD2-15*01	IGHJ5*02	GFTFTTYG	812	IWADGSNQ	813	AREGHVATPILDL	814	IGKV1-39*01	IGKJ4*01	QSIANY	815	VAS	QQSYSMPTLT	816								
	146	IGHV3-33*01	IGHD3-10*01	IGHJ3*01	GFTFSSYG	817	IWYDGSIK	818	VRDNFGLNAFDV	819	IGKV3-11*01	IGKJ2*01	QSVTRY	820	EAT	QHRSNWPYT	821								
	146	IGHV3	IGHD6-	IGHJ4*02	GFTFSNYG	822	IWHDGSNQ	823	ATERRIAAP	824								IGLV5-	IGLJ	SGISVDRSR	825	SXSDK	826	MIXHSS	827

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-33*01	13*01						GCLDY								48*02	2*01					AMW	
	146	IGHV3-33*01	IGHD6-13*01	IGHJ4*02	GFTFSSHG	828	IWYDGSTK	829	AREALIAAPATFDY	830	IGKV1-5*03	IGKJ1*01	QSIDTW	831	KAS	QYYSVYST	832	IGLV3-21*02	IGLJ3*02	NIGSKN	833	DDN		QVWDNNSDHVV	834
	60	IGHV3-33*02	IGHD5-12*01	IGHJ6*02	GFSFSRYG	835	IWYDGSTR	836	AGGGYSSRGYYNYGLDV	837	IGKV1-33*01	IGKJ4*01	QDISNY	838	DAS	QQYDNLPPLT	839	IGLV3-10*01	IGLJ2*01			EDN		YSTDRSGDQRV	840
	99	IGHV3-33*06	IGHD2-15*01	IGHJ4*02	GFTFSRYG	841	IWSDGSNK	842	AKATCGDGSCGLYYFDY	843								IGLV1-40*01	IGLJ3*02	SSNIGAGYD	844	GNS		QSYDSNLSGWV	845
	55	IGHV3-43*02	IGHD2-21*01	IGHJ5*02			INGNGRDT	846	AKDIWIFDGRRWIAGSPDA	847	IGKV2-30*01	IGKJ1*01	QSLVYSDGNTY	848	KVS	MQQTHWPWA	849								
	49	IGHV3	IGHD1-	IGHJ6*02	GFSFSSYS	850	ITSNSATI	851	ARAGPPSPP	852	IGKV4-	IGKJ4*01	QSLLYR	853	WAS	QQYYTA	854								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-48*01	1*01						NYGMDV		1*01		SNNKNY			PLL									
H0166	69	IGHV3-48*02	IGHD3/OR15-3a*01	IGHJ2*01	GFTFPSHT	855	ISTTSEAI	856	ASVGLDSKISGYWYFDL	857	IGKV3-15*01	IGKJ4*01	QSISSN	858	RAS	QQYDHWPLT	859								
	69	IGHV3-48*02	IGHD3/OR15-3a*01	IGHJ2*01	GFTFSTYT	860	ISSSGDTI	861	ARVGLALTISGYWYFDL	862	IGKV3-15*01	IGKJ4*01	QSVSSN	863	GAS	QQYNDWPLT	864								
	146	IGHV3-48*02	IGHD7-27*01	IGHJ2*01	GFTFSSSV	865	ISTTSAAI	866	ARAKLGSGSYWYFDL	867	IGKV3-15*01	IGKJ4*01	QSVGSN	868	AAS	QQYNNWPLT	869								
	13	IGHV3-48*03	IGHD1-1*01	IGHJ3*02	GITLRTYK	870	ISSDDKTI	871	ARDTGIWNGAYDAFDI	872								IGLV5-45*02	IGLJ1*01	SGINVGTYR	873	YRSDSDM	874	MIWHSTAYV	875
	13	IGHV3		IGHJ4*02	GFTFSSYE	876	ISNSGNTI	877	VGFDH	878	IGKV4-	IGKJ5*01	RSLLYT	879	WAS	QQYY	880								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-48*03									1*01		SVNKNH			SPPIT									
	55	IGHV3-48*03	IGHD2-2*02	IGHJ4*02	GFTFSNNE	881	ISSSGSVM	882	AGHCSSNKCYKY	883								IGLV1-40*01	IGLJ2*01	SSNIGAGYD	884	RNS		QSYDSSLSGSI	885
	69	IGHV3-49*03	IGHD3-22*01	IGHJ4*02	GFTFGDYG	886	IKPKAYGGAT	887	ARDLTINKIIVANDF	888	IGKV4-1*01	IGKJ5*01	QSLLYSSNNKNY	889	WAS	QQYYSTPIT	890								
	146	IGHV3-49*03	IGHD6-13*01	IGHJ4*02	GFTFGDYA	891	IRSKGYGGTR	892	ARVPYSSSWYVAWADY	893	IGKV4-1*01	IGKJ4*01	QSVLYSFNNKNY	894	WAS	QQYYSTPLT	895								
	99	IGHV3-49*04	IGHD3-10*01	IGHJ4*02	GFTFGDYG	896	IRRKANRGTT	897	TRGDYYGSRNSYFWLFDY	898	IGKV2D-29*01	IGKJ1*01	QSLLYSDGKTY	899	ELS	MQSIQLRT	900								
	69	IGHV3	IGHD6-	IGHJ4*02	GFTVISNY	901	IYSGVNT	902	ARVIAVAGT	903								IGLV7-	IGLJ	SGTVTT	904	STT		LLYCSGVRV	905

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-53*01	19*01						NRGGPRWRSTYYFDY								43*01	3*02	ANY					
	9	IGHV3-7*01	IGHD3-3*01	IGHJ4*02	GLTFSRYW	906	INEEGSHS	907	ASELWTAFNKDWSGYNDY	908								IGLV1-51*01	IGLJ3*02	SSNVGKNY	909	DSY		GTWDSSLKVVV	910
	9	IGHV3-7*01	IGHD1-26*01	IGHJ4*02	GFTFTNFK	911	IKQDGSEK	912	TRDTWVDS	913	IGKV1-17*03	IGKJ3*01	QGISKY	914	ASS	LQHQSYPFT	915								
	13	IGHV3-7*01	IGHD2-21*01	IGHJ4*02	GFSFSNYW	916	IKEDGSEK	917	ASSHYSAGDVSYNFDY	918								IGLV10-54*01	IGLJ3*02	NKNVGNKG	919	RHN		SAWDFSLRAWV	920
	55	IGHV3-7*03	IGHD6-13*01	IGHJ5*02	GFIFSSSW	921	IKQDGSDK	922	ARSHVAAGVTRWFDP	923	IGKV3-11*01	IGKJ2*01	QSVSSY	924	DAS	QHRSK	925								
	55	IGHV3-	IGHD6-13*01	IGHJ5*01	SFTFSTSW	926	INQDGSER	927	ARSHVAAGGTR	928	IGKV3-11*01	IGKJ2*01	QNINSQ	929	DAS	HHRIN	930								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		7*03							WIDS																
	55	IGHV3-7*03	IGHD3-16*02	IGHJ3*01	GFTFSDYW	931	INQDGSEY	932	ARLDRGTGESGYRSSDV	933								IGLV1-44*01	IGLJ2*01	SSNIGSRS	934	IN N		AAWDDSLNGVV	935
	55	IGHV3-7*03	IGHD1-7*01	IGHJ5*02	GFIFSSNW	936	INQDGSDI	937	ARSHVASGTRWFDP	938	IGKV3-11*01	IGKJ2*01	QSVSSY	939	DAS	QHRSY	940								
	55	IGHV3-72*01	IGHD3-9*01	IGHJ4*02	GFTFSDHF	941	TRNKANSYTT	942	ARDGYDILNHFVRFDF	943	IGKV3-11*01	IGKJ2*01	QSVSSY	944	DAS	QHRSY	945								
	60	IGHV3-72*01	IGHD3-16*01	IGHJ3*02	GFTFSDHY	946	IRNKAKSYTT	947	AREGLGSPTSDAFDI	948								IGLV2-14*01	IGLJ3*02	SSDVGGYNY	949	EV T		SSYTTSSTLV	950
	60	IGHV3-73*02	IGHD4-17*01	IGHJ6*02	GFTLSGSA	951	IRSKANNYAT	952	TSQYGDGYYYAMDV	953	IGKV3-15*01	IGKJ3*01	QNIRNN	954	GAS	QHYNNWPLFT	955								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	9	IGHV3-74*01		IGHJ6*02			ISDDERST	956	VRGLNHAMDV	957								IGLV2-14*01	IGLJ3*02	NSDVGGYNF	958	DVT		CSFTTRNTWV	959
	13	IGHV3-74*01	IGHD3-22*01	IGHJ4*02	GFTFSTYR	960	IKYDGSST	961	ARVYRDSRDGSDFRHFDS	962	IGKV4-1*01	IGKJ4*01	QSLLYSSNKKNY	963	WAS	QQYYDIPYT	964								
H017	55	IGHV3-74*01	IGHD3-10*01	IGHJ4*02	GFTFSNYW	965	ISTDGSST	966	ARGSTYYFGSGSVDY	967								IGLV2-14*01	IGLJ1*01	SSDIGVYNY	968	DVT		SSYRGSSTPYV	969
	55	IGHV3-74*01	IGHD1-26*01	IGHJ4*02	GFTFSDYW	970	IESDGSGT	971	ARGSLDF	972								IGLV2-14*01	IGLJ2*01	RSDVGAYNY	973	DVS		YSYTTSNTLV	974
	55	IGHV3-74*01	IGHD1-26*01	IGHJ4*02	GFTFSDYW	975	IDDGGSAT	976	SRGSLDY	977								IGLV2-14*01	IGLJ2*01	RSDVGAYNY	978	DVS		YSYTTSNTLV	979

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	99	IGHV3-74*01	IGHD4/OR15-4a*01	IGHJ4*02	GFTFSNYW	980	INSDGTNT	981	ACLRVPDRN	982								IGLV7-46*01	IGLJ2*01	TGAVTSGHY	983	DAS		LLSYSGAQV	984
	13	IGHV3-9*01	IGHD2-2*01	IGHJ4*02	GFIFDDYS	985	ISWNSEFM	986	VKANVKKGSTSCFDY	987	IGKV3-20*01	IGKJ1*01	QSVSSSY	988	DAS	QQYSGSSPRT	989								
	60	IGHV3-9*01	IGHD6-19*01	IGHJ4*01	GFNFNMYA	990	ISYNGGAR	991	VKDKSQGIPVAGLEY	992								IGLV1-51*01	IGLJ2*01	NSNIGNNY	993	DDS		GTWDSSLSAA	994
	60	IGHV3-9*01	IGHD6-19*01	IGHJ4*02	GFTFNMYA	995	ISFNGGAR	996	VKDKSQGIPLAGLEY	997								IGLV1-51*01	IGLJ2*01	SSNIGNNY	998	DDS		ATWDSSLTAA	999
H018	60	IGHV3-9*01	IGHD6-19*01	IGHJ4*01	GFNFNMYA	1000	ISYNGGAR	1001	VKDKSQGIPVAGLEY	1002								IGLV1-51*01	IGLJ2*01	NSNIGNNF	1003	DDS		GTWDSSLSAA	1004
	69	IGHV4-	IGHD2-2*03	IGHJ3*02	GGSITTGDYY	1005	IYYSGST	1006	AIYMDEAWAFEI	1007	IGKV1-39*01	IGKJ2*01	QSIGNY	1008	AVS	QQSYTIS	1009								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		30-4*01														LFT									
H019	69	IGHV4-30-4*01	IGHD2-2*03	IGHJ3*02	GGSITTGDYY	1010	IYYSGST	1011	AIYMDEAWAFEI	1012	IGKV1-39*01	IGKJ2*01	QSVGNY	1013	AVS	QQSYTISLFT	1014								
	146	IGHV4-30-4*01	IGHD3-10*01	IGHJ4*02	GGSISGGDYY	1015	IYYSGNT	1016	VRENYITSPLSR	1017								IGLV2-8*01	IGLJ3*02	SSDVGGYNY	1018	EVT		SSYAGSNDVV	1019
	146	IGHV4-30-4*01	IGHD4-17*01	IGHJ4*02	GGSINSGDYY	1020	VYSSGST	1021	ASYTVTTWGGFDY	1022								IGLV3-10*01	IGLJ3*02	ALPKKY	1023	EDH		YSTDSSGNYRV	1024
	99	IGHV4-31*02	IGHD4/OR15-4a*01	IGHJ4*02	GGSISSGNYY	1025	IHYSGST	1026	ARGVLH	1027	IGKV3-20*01	IGKJ2*01	QSVSSSY	1028	GVS	QQYGSSPYT	1029								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	13	IGHV4-31*03	IGHD3-22*01	IGHJ4*02	GGSISSGGYY	1030	IYYSDTTYYSGST	1031	ARVVSSGHRHYYFDY	1032	IGKV1-27*01	IGKJ1*01	QGISNY	1033	SAS	QKYWT	1034								
	60	IGHV4-31*03	IGHD1-1*01	IGHJ5*02	RGSVGWGENF	1035	ILNTGID	1036	AQSRRLVGPFVS	1037	IGKV3-15*01	IGKJ2*03	SININ	1038	DAS	QQYDKWPRS	1039	IGLV6-57*01	IGLJ3*02	SGSIASNY	1040	EDN		QSYDSSNHGV	1041
	99	IGHV4-31*03	IGHD2-8*02	IGHJ4*02	GGSISSGGYY	1042	ISYSGST	1043	ARGVLV	1044	IGKV3-20*01	IGKJ2*01	QSVSRAY	1045	GAS	QQYDSSPYT	1046								
	146	IGHV4-31*03	IGHD3-10*01	IGHJ3*01	GGSINSDDYY	1047	IYYDGSA	1048	ARVHASANAFDV	1049	IGKV1-6*01	IGKJ4*01	QGIRND	1050	AAS	LQDYNYPLT	1051	IGLV1-51*01	IGLJ3*02	SSNIGNTF	1052	DNY		GTWDSSLNGWV	1053
	146	IGHV4-31*03	IGHD3-10*01	IGHJ3*01	GGSISNDNYY	1054	IYYDGSA	1055	ARVHASANAFDV	1056	IGKV1-39*01	IGKJ5*01	QSINKF	1057	DAS	QQTYSTPT	1058								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	146	IGHV4-31*03	IGHD4-11*01	IGHJ3*02	GVPINNAGFY	1059	IHASGAT	1060	ARVPLRDFYSNYSPSAFDI	1061	IGKV3-15*01	IGKJ4*01	QSVSSD	1062	GAS	QQYKNWPPLT	1063								
	9	IGHV4-34*01	IGHD3-16*02	IGHJ5*02	RGSFSDYY	1064	INHSGST	1065	AGGRFTNDFVWGSYRYES	1066	IGKV2-28*01	IGKJ4*01	QSLLHSNGYNY	1067	LGS	MQALQTLLLT	1068								
	60	IGHV4-34*01	IGHD6-19*01	IGHJ4*02	GGSFIGHY	1069	ISHSGSA	1070	VRGGYSSAPYPREWRY	1071								IGLV1-44*01	IGLJ3*02	SSNIGSNT	1072	SNN		AAWDDSLNGWV	1073
	69	IGHV4-34*01	IGHD5-24*01	IGHJ6*03	GGSFSGDF	1074	INQSGST	1075	ARGRDGYNYVGYYYYYMDV	1076	IGKV3-11*01	IGKJ1*01	QSVTNY	1077	DGS	QQRSNWQWT	1078								
	146	IGHV4-34*01	IGHD3-3*01	IGHJ6*02	GGTFSGYY	1079	IDHSGGT	1080	ARGIFEVVIPYYSYRVDV	1081	IGKV3-15*01	IGKJ3*01	QTISNN	1082	GAS	QQYNNWPPFT	1083	IGLV3-19*01	IGLJ2*01	SLRSYY	1084	GRN		SSRSGNRLV	1085

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	9	IGHV4-34*02	IGHD6-13*01	IGHJ5*02	GGPFSGYY	1086	INHSGST	1087	GRGLGREYSSSWYGGRRFDP	1088								IGLV2-14*01	IGLJ3*02	SRQDGRYX	1089	EVN		RSYISNNXXWV	1090
	9	IGHV4-38-2*02	IGHD3-22*01	IGHJ3*02	GYSIRNRYY	1091	MYHSGST	1092	ARDRSGYVFFYDAFDI	1093	IGKV3-20*01	IGKJ4*01	QSVSSSY	1094	GAS	QQYGSSPLT	1095								
	146	IGHV4-38-2*02	IGHD2-21*02	IGHJ4*02	GYSISRDYY	1096	FSHSGTT	1097	GGGVTRADY	1098								IGLV1-47*02	IGLJ3*02	SSNIGKNY	1099	TND		AVWDDNLSAWE	1100
	60	IGHV4-39*01	IGHD2-8*01	IGHJ4*02	GGSISSSSYY	1101	IDYYGST	1102	ARRIQLMVFDF	1103	IGKV1-5*03	IGKJ1*01	QSISSW	1104	KAS	HQYNTYPWT	1105								
	60	IGHV4-39	IGHD3-3*01	IGHJ2*01	GGSISSNSNYY	1106	IYYSGST	1107	ARHPYYNFWIY	1108								IGLV1-44*01	IGLJ2*01	SSTIGSNT	1109	LNN		ASWDDSLNGLVV	1110

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*01							WYFDL															
	99	IGHV4-39*01	IGHD3-10*01	IGHJ3*01	GGSIRSSGYF	1111	VSSKGKT	1112	TRHWLGGDKWSQSPFLAV	1113								IGLV1-44*01	IGLJ3*02	SSNIGVNT	1114	ANN		AVWDDSLNTWV	1115
	99	IGHV4-39*01	IGHD5-12*01	IGHJ3*02	GGSISTSNYY	1116	IYYGGST	1117	AKGRYSGYNDYNAFDI	1118								IGLV1-47*02	IGLJ3*02			SNN		AAWDDSPEWLG	1119
	146	IGHV4-39*01	IGHD3-10*01	IGHJ3*01	GGSISSMSYY	1120	IYYSGTT	1121	TRPASGAHDYVSRSYYPGQGAFGV	1122	IGKV3-20*01	IGKJ5*01	QSVSSSY	1123	GAS	QQYGSSSIT	1124								
	146	IGHV4-39*01	IGHD6-13*01	IGHJ4*02	GGSIISYTYY	1125	LYYTGIT	1126	ARLLGIAATGHFDS	1127								IGLV10-54*01	IGLJ3*02	SNNIDNQG	1128	RNN		STWDSSLSTWL	1129
	146	IGHV4-	IGHD3-10*01	IGHJ3*02	GGSISSISYY	1130	IYYSGTP	1131	TRPASGAHDYAS	1132	IGKV3-20*01	IGKJ5*01	QSVSTTY	1133	GAS	QQYGSSSTT	1134								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		39*01							RSYYPGLGAFGI																
	146	IGHV4-39*01	IGHD3-3*01	IGHJ3*02	GGSITSLSYW	1135	IYYSGTT	1136	ARPLLNPMTLYGVTPGIGPFEI	1137	IGKV3-20*01	IGKJ4*01	QSVSSKC	1138	GAS	QQHDNSLS	1139								
	146	IGHV4-39*01	IGHD6-6*01	IGHJ4*02	GDSMSRNSFY	1140	INYNGIT	1141	AAHRVSSSYPADY	1142	IGKV1-39*01	IGKJ1*01	QNIDDY	1143	AAS	QQSYNTPT	1144								
	146	IGHV4-39*01	IGHD3-3*01	IGHJ3*02	GGSISSLSYY	1145	IYYSGTA	1146	ARPLLNPSTIYGVTPGIGPFEM	1147	IGKV3D-15*01	IGKJ1*01	QSIRSN	1148	GAS	QQYINWPPWT	1149								
	146	IGHV4-4*02	IGHD3-16*02	IGHJ6*02	GYSVSTSNW	1150	IYHIGST	1151	ARGNYDYVWGSYRSDQGYGLDV	1152	IGKV1-39*01	IGKJ2*01	QSIDNY	1153	LAS	QRSYSTPYT	1154								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	49	IGHV4-4*07	IGHD6-13*01	IGHJ6*03	GASIRSHY	1155	VHSSGGT	1156	AREGGSSYYYYYMDV	1157								IGLV2-8*01	IGLJ2*01	SSDVGSYNY	1158	DVT		SSYAGINSYVI	1159
	13	IGHV4-59*01	IGHD2-2*01	IGHJ5*02	GGSISTYF	1160	IYYNGGT	1161	ARSKNQLLLFDP	1162	IGKV3-15*01	IGKJ4*01	QSVGSD	1163	GAS	QQYNDWPPLT	1164								
	13	IGHV4-59*01	IGHD4-23*01	IGHJ5*01	GDSIGTYF	1165	VYHTGGT	1166	ARSKNQLLLFEF	1167	IGKV1-33*01	IGKJ4*01	QDISNY	1168	DAS	QQYDNLPLT	1169								
	55	IGHV4-59*01	IGHD7-27*01	IGHJ3*01	GASISSNY	1170	MYSSGSV	1171	ARTNWAYDPFNV	1172	IGKV1-5*03	IGKJ1*01	QNINSW	1173	KAS	QQYYSYST	1174	IGLV1-36*01	IGLJ2*01	NNNIGRSA	1175	ED		SAWDFSLSVQV	1176
	60	IGHV4-59*01	IGHD2-15*01	IGHJ6*02	GGSISSYY	1177	IYDSGST	1178	ARDRGYCSGGSCLGGMDV	1179	IGKV1-5*03	IGKJ4*01	QSISRW	1180	KAS	QQYNSYFPLT	1181								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	60	IGHV4-59*01	IGHD2-8*02	IGHJ6*02	GGSISSGSY	1182	IYDSGNT	1183	VRDRGFCTGKSCLGGMDV	1184	IGKV1-5*03	IGKJ1*01	QSISSW	1185	KAS	QQYNSYRT	1186								
	60	IGHV4-59*01	IGHD2-8*02	IGHJ4*02	GGSISNYF	1187	VYSSGTT	1188	ARLRRRGLTGTDFDY	1189								IGLV1-44*01	IGLJ2*01	TSNIGDNN	1190	IN		AAWDDSLNGPNVV	1191
	69	IGHV4-59*01	IGHD3-22*01	IGHJ6*03	GGSIRSYY	1192	IYYSGST	1193	ARSYYYDSSGYRPSFYYYYMDV	1194								IGLV3-1*01	IGLJ2*01	KLGDKY	1195	QDT		QAWDSSVV	1196
	146	IGHV4-59*01	IGHD1-26*01	IGHJ6*02	GGSISGYY	1197	IYYSGTT	1198	ARGILGSTWYYYYGLDV	1199	IGKV1-39*01	IGKJ2*01	QSISSY	1200	ATS	HQSYSSPYT	1201								
	55	IGHV4-59	IGHD5-18*01	IGHJ4*02	GGSISNDY	1202	IHSKGDT	1203	ARHLYRYGYRNYFDY	1204	IGKV1-12*01	IGKJ4*01	QGISSG	1205	AAS	QQANSFPLT	1206								

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		*08																						
H020	55	IGHV4-59*08	IGHD5-18*01	IGHJ4*02	GGSISSNDY	1207	IHSKGDT	1208	ARHLYRYGYRNYFDY	1209	IGKV1-12*01	IGKJ4*01	QGISSG	1210	AAS	QQANSFPLT	1211								
	69	IGHV4-61*08	IGHD6-13*01	IGHJ3*02	GGSVRSTGYF	1212	IYTGGAT	1213	ARMTSFKQSGGWYRGRHDGFDI	1214	IGKV1-5*01	IGKJ2*01	QTIGTY	1215	EAS	QEYNSYSYT	1216								
	69	IGHV4-61*08	IGHD6-19*01	IGHJ3*02	RGSVSNGGYY	1217	VYYTGSS	1218	ARLTSYKQRGGWYRGRHDAFDI	1219	IGKV1-5*01	IGKJ2*01	QSISTL	1220	DGS	QEYSSYSYT	1221								
	9	IGHV5-51*01	IGHD3-22*01	IGHJ4*02	GYSFTSYW	1222	IQSGDYNT	1223	ARRARNVGNYGTSDFYPYFDH	1224								IGLV2-14*01	IGLJ3*02	SSDVGRYNY	1225	DVT		SSYISSNTLWV	1226
	60	IGHV5	IGHD1-	IGHJ3*02	GYTFASYW	1227	INPPNSDT	1228	ARRVSVTG	1229								IGLV2-	IGLJ	SSDVGGYNY	1230	EVN		SSYAGT	1231

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		-51*01	14*01						TDAFDI									8*01	2*01					NTFVV	
	60	IGHV5-51*01	IGHD1-14*01	IGHJ3*02	GYTFASYW	1232	INPPNSDT	1233	ARRRVSVTGTDAFDI	1234								IGLV2-8*01	IGLJ2*01	SSDVGGYNY	1235	EVN		SSYAGTNTFVV	1236
	69	IGHV5-51*01	IGHD1-1*01	IGHJ4*02	GDTFGNYW	1237	ILLSDSDT	1238	ARATPGNYYFDS	1239								IGLV2-14*01	IGLJ1*01	SSDVGAYNY	1240	DVT		SSYTDSSPNCV	1241
	99	IGHV5-51*01	IGHD2-2*01	IGHJ1*01	GYSFSNFW	1242	IYPGDSDT	1243	ARPSRSRDINKWYLSTSEYFHY	1244	IGKV3-20*01	IGKJ4*01	QSVSSRS	1245	GAS	QQYANSPLT	1246								
	9	IGHV6-1*01	IGHD1-1*01	IGHJ4*02	GDSVSNTAV	1247	TYYRSKWFN	1248	AVGHHWHFKY	1249								IGLV2-8*01	IGLJ1*01	SSDVGGYSH	1250	EVS		SSHAGSNYGV	1251
	9	IGHV6	IGHD1-	IGHJ4*02	GDSVSN	1252	TYYRSK	1253	AVGHH	1254								IGLV2-	IGLJ	SSDVGGYSH	1255	EVS		SSHAGS	1256

		HEAVY CHAIN									KAPPA LIGHT CHAIN							LAMBDA LIGHT CHAIN							
	DONOR ID	V	D	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	CDR3	SEQ ID NO:	V	J	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		IGHV-1*01	IGHD1*01		NTAV		WFN		WHFKY									8*01	1*01					NYGV	
	55	IGHV6-1*01	IGHD3-10*01	IGHJ4*02	GSSIFTNSAG	1257	TYYRSKWYN	1258	ARDTYYYTSASYYNVDY	1259	IGKV1-39*01	IGKJ5*01	ESIRSN	1260	AAS	QQSYRTPIT	1261								
	55	IGHV7-4-1*02	IGHD1-7*01	IGHJ4*02	GYTFTSYG	1262	INTDTGNP	1263	ARLGEYSWNSIGYFDY	1264								IGLV1-40*01	IGLJ2*01	SSNIGAGYD	1265	GNN		QSYDRSLILVV	1266
	99	IGHV7-4-1*02	IGHD3-10*01	IGHJ4*02	GYVFTNYA	1267	INTNTGNP	1268	ARSYAYGDF	1269	IGKV1-39*01	IGKJ1*01	QNIAIR	1270	EAS	QQSDTLPWT	1271								
	99	IGHV7-4-1*02	IGHD3-22*01	IGHJ4*02	GYTFSNYA	1272	INTNTGNP	1273	ARGARSYYDSSGYYSWSDY	1274	IGKV4-1*01	IGKJ1*01	QSVLYRSNNKNY	1275	WAS	QQYYNTLTWA	1276								

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

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
F1-HC	5'-ACAGGTGCCCACTCCCAGGTGCAG	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'-GTTCGGGGAAGTAGTCCTTGAC	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'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CCCAGGCGC	1305
F-H003-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAGATGCAGCTGCTGGAGTCTGG	1306
R-H003-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACAGTGACCAGGGTGC	1307
F-H003- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATATGCTGA CTCAGGCACCC	1308
F-H004-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAGATGCAACTGGTGGAGTCTGG	1309
R-H004-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGATGACCGTGGTCC	1310
F-H004- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1311
F-H005-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGCGTCTGGTGGAATCTGG	1312
R-H005-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCGGGGT	1313
F-H005- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1314
F-H006-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGCGTCTGGTGGAATCGGG	1315
R-H006-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCGGGATC	1316
F-H006- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC 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 TTTGATCTCCAACTTG GTCCCCTGG	1321
F-H008-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGCACCTATTGGAGTCTGGG	1322

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-H008-HC	5'-CCGATGGGCCCTTGGTCGACGC TGACGAGACGGTGACCCTGGTC	1323
F-H008- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1324
F-H009-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGATGAAGTTGGTGGAGTCTGGG	1325
R-H009-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCGTGGTC	1326
F-H009- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1327
F-H010-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGGTGGAGTCTG	1328
R-H010-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGGTT	1329
F-H010- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1330
F-H011-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTTCACTTGGCGGAGTCTGG	1331
R-H011-HC	5'-CCGATGGGCCCTTGGTCGACGC 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'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGGTTC	1336
F-H012- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1337
F-H013-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGGTGGAGTCTG	1338
R-H013-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGGCT	1339
F-H013- Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGCCACC	1340
F-H014-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTACAACTGATGGAGTCTGGG	1341

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-H014-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGGCT	1342
F-H014-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC TCCTATGTGCTGA CTCAGACACCC	1343
F-H015-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGGTGGAGTCTG	1344
R-H015-HC	5'-CCGATGGGCCCTTGGTCGACGC 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'-CCGATGGGCCCTTGGTCGACGC 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'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGGTTC	1353
F-H017-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC CAGTCTGCCCTGA CTCAGCCTG	1354
F-H018-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GAAGGACAGCTGGTGGAGTCTGG	1355
R-H018-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGGTTC	1356
F-H018-Lambda	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCC CAGTCTGTGTTGA CGCAGCCGC	1357
F-H019-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGGTGCTGCAGGAGTCG	1358
R-H019-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAAGAGACGGCGACCAGTGTCC	1359
F-H019-Kappa	5'- CTAGTAGCAACTGCAACCGGTGTACATTCT GACATCCAGATGA CCCAGTCTCCG	1360

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
R-H019-Kappa	5'-GAAGACAGATGGTGCAGCCACCGTACG TTTGATCTCCAGCTTGGTCCCCTG	1361
F-H020-HC	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT CAGGTGCAGCTGCAGGAGTCG	1362
R-H020-HC	5'-CCGATGGGCCCTTGGTCGACGC TGAGGAGACGGTGACCAGGTTTCC	1363
F-H020-Kappa	5'-CTAGTAGCAACTGCAACCGGTGTACATTCT GACATCCAGATGACCCAGTCTCCA	1364
R-H020-Kappa	5'-GAAGACAGATGGTGCAGCCACCGTACG TTTGAACTCCACCTTGGTCCCTCC	1365
R-Lambda	5'-GGCTTGAAGCTCCTCACTCGAGGGYGGGAACAGAGTG	1366
gBlock Synthesis for Alanine Mutations		
101Q	5'-ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCAAAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTATTGGTTCTTCTGGATTATGCAGGTATGTTGCCCGTTTGTCCTCTAATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACCTGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCATCCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCCTCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTCAGTGGTTCGTAGGG	1367
102G	5'-ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCAAAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTATTGGTTCTTCTGGATTATCAAGCAATGTTGCCCGTTTGTCCTCTAATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACCTGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCATCCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCCTCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTCAGTGGTTCGTAGGG	1368

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
103M	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTGCATTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1369
104L	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGGCACCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1370
105P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGGCAGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1371

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
106V	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGCATGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1372
108P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTGCACT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1373
109L	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTGC AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1374

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
110I	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AGCACCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1375
111P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTGCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1376
112G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGCATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1377

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
113S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGAGCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1378
114T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAGCAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1379
115T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAGCAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1380

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
116T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAGCAAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1381
117S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCGCAACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1382
118T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTGCAGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1383

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
119G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGCACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1384
120P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGAGCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1385
122K	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCGCAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1386

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
123T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAGCA TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1387
125T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCGCAACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1388
126T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGGCACCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1389

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
127P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTGCAGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1390
129Q	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTGCAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1391
130G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGCAAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1392

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
131N	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCGCATCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1393
132S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACGCAATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1394
133M	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTGCATTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1395

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
134F	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGGCACCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1396
135P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTGCATCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1397
136S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCGCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1398

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
140T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTGCAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1399
141K	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAGCACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1400
142P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAAGCAACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1401

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
143T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTGCAGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1402
144D	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGCAGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1403
145G	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGCAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1404

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
146N	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAGCATGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1405
148T	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCGCATGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1406
150I	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTGCACCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1407

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
151P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTGCAAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1408
152I	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCGC ACCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1409
153P	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CGCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1410

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
154S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCAGCATCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1411
155S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGGCATGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1412
156W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCGCAGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1413

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
158F	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTGCAGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1414
160K	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAGCATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1415
161Y	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAAGCACTATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1416

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
162L	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACGCATGGGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1417
163W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTAGCAGAGTGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1418
164E	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGCATGGGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1419

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
165W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGGCAGCC TCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1420
167S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC GCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1421
168V	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGCACGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1422

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
169R	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCGCATTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1423
170F	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTGCATCTTGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1424
171S	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCGCATGGCTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1425

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
172W	5'- ACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGA CTTCTCTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCA AAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTC CTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT TATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTAT TGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACC TGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTT GCTGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCAT CCCATCGTCCTGGGCTTTCGCAAAATACCTATGGGAGTGGGCC TCAGTCCGTTTCTCTGCACTCAGTTTACTAGTGCCATTTGTTC AGTGGTTCGTAGGG	1426
gBlock Synthesis for Germline Antibodies		
H006- HC_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTCAGGTGCAGCTGG TGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAG ACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGC ATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGG TGGCAGTTATATCATATGATGGAAGTAATAAATACTATGCAG ACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAA GAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGAC ACGGCTGTGTATTACTGTGCGAAAGATGCTTATCTTTCTGCAG CGAGAGGATACGGTATGGACGTCTGGGGCCAAGGGACCACGGT CACCGTCTCCTCAGCGTCGACCAAGGGCCCATCGG	1427
H006- Lambda_GL	5'- CTAGTAGCAACTGCAACCGGTTCCTGGGCCTCCTATGTGCTGA CTCAGCCACCCTCGGTGTCAGTGGCCCCAGGACAGACGGCCAG GATTACCTGTGGGGGAAACAACATTGGAAGTAAAAGTGTGCAC TGGTACCAGCAGAAGCCAGGCCAGGCCCCTGTGCTGGTCGTCT ATGATGATAGCGACCGGCCCTCAGGGATCCCTGAGCGATTCTC TGGCTCCAACTCTGGGAACACGGCCACCCTGACCATCAGCAGG GTCGAAGCCGGGGATGAGGCCGACTATTACTGTCAGGTGTGGG ATAGTAGTAGTGATCATGTGGTATTCGGCGGAGGGACCAAGCT GACCGTCCTAGGTCAGCCCAAGGCTGCCCCCTCGGTCACTCTGT TCCCACCCTCGAGTGAGGAGCTTCAAGCC	1428

Single-Cell Antibody Cloning Primers A2		SEQ ID NO:
H019- HC_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTCAGGTGCAGCTGC AGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTGGTGAT TACTACTGGAGTTGGATCCGCCAGCCCCCAGGGAAGGGCCTGG AGTGGATTGGGTACATCTATTACAGTGGGAGCACCTACTACAA CCCGTCCCTCAAGAGTCGAGTTACCATATCAGTAGACACGTCC AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACTGCCGCAG ACACGGCCGTGTATTACTGTGCCATCTACATGGATGAGGCCTG GGCTTTTGATATCTGGGGCCAAGGGACAATGGTCACCGTCTCT TCAGCGTCGACCAAGGGCCCATCGG	1429
H019- Kappa_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTGACATCCAGATGA CCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAA ATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGAT CTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCA GTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAG TTACAGTATTTCCTTATTCACTTTTGGCCAGGGGACCAAGCTG GAGATCAAACGTACGGTGGCTGCACCATCTGTCTTC	1430
H020- HC_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTCAGGTGCAGCTGC AGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACT GGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGAT TGGGTATATCTATTACAGTGGGAGCACCAACTACAACCCCTCC CTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAACC AGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCAGACACGGC CGTGTATTACTGTGCGAGACACCTTTATCGCTATGGTTATAGG AACTACTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCT CCTCAGCGTCGACCAAGGGCCCATCGG	1431
H020- Kappa_GL	5'- CTAGTAGCAACTGCAACCGGTGTACATTCTGACATCCAGATGA CCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGT CACCATCACTTGTCGGGCGAGTCAGGGTATTAGCAGCTGGTTA GCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA TCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTT CAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC AGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGG CTAACAGTTTCCCGCTCACTTTCGGCGGAGGGACCAAGGTGGA 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.

CLAIMS

What is claimed is:

1. A combination of isolated or recombinant antibodies or antigen binding fragments thereof,

the combination comprising H019 and H017,

wherein H019 comprises a heavy chain variable region that is IGHV4-30-4*01; a heavy chain diverse region that is IGHD2-2*03; a heavy chain joining region that is IGHJ3*02, a heavy chain CDR1 that is GGSITTGDYY (SEQ ID NO: 18), a heavy chain CDR2 that is IYYSGST (SEQ ID NO: 19), and a heavy chain CDR3 that is AIYMDEAWAFEI (SEQ ID NO: 1012); and a kappa light chain variable region that is IGKV1-39*01, a kappa light chain joining region that is IGKJ2*01, a light chain CDR1 that is QSVGNY (SEQ ID NO: 21), a light chain CDR2 that is AVS, and a light chain CDR3 that is QQSYTISLFT(SEQ ID NO: 22),

and wherein H017 comprises a heavy chain variable region that is IGHV3-74*01, a heavy chain diverse region that is IGHD3-10*01, a heavy chain joining region that is IGHJ4*02, a heavy chain CDR1 that is GFTFSNYW (SEQ ID NO: 13), a heavy chain CDR2 that is ISTDGSST (SEQ ID NO: 14), and a heavy chain CDR3 that is ARGSTYYFGSGSVDY (SEQ ID NO: 15); and a lambda light chain variable region that is IGLV2-14*01, a lambda light chain joining region that is IGLJ1*01, a light chain CDR1 that is SSDIGVYNY (SEQ ID NO: 16), a light chain CDR2 that is DVT, and a light chain CDR3 that is SSYRGSSTPYV (SEQ ID NO: 17).

2. The combination of claim 1, comprising at least 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;

optionally comprising the modification that increases in vivo half-life of the antibody; or

optionally comprising the modification that alters the ability of the antibody to bind to Fc receptors.

3. The combination of claim 1 that further comprises the H016 antibody,

wherein H016 comprises a heavy chain variable region that is IGHV3-48*02; a heavy chain diverse region that is IGHD3/OR15-3a*01; a heavy chain joining region that is IGHJ2*01, a heavy chain CDR1 that is GFTFPSHT (SEQ ID NO: 8), a heavy chain CDR2 that is ISTTSEAI (SEQ ID NO: 9), and a heavy chain CDR3 that is ASVGLDSKISGYWYFDL (SEQ ID NO: 10); and a kappa light chain variable region that is IGKV3-15*01, a kappa light chain joining region that is IGKJ4*01, a light chain CDR1 that is QSISSN (SEQ ID NO: 11), a light chain CDR2 that is RAS, and a light chain CDR3 that is QQYDHWPLT (SEQ ID NO: 12).

4. A pharmaceutical composition comprising the combination of any one of claims 1-3.

5. The pharmaceutical composition of claim 4, wherein the composition futher comprises the H016 antibody,

wherein H016 comprises a heavy chain variable region that is IGHV3-48*02; a heavy chain diverse region that is IGHD3/OR15-3a*01; a heavy chain joining region that is IGHJ2*01, a heavy chain CDR1 that is GFTFPSHT (SEQ ID NO: 8), a heavy chain CDR2 that is ISTTSEAI (SEQ ID NO: 9), and a heavy chain CDR3 that is ASVGLDSKISGYWYFDL (SEQ ID NO: 10); and a kappa light chain variable region that is IGKV3-15*01, a kappa light chain joining region that is IGKJ4*01, a light chain CDR1 that is QSISSN (SEQ ID NO: 11), a light chain CDR2 that is RAS, and a light chain CDR3 that is QQYDHWPLT (SEQ ID NO: 12).

6. The combination of any of claims 1-3 for use in a method for prophylaxis or therapy of a Hepatitis B virus infection, wherein an effective amount of the combination of any one of claims 1-3 is to be administered to an individual in need thereof, and wherein optionally the at least one antibody comprises at least one modification of the constant region.

7. The combination for use of claim 6, wherein the H016 antibody is to be further administered.

8. The combination for use of claim 6, wherein a combination of at least two of the antibodies comprising the H017 and H019 antibodies is to be administered to provide 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;

wherein, optionally, the combination of at least two of the antibodies further comprises the H016 antibody.

9. One or more recombinant expression vectors encoding the heavy chain and the light chain of any one of the antibodies or antigen binding fragments thereof of any one of claims 1–3.

10. Cells comprising one or more recombinant expression vectors of claim 9.

11. A method comprising culturing cells of claim 10 and separating antibodies from the cells.

12. A kit comprising one or more expression vectors encoding according to claim 9.

13. A method for detecting Hepatitis B virus comprising:

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.

14. 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 complex formed by the peptide and an antibody of any one of claims 1–3.