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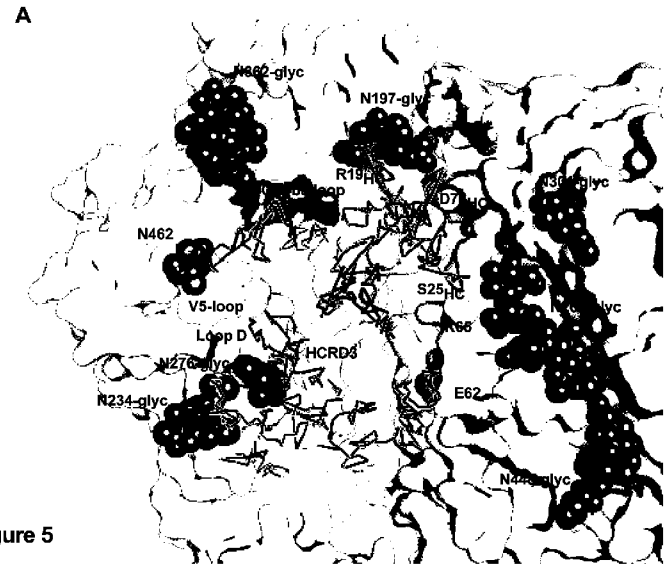


Figure 5

(57) Abstract: The present disclosure relates to anti-HIV Env antibodies and their use in the treatment or prevention of HIV/AIDS.

WO 2020/086446 A1

Anti-HIV Antibodies

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority of U.S. Provisional Application No. 62/748,610 filed October 22, 2018, which is incorporated herein in its entirety.

FIELD OF THE INVENTION

[0002] The field of the invention generally relates to anti-HIV Env antibodies and their use in the treatment or prevention of HIV/AIDS.

GOVERNMENT INTEREST

[0003] The invention was made with government support under Grant No. USAID Cooperative Agreement AID-OAA-A-11-00020 awarded by the USAID. The U.S. government has certain rights in the invention.

BACKGROUND

[0004] In 2015, there were approximately 2.1 million new human immunodeficiency virus (HIV) infections, over 36.7 million people living with HIV, and 1.1 million acquired immune deficiency syndrome (AIDS) related deaths. unaids.org/en/resources/fact-sheet (accessed on June 29, 2017) While great progress has been made in the treatment of HIV/AIDS, all individuals living with HIV will have to be treated with anti-retroviral therapy (ART) for the rest of their lives since drug therapy is unable to clear latent viral reservoirs that exist in resting CD4+ T cells at a frequency of about $1/10^6$ cells. *See*, Eriksson, S. 2013. *PLoS Pathog* 9:e1003174.

[0005] HIV isolates can be classified into different groups and clades based on genotype and geographic location. For example, the population episensus (i.e., epitope based consensus sequence) antigen is central to the B clade epidemic in the United States while the population episensus antigen is central to the HIV C clade epidemic in South Africa. Broadly neutralizing anti-Env antibodies, for example PGT-121 can neutralize more than one HIV isolate. U.S. patent No. 9464131.

[0006] Until a vaccine is discovered, many agree that a single product or approach will not completely halt new HIV infections. Accordingly, the use of HIV broadly neutralizing

antibodies (bnAbs) has the potential to complement existing prevention methods by addressing important shortfalls or gaps in current product profiles. To achieve the goal of making bnAbs affordable and feasible products for widespread use in HIV prevention efforts, maximizing the potency of current and future bnAb candidates represents a promising and inadequately explored opportunity.

[0007] Thus, there remains a need for the development of broadly neutralizing antibodies that can be used in the treatment and prevention of HIV.

BRIEF SUMMARY

[0008] In one aspect, provided herein are monoclonal antibodies that specifically bind to HIV Env. In some embodiments, an antibody described herein is a monoclonal antibody. In some embodiments, an antibody described herein is a human antibody. In some embodiments, an antibody described herein is a broadly neutralizing antibody. In some embodiments, an antibody described herein specifically binds the Env of at least one HIV isolate in the indicator virus panels of Figure 8 and 9. In some embodiments, an antibody described herein specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 8 and 9. In some embodiments, an antibody described herein is a VRC01 class antibody. In some embodiments, an antibody described herein binds Env at the CD4 receptor binding site (CD4bs) epitope region.

[0009] In one aspect, provided herein are pharmaceutical compositions comprising a monoclonal antibody that specifically binds to HIV Env described herein.

[0010] In one aspect, provided herein are isolated polynucleotides encoding a monoclonal antibody that specifically binds to HIV Env described herein.

[0011] In one aspect, provided herein are methods of producing a monoclonal antibody that specifically binds to HIV Env described herein.

[0012] In one aspect, provided herein are methods of neutralizing an HIV virus, comprising contacting the virus with a monoclonal antibody that specifically binds to HIV Env described herein.

[0013] In one aspect, provided herein are methods of reducing the likelihood of HIV infection in a subject exposed to HIV comprising administering to the subject a monoclonal antibody that specifically binds to HIV Env described herein.

[0014] In one aspect, provided herein are methods of treating HIV/AIDS comprising administering to a subject in need thereof a monoclonal antibody that specifically binds to HIV Env described herein.

[0015] In one aspect, provided herein are methods of producing an engineered variant of a monoclonal antibody that specifically binds to HIV Env described herein.

[0016] In some embodiments, the disclosure provides:

[1.] An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[2.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[3.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-71I1a, or PCIN63-71L;

[4.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37-54;

[5.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37, 39, 40, 42-48, or 50-53;

[6.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 44 or 47;

[7.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[8.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[9.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[10.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[11.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[12.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH

CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[13.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[14.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[15.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-71I1a, or PCIN63-71L;

[16.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 1-18;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 19-36; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37-54;

[17.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 1, 3, 4, 6-12, or 14-17;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 19, 21, 22, 24-30, or 32-35; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37, 39, 40, 42-48, or 50-53;

[18.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 8 or 11;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 26 or 29; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 44 or 47;

[19.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[20.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[21.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[22.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[23.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1, 3, 4, 6-12, or 14-17 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19, 21, 22, 24-30, or 32-35 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[24.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 8 or 11 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 26 or 29 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[25.] An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[26.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[27.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L;

[28.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54;

[29.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1, 3, 4, 6-12, or 14-17;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19, 21, 22, 24-30, or 32-35; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53;

[30.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 8 or 11;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 26 or 29; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47;

[31.] the isolated monoclonal antibody of any one of [1] to [30] comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62;

[32.] the isolated monoclonal antibody of any one of [1] to [30] comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62;

[33.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[34.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[35.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-71I1a, or PCIN63-71L;

[36.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[37.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[38.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[39.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[40.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[41.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-71I1a, or PCIN63-71L;

[42.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 55-72;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 73-90; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 91-108;

[43.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 55, 57, 58, 60-66, or 68-71;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 73, 75, 76, 78-84, or 86-89; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 91, 93, 94, 96-102, or 104-107;

[44.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 62 or 65;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 80 or 83; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 98 or 101;

[45.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[46.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55, 57, 58, 60-66, or 68-71 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73, 75, 76, 78-84, or 86-89 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91, 93, 94, 96-102, or 104-107 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[47.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 62 or 65 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 80 or 83 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 98 or 101 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

[48.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108;

[49.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55, 57, 58, 60-66, or 68-71;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73, 75, 76, 78-84, or 86-89; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91, 93, 94, 96-102, or 104-107;

[50.] the isolated monoclonal antibody of any one of [1] to [32], wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 62 or 65;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 80 or 83; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 98 or 101;

[51.] the isolated monoclonal antibody of any one of [33] to [50] comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[52.] the isolated monoclonal antibody of any one of [33] to [50] comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[53.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively;

[54.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively;

[55.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-71I1a, or PCIN63-71L VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively;

[56.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of

(a) SEQ ID NO: 1, 19, 37, 55, 73, and 91, respectively;

(b) SEQ ID NO: 2, 20, 38, 56, 74, and 92, respectively;

(c) SEQ ID NO: 3, 21, 39, 57, 75, and 93, respectively;

(d) SEQ ID NO: 4, 22, 40, 58, 76, and 94, respectively;

(e) SEQ ID NO: 5, 23, 41, 59, 77, and 95, respectively;

(f) SEQ ID NO: 6, 24, 42, 60, 78, and 96, respectively;

(g) SEQ ID NO: 7, 25, 43, 61, 79, and 97, respectively;

(h) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively;

(i) SEQ ID NO: 9, 27, 45, 63, 81, and 99, respectively;

(j) SEQ ID NO: 10, 28, 46, 64, 82, and 100, respectively;

(k) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively;

(l) SEQ ID NO: 12, 30, 48, 66, 84, and 102, respectively;

(m) SEQ ID NO: 13, 31, 49, 67, 85, and 103, respectively;

(n) SEQ ID NO: 14, 32, 50, 68, 86, and 104, respectively;

(o) SEQ ID NO: 15, 33, 51, 69, 87, and 105, respectively;

(p) SEQ ID NO: 16, 34, 52, 70, 88, and 106, respectively;

(q) SEQ ID NO: 17, 35, 53, 71, 89, and 107, respectively; or

(r) SEQ ID NO: 18, 36, 54, 72, 90, and 108, respectively;

[57.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of

(a) SEQ ID NO: 1, 19, 37, 55, 73, and 91, respectively;

(b) SEQ ID NO: 3, 21, 39, 57, 75, and 93, respectively;

(c) SEQ ID NO: 4, 22, 40, 58, 76, and 94, respectively;

(d) SEQ ID NO: 6, 24, 42, 60, 78, and 96, respectively;

(e) SEQ ID NO: 7, 25, 43, 61, 79, and 97, respectively;

(f) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively;

(g) SEQ ID NO: 9, 27, 45, 63, 81, and 99, respectively;

(h) SEQ ID NO: 10, 28, 46, 64, 82, and 100, respectively;

(i) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively;

(j) SEQ ID NO: 12, 30, 48, 66, 84, and 102, respectively;

(k) SEQ ID NO: 14, 32, 50, 68, 86, and 104, respectively;

(l) SEQ ID NO: 15, 33, 51, 69, 87, and 105, respectively;

(m) SEQ ID NO: 16, 34, 52, 70, 88, and 106, respectively; or

(n) SEQ ID NO: 17, 35, 53, 71, 89, and 107, respectively;

[58.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of

(a) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively; or

(b) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively;

[59.] the isolated monoclonal antibody of any one of [53] to [58], wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises one or more of

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[60.] the isolated monoclonal antibody of any one of [53] to [58], wherein the VH comprises the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56, and the VL comprises the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34, and the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70;

[61.] the isolated monoclonal antibody of any one of [53] to [58], wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[62.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[63.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[64.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-71I1a, or PCIN63-71L;

[65.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235-252;

[66.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235, 237, 238, 240-246, or 248-251;

[67.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH

comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 242 or245;

[68.] the isolated monoclonal antibody of any one of [62] to [67], wherein the VH CDR1, VH CDR2, and VH CDR3, comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH CDR1, VH CDR2, and VH CDR3, respectively;

[69.] the isolated monoclonal antibody of any one of [62] to [67], wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54;

[70.] the isolated monoclonal antibody of any one of [62] to [69], wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62;

[71.] the isolated monoclonal antibody of any one of [60] to [68], wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62;

[72.] the isolated monoclonal antibody of any one of [62] to [71], wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L,

PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[73.] the isolated monoclonal antibody of any one of [62] to [71], wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[74.] the isolated monoclonal antibody of any one of [62] to [71], wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-71I1a, or PCIN63-71L;

[75.] the isolated monoclonal antibody of any one of [62] to [71], wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253-270;

[76.] the isolated monoclonal antibody of any one of [62] to [71], wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253, 255, 256, 258-264, or 266-269;

[77.] the isolated monoclonal antibody of any one of [62] to [71], wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 260 or 263;

[78.] the isolated monoclonal antibody of any one of [72] to [77], wherein the VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VL CDR1, VL CDR2, and VL CDR3, respectively;

[79.] the isolated monoclonal antibody of any one of [72] to [77], wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108.;

[80.] the isolated monoclonal antibody of any one of [72] to [79], wherein the VL comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[81.] the isolated monoclonal antibody of any one of [72] to [79], wherein the VL comprises

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[82.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH and VL, respectively;

[83.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-

71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C VH and VL, respectively;

[84.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-71I1a, or PCIN63-71L VH and VL, respectively;

[85.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235-252 and the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253-270;

[86.] an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to

(a) SEQ ID NO: 235 and 253, respectively;

(b) SEQ ID NO: 236 and 254, respectively;

(c) SEQ ID NO: 237 and 255, respectively;

(d) SEQ ID NO: 238 and 256, respectively;

(e) SEQ ID NO: 239 and 257, respectively;

(f) SEQ ID NO: 240 and 258, respectively;

(g) SEQ ID NO: 241 and 259, respectively;

(h) SEQ ID NO: 242 and 260, respectively;

(i) SEQ ID NO: 243 and 261, respectively;

(j) SEQ ID NO: 244 and 262, respectively;

(k) SEQ ID NO: 245 and 263, respectively;

(l) SEQ ID NO: 246 and 264, respectively;

(m) SEQ ID NO: 247 and 265, respectively;

(n) SEQ ID NO: 248 and 266, respectively;

(o) SEQ ID NO: 249 and 267, respectively;

(p) SEQ ID NO: 250 and 268, respectively;

(q) SEQ ID NO: 251 and 269, respectively; or

(r) SEQ ID NO: 252 and 270, respectively;

[87.] the isolated monoclonal antibody of any one of [82] to [86], wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively;

[88.] the isolated monoclonal antibody of any one of [82] to [86], wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36;

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54,

(d) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72;

(e) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90; and

(f) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108.;

[89.] the isolated monoclonal antibody of any one of [82] to [88], wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises one or more of

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[90.] the isolated monoclonal antibody of any one of [82] to [88], wherein the VH comprises the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56, and the VL comprises the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34, and the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70;

[91.] the isolated monoclonal antibody of any one of [82] to [88], wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97;

[92.] the isolated antibody of any one of [1] to [91], wherein the antibody is not PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

[93.] the isolated antibody of any one of [1] to [91], wherein the antibody is not PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

[94.] the isolated antibody of any one of [1] to [91], wherein the antibody is not PCIN63-71I1a, or PCIN63-71L;

[95.] the monoclonal antibody of any one of [1] to [94, further comprising a heavy and/or light chain constant region;

[96.] the monoclonal antibody of any one of [1] to [94], further comprising a human heavy and/or light chain constant region;

[97.] the antibody of [95] or [96], wherein the heavy chain constant region is selected from the group consisting of a human immunoglobulin IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2 constant region;

[98.] the antibody of any one of [95] to [97], wherein the heavy chain constant region comprises a native amino acid sequence;

[99.] the antibody of any one of [95] to [97], wherein the heavy chain constant region comprises a variant amino acid sequence;

[100.] the isolated monoclonal antibody of any one of [1] to [99], wherein the antibody is a recombinant antibody, a chimeric antibody, a human antibody, an antibody fragment, a bispecific antibody, or a trispecific antibody;

[101.] the isolated monoclonal antibody of [100], wherein the antibody fragment comprises a single-chain Fv (scFv), F(ab) fragment, F(ab')2 fragment, or an isolated VH domain;

[102.] the monoclonal antibody of any one of [1] to [101], wherein the antibody is capable of neutralizing at least two cross-clade isolates of HIV;

[103.] the monoclonal antibody of any one of [1] to [101], wherein the antibody is capable of neutralizing at least one clade A HIV isolate, at least one clade B HIV isolate, and at least one clade C HIV isolate;

[104.] the antibody of [102], wherein the antibody is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 8;

[105.] the antibody of [102], wherein the antibody is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 9;

[106.] the antibody of [104] or [105], wherein the antibody is capable of neutralizing the cross-clade HIV isolates with a median IC50 equal to or less than about 1 microg/ml, about 0.8 microg/ml, 0.5 microg/ml, or 0.3 microg/ml;

[107.] the antibody of [104] or [105], wherein the antibody is capable of neutralizing the cross-clade HIV isolates with a mean IC50 equal to or less than about 1 microg/ml, about 0.8 microg/ml, 0.5 microg/ml, or 0.3 microg/ml;

[108.] a pharmaceutical composition comprising the monoclonal antibody of any one of [1] to [101] and a pharmaceutically acceptable excipient;

[109.] the pharmaceutical composition of [108], which is lyophilized;

[110.] an isolated polynucleotide encoding the heavy chain variable region or heavy chain of the antibody of any one of [1] to [101];

[111.] an isolated polynucleotide encoding the light chain variable region or light chain of the antibody of any one of [1] to [101];

[112.] an isolated polynucleotide encoding the heavy chain variable region or heavy chain of the antibody of any one of [1] to [101] and the light chain variable region or light chain of the antibody of any one of [1] to [101];

[113.] the isolated polynucleotide of [110] or [112], wherein the polynucleotide encodes a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 235-252;

[114.] the isolated polynucleotide of [111] or [112], wherein the polynucleotide encodes a light chain variable region comprising the amino acid sequence of SEQ ID NO: 253-270;

[115.] the isolated polynucleotide of any one of [110] to [114], which is a DNA;

[116.] the isolated polynucleotide of any one of [110] to [114], which is an mRNA;

[117.] the isolated polynucleotide of [116], wherein the mRNA comprises a modified nucleotide;

[118.] an isolated vector comprising the polynucleotide of any one of [110] to [114];

[119.] the isolated vector of [117], wherein the vector is a viral vector;

[120.] a recombinant virus comprising the polynucleotide of any one of [110] to [114];

[121.] the recombinant virus of [119], which is a recombinant adeno-associated virus (AAV);

[122.] a host cell comprising the polynucleotide of any one of [110] to [115], the vector of [118] or [119], or a first vector comprising the nucleic acid of [110] and a second vector comprising the nucleic acid of [111];

[123.] the host cell of [122], which is selected from the group consisting of E. coli, Pseudomonas, Bacillus, Streptomyces, yeast, CHO, YB/20, NS0, PER-C6, HEK-293T, NIH-3T3, HeLa, BHK, Hep G2, SP2/0, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, BMT10 cell, plant cell, insect cell, and human cell in tissue culture;

[124.] a method of producing an antibody that binds to HIV comprising culturing the host cell of [123] so that the polynucleotide is expressed and the antibody is produced;

[125.] an isolated antibody that specifically binds to HIV Env and is encoded by the isolated polynucleotide of any one of [110] to [117];

[126.] a method of neutralizing an HIV virus comprising contacting the virus with a sufficient amount of the antibody of any one of [1] to [101], or the pharmaceutical composition of [108];

[127.] a method of reducing the likelihood of HIV infection in a subject exposed to HIV comprising administering to the subject a therapeutically sufficient amount of the antibody of any one of [1] to [101], or of the pharmaceutical composition of [108];

[128.] a method of reducing the risk of a subject becoming infected with HIV comprising administering to the subject in need thereof an effective amount of the antibody of any one of [1] to [101], or the pharmaceutical composition of [108];

[129.] a method for passively immunizing a subject comprising administering to the subject in need thereof an effective amount of the antibody of any one of [1] to [101], or the pharmaceutical composition of [108];

[130.] a method of preventing HIV infection comprising administering to a subject in need thereof a therapeutically sufficient amount of the antibody of any one of [1] to [101], the pharmaceutical composition of [108], the isolated polynucleotide of any one of [110] to [117], or the recombinant virus of any [120] or [121];

[131.] a method of treating HIV/AIDS comprising administering to a subject in need thereof a therapeutically sufficient amount of the antibody of any one of [1] to [101], the pharmaceutical composition of [108], the isolated polynucleotide of any one of [110] to [117], or the recombinant virus of any [120] or [121];

[132.] the method of any one of [127] to [131], wherein the administering to the subject is by at least one mode selected from oral, parenteral, subcutaneous, intramuscular, intravenous, vaginal, rectal, buccal, sublingual, and transdermal;

[133.] the method of any one of [127] to [132], further comprising administering at least one additional therapeutic agent;

[134.] the method of [133], wherein the additional therapeutic agent is an antiretroviral agent or a second antibody;

[135.] the method of [134], wherein the additional therapeutic agent comprises a broadly neutralizing antibody;

[136.] the method of [134], wherein the additional therapeutic agent comprises two broadly neutralizing antibodies;

[137.] the method of [134], wherein the additional therapeutic agent comprises three broadly neutralizing antibodies;

[138.] a method for detecting HIV in a sample comprising contacting the sample with the antibody of any one of [1] to [101];

[139.] a method of purifying HIV from a sample comprising contacting the sample with the antibody of any one of [1] to [101];

[140.] a kit comprising the antibody of any one of [1] to [101], or the pharmaceutical composition of [108] and a) a detection reagent, b) an HIV antigen, c) a notice that reflects approval for use or sale for human administration, or d) any combination thereof;

[141.] the antibody of any one of [1] to [101], wherein the antibody specifically binds the Env of at least one HIV isolate in the indicator virus panel of Figure 8;

[142.] the antibody of any one of [1] to [101], wherein the antibody specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 8;

[143.] the antibody of any one of [1] to [101], wherein the antibody specifically binds the Env of at least one HIV isolate in the indicator virus panel of Figure 9;

[144.] the antibody of any one of [1] to [101], wherein the antibody specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 9;

[145.] a method of producing an engineered variant of a PCIN63 antibody comprising

(a) substituting one or more amino acid residues of the VH; and/or substituting one or more amino acid residues of the VL to create an engineered variant antibody, and

(b) and producing the engineered variant antibody,

wherein the PCIN63 antibody is

i. PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

ii. PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; or PCIN63-71I1a, or PCIN63-71L.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] **Figure 1.** PCIN63 antibodies define a minimally mutated VRC01-like bnAb lineage. (A) Longitudinal plasma samples from donor PC063 were tested for neutralization against heterologous pseudoviruses. The percent of viruses neutralized (>50% inhibition of infectivity at the lowest plasma dilution, 1:50) from a cross-clade (A, B, C) 37-virus panel is shown as shaded blue bars. The blue line represents the neutralization score calculated for each sample and taking into account breadth and potency (see Landais et al, 2016). The evolution of the viral load (red circles) in the plasma is also plotted. The time points at which PCIN63 antibodies were isolated are indicated by antibody symbols. See also Figure 6A, 6B. (B) Comparison of CD4bs Abs genetic characteristics. Antibodies are listed and color-coded by classes as defined in Zhou et al., 2016: PCIN63 (Black), DRVI07 (Violet), VRC01-class bnAbs (Blue), HCDR3 dominated bnAbs (Red), VH1-46+ bnAbs (Brown). Top left inlet: Heavy (VH) and light chains (VL) putative V-genes nucleotide variation from IMGT database reference (% SHM). Top right inlet: light chain V-gene usage. Bottom left inlet: length the HCDR3s, with mean ± SEM showed as lines. Bottom right inlet: Logogram of the LCDR3 amino acid sequences for PCIN63 and other VRC01-class Abs. Residues common or unique to each category are colored in blue and red, respectively. See also Figure 6C, 6D, 7, 13. (C) Comparison of PCIN63-71b, min12A21, 12A21, VRC01 and minVRC01 Abs neutralization breadth and potency on a 120-virus panel (Seaman et al, 2010). See also Figure 8 and 9. (D) Comparison of the PCIN63 Ab lineage (Blue) development kinetics with other bnAbs lineages isolated as reported in original publications. Time to maturation (Mat.) is defined as the time between first detection of the lineage in the periphery (Init.) and peak neutralization breadth in plasma. See also Figure 10A.

[0018] **Figure 2.** SHM Motifs are selected sequentially in the PCIN63 bnAb lineage. PC063 IgG libraries prepared from total PBMCs were amplified with IgG-specific primers for all human VH gene families. See Figure 10A-C. (A) Delineation of PCIN63 Ab SHM Motifs (gray) on heavy (HC) and light (KC) chains V-segments amino-acid sequences of mature VRC01, minVRC01, 12A21 and min12A21 and respective germlines. Residues varying from VH1-2 and VL putative germlines are indicated by a single letter code. (B, C) Longitudinal frequency of PCIN63 Ab lineage NGS sequences containing 1-5 Motif residues mutated from germline to any of the amino-acid found in the isolated mature PCIN63 Abs. (B) Left Panel: Motifs containing the same number of SHMs but varying in aa sequence are separated by white lines within each shade of the Motif-coded color. Motifs are arranged from top to bottom based on the extent of maturation, i.e. the number of intermediate versions, necessary to achieve fixation of the mature sequence found

in the PCIN63 mAbs. Right panel: Logogram representing the distribution of amino-acids at each position of the Motif for the isolated mature PCIN63 Abs, the entire PCIN63 lineage NGS sequences and random Ab sequences from the same NGS dataset. Germline residues are indicated in black while mutated amino-acids found in the isolated matured PCIN63 Abs are colored using the pattern defined in (A). (C) Motifs are grouped based on time between emergence of first mutation to fully mutated sequence (thick line), as found in the PCIN63 mAbs.

[0019] **Figure 3**. Role of SHM Motifs in acquisition of neutralization by PCIN63 lineage. PCIN63-71I HC and KC SHM Motifs were either introduced into the PCIN63-UCA-HC and PCIN63-UCA-KC1 (mut) (A) or reverted to germline (rev) (B). SHM Motifs are color-coded as in Figure 2 and their position is indicated with diagrams. Mutated constructs were paired with WT PCIN63-UCA (left) or PCIN63-71 (right) HC or LC. The chimeric Abs were tested for neutralization of the indicated WT and N276A autologous Env clones sensitive to neutralization by PCIN63-71I. See also Figure 10D, 10E, 11.

[0020] **Figure 4.** N276-glycan dependent neutralization of PCIN63 Abs and other VRC01-like Abs. (A) Fold decrease in neutralization IC_{50} of PCIN63 Abs (Lower panel) and the listed VRC01-class Abs (Upper panel) for N276A mutant of the indicated pseudotyped Env strains produced in 293-T or 293-S (GtnI-/1) cells compared to WT. The geomean with standard deviation are indicated. Relevant features of the selected Env strains are indicated above. Symbols are color-coded according to the permissive (blue) versus obstructive (red) potential regarding access to the CD4bs. See also Figure 12. (B) Logogram of the PCIN63 SHM Motifs amino acid sequences for PCIN63 Abs segregated according to their sensitivity to N276-glycan removal (A) and compared to corresponding sequences of 12A12, 12A21 and min12A21 Abs. Residues common to 12A21 and PCIN63 N276-glycan tolerant Abs are colored in red. Residues shared between 12A21 and all PCIN63 Abs are colored in blue. SHM Motifs are color-coded as in Figure 2 and their position is indicated with diagrams. See also Figure 7, 13.

[0021] **Figure 5.** Modelling PCIN63 maturation. (A) *In silico* modelling of 12A21 bound to BG505 SOSIP.664 using the published structures of 12A21 bound to gp120 (PDB ID: 4JPW) (Klein et al, 2013) and glycosylated BG505 SOSIP.664 bound to 35O22 and PGT122 (PDB ID: 6DE7) (Zhang et al, 2018). Two of the three Env protomers are displayed in shades of gray as transparent surfaces highlighting the CD4bs loop (red), loop D (orange), the V5 loop (yellow) on one protomer and other putative contact residues (cyan) on the second protomer. Glycans surrounding the CD4bs protruding from both protomers are shown as brown spheres and labeled. 12A21 HC and LC residues corresponding to PCIN63 SHM Motifs are shown as ribbon and color-

coded as defined in Figure 2A and represented in a diagram (B). Additional Motifs in HFR1 (aa19-25 – pink) and HRF3 (aa71-76 – brown) are also highlighted. (B) PC63 infection timeline summary showing the evolution of viral load (red), serum neutralization breadth and potency (score, blue), and overall PCIN63 Ab lineage frequency in the periphery (green line). PCIN63 Ab lineage maturation is further detailed above for each SHM Motif as shaded bars from unmutated (white) to fully mature (full Motif-specific color) according to the kinetic analysis detailed in Figure 2. Putative functional impact of SHM Motifs maturation regarding contact with Env (gray filled boxes) or internal structural stabilization (open boxes) inferred from the model in (A) are indicated color-coded accordingly.

[0022] **Figure 6.** Isolation of CD4bs-specific antibodies in participant PC063. (A) Neutralization of HIV-1 pseudoviruses by titrated amount of PC063 month-66 (M66) untreated plasma or after adsorption on BSA- or rgp140-coated beads. (B) Fluorescence Activated Cell Sorting (FACS) cell plots highlighting cell selection strategy for CD4bs specific B-cell isolation from PC063. Pie charts detail the distribution of VH-gene IMGT assignment of IgG amplicons generated from rgp140 WT+D368R- and rgp140 WT+D368R+ single sorted cells in (Quadrant #1, Q1, left) and (Quadrant #2, Q2, right). (C) Statistics for the PCIN63 heavy chain and light chain sequences obtained from the VH1-2+ single B-cell isolated in (B). The percent of somatic hyper mutations at the nucleotide (nt) and amino-acid (aa) levels compared to the IMGT database germline gene sequences and NGS-identified unmutated common ancestor (UCA) (see Figure 10D), were calculated for V and J heavy chain (VH+JH) and light chain (VK+JK) segments. The CDR3 definitions are based on IMGT database guidelines. (D) Logogram of the HCDR3 amino acid sequences for PCIN63 and VRC01-class Abs. (E) Frequency of 5-amino acid LCDR3 immunoglobulin sequences in the naïve repertoire of PC63 (from Zambia) at different time points compared to HIV negative individuals from the United States (Southern California) and sub-Saharan Africa (Protocol C clinical research site in Zambia, Uganda, Rwanda and South Africa).

[0023] **Figure 7.** PCIN63 mAbs heavy chain and light chain amino acid alignments with putative germline genes. PCIN63 mAbs HC (top) and LC (bottom) amino-acid sequences are aligned to the IMGT database V_H1-2*02, D_H6-13, J_H5*02, Vκ1-5*03 and Jκ1*01 sequences and compared to alignment with VRC01, minVRC01, 12A21 and min12A21 amino-acid sequences. Identical residues are marked as a dot and somatically mutated residues are specified using one-letter coding. Deletions are marked by a ~ symbol. CDR regions are indicated.

[0024] **Figure 8.** Neutralization breadth and potency in the PCIN63 lineage on a medium cross-clade pseudovirus panel. (A) The neutralization IC_{50}s (Ab concentration in μg/mL allowing

50% loss of infectivity) of PCIN63 mAbs, PC063-M66 plasma sample and other VR01-class bnAbs on a medium cross-clade pseudotyped virus panel (N=40) are tabulated and color-coded as indicated. PCIN63 Abs are organized from least to most mutated. (B) Neutralization breadth (% virus neutralized for the indicated IC_{50} threshold) and potency (GeoMean IC_{50} in μg/mL) are tabulated and color-coded as indicated

[0025] **Figure 9.** Neutralization breadth and potency in the PCIN63 lineage on a large cross-clade pseudovirus panel. (A) The neutralization of PCIN63 mAbs, PC063-M66 plasma sample and other VRC01-class bnAbs was evaluated on a large cross-clade pseudotyped virus panel (N=120) (Seaman et al., 2010). Viruses are organized by subtypes while Abs are organized by level of somatic hypermutation from least to most mature. (B) Neutralization breadth (% virus neutralized at 10μg/mL) and potency (GeoMean IC_{50} in μg/mL) are tabulated and color-coded as indicated. (C) Neutralization breadth (% virus neutralized) of the indicated Abs is plotted as a function of neutralization IC_{50} in μg/mL

[0026] **Figure 10.** Emergence and maturation of the PCIN63 bnAb lineage (A) Comparison of the PCIN63 Ab lineage (blue) development kinetics with other bnAbs lineages isolated from two Protocol C participants (PC076: high-mannose patch targeting PCDN lineage in orange; PC064: V2-apex targeting PCT64 lineage in green) as detected in the periphery. Lineage sequences frequencies are plotted as a percentage of total lineage sequences from all time points. Plasma neutralization score (see (Landais et al., 2016)) from a heterologous medium panel is plotted as a dashed line. Related to Figure 1D. (B) Somatic hypermutation frequency was calculated for each timepoint as divergence (number of amino acid changes compared to LMCA). Data are presented as whisker plot showing mean, 95% upper and lower quartiles, standard deviation and outliers. (C) Longitudinal phylogeny of PCIN63 heavy chain and light chain NGS sequences (colored by time-point, mpi). (D) Identification of PCIN63 lineage precursor sequences. The CDR3 of putative PCIN63-UCA NGS sequences (100% identity to PCIN63 Abs HC and LC germline V+J genes) are aligned with IMGT V_H1-2*02, D_H6*13, J_H5*03, Vκ1-5*03 and Jκ1*01 germline genes sequences. The N regions of the junctions are indicated. For putative PCIN63-UCA-KCs, the number of sequences found in the NGS dataset and the corresponding CDRL3 amino-acid sequences are also indicated. Residues previously described as important for binding to the HIV Env CD4bs are colored in red. (E) Binding affinity of PCIN63 mature and putative UCA Abs and VRC01-class inferred germline (VRC01, VRC03, VRC07, 12A12, 12A21, 3BNC60, 3BNC117, VRC-PG04, VRC-CH31) and mature Abs (minVRC01, VRC01, VRC03, VRC07, VRC23,

VRC27, 12A12, min12A21, 12A21, 3BNC117, VRC-PG19, VRC-CH31, VRC-N6) for the indicated previously described VH1-2 germline targeting immunogens, as measured by SPR.

[0027] **Figure 11.** PCIN63 Ab lineage elicitation by the autologous virus donor PC063. (A) Phylogeny of PC063 HIV subtype C *env*, estimated by maximum likelihood from full-length *env* PacBio high-quality consensus sequences (HQCSs) obtained by next-generation sequencing of longitudinal plasma samples (with bubbles representing sample proportion), and color-coded by samples date. (B) PCIN63 UCA sequences were inferred from the NGS dataset (see Figure 10D). All possible corresponding PCIN63-UCA Abs were expressed and tested for neutralization (upper panel) of representative pseudotyped autologous Env clones, selected from all time points prior to detection of the PCIN63 lineage in the periphery, and binding to captured gp120 from corresponding pseudovirus stock lysates (lower left panel) or recombinantly expressed (lower right panel). (C) PCIN63-71I-KC SHM Motifs were either introduced into the PCIN63-UCA-KC1 (top panels) or reverted to germline (bottom panels), individually or in combination. Motifs are color-coded and their sequence position on the LC is indicated with a diagram. Motif#4 variants details are also indicated. Mutated constructs were paired with WT PCIN63-UCA (left) or PCIN63-71 (right) HC. The chimeric Abs were tested for neutralization of the indicated WT and N276A autologous Env clones sensitive to neutralization by PCIN63-71I. Related to Figure 3.

[0028] **Figure 12.** Effect of CD4bs N-glycan removal on neutralization by PCIN63 Abs. PCIN63 Abs, VRC01-class, PGT151 and PGT121 Abs were tested for neutralizing activity against the indicated pseudoviruses carrying the indicated CD4bs N-glycan single mutation. The fold decrease or increase in neutralization IC_{50} is plotted. The gray bars indicate the range of variation for the PCIN63 Abs only (upper panel) or VRC01-class reference Abs (lower panel).

[0029] **Figure 13.** VRC01-class Abs sequence alignment. (A) VRC01-class bnAbs heavy chain and light chain amino acid alignments with putative germline V-genes. CDR3 Sequences are highlighted in grey. Motifs (as defined in Figure 2) are highlighted in the corresponding colors.

DETAILED DESCRIPTION

[0030] In one aspect, provided herein are anti-HIV Env antibodies generated from a HIV subtype C infected human patient and variants of the antibodies. In some embodiments, an antibody described herein has the hallmark VRC01-class features and demonstrates similar neutralization breath to the prototype VRC01 antibody. In another aspect, the present disclosure relates to nucleotide sequences encoding, compositions comprising, and kits comprising an antibody described herein. In another aspect, the present disclosure relates to methods of treatment and

prevention of HIV using an antibody described herein. In another aspect, the present disclosure relates to methods of diagnosing and monitoring of HIV infection using an antibody described herein.

I. Definitions

[0031] To facilitate an understanding of the present invention, a number of terms and phrases are defined below.

[0032] The terms "human immunodeficiency virus" or "HIV," as used herein, refer generally to a retrovirus that is the causative agent for acquired immunodeficiency syndrome (AIDS), variants thereof (e.g., simian acquired immunodeficiency syndrome, SAIDS), and diseases, conditions, or opportunistic infections associated with AIDS or its variants, and includes HIV-Type 1 (HIV-1) and HIV-Type 2 (HIV-2) of any clade or strain therein, related retroviruses (e.g., simian immunodeficiency virus (SIV)), and variants thereof (e.g., engineered retroviruses, e.g., chimeric HIV viruses, e.g., simian-human immunodeficiency viruses (SHIVs)). In some embodiments, an HIV virus is an HIV-Type -1 virus. Previous names for HIV include human T-lymphotropic virus-Ill (HTLV-III), lymphadenopathy-associated virus (LAV), and AIDS-associated retrovirus (ARV).

[0033] As used herein, the term "clade" refers to related human immunodeficiency viruses (HIVs) classified according to their degree of genetic similarity. There are currently four known groups of HIV-1 isolates: M, N, O, and P. Group M (major strains) viruses are responsible for the majority of the global HIV epidemic. The other three groups, i.e., N, O and P are quite uncommon and only occur in Cameroon, Gabon and Equatorial Guinea. In some embodiments, an HIV virus is a Group M HIV virus. Within group M there are known to be at least nine genetically distinct subtypes or clades of HIV-1: subtypes or clades A, B, C, D, F, G, H, J and K. Additionally, different subtypes can combine genetic material to form a hybrid virus, known as a 'circulating recombinant form' (CRFs). Subtype/clade B is the dominant HIV subtype in the Americas, Western Europe and Australasia. Subtype/clade C is very common in the high AIDS prevalence countries of Southern Africa, as well as in the horn of Africa and India. Just under half of all people living with HIV have subtype C. In certain exemplary embodiments, methods described herein can be used to treat a subject (e.g., a human) infected with HIV (e.g., HIV-1) or to block or prevent HIV (e.g., HIV-1) infection in subject (e.g., a human) at risk of HIV transmission. The HIV may be of two, three, four, five, six, seven, eight, nine, ten, or more clades and/or two or more groups of HIV.

[0034] Acquired immune deficiency syndrome ("AIDS") is a disease caused by the human immunodeficiency virus, or HIV.

[0035] As used herein, the term "envelope glycoprotein" or "Env" refers to the glycoprotein that is expressed on the surface of the envelope of HIV virions and the surface of the plasma membrane of HIV infected cells. "Envelope glycoprotein" or "Env" encompass, but are not limited to, native Env, an isoform of Env, or a recombinant variant of Env (e.g., SOSIP) derived from an HIV isolate. Env is the sole virally encoded gene product on the surface of the virus and, as such, is the only target of neutralizing antibodies. Env is a trimer of heterodimers composed of two non-covalently associated subunits: the receptor-binding gp120 and the fusion machinery-containing gp41. Each subunit is derived from a gp160 precursor glycoprotein following cleavage by cellular furins. HIV-1 gp120 binds the CD4 molecule on the surface of human target T cells to initiate the viral entry process, and following co-receptor engagement, fusion is mediated by gp41. gp140 env is the uncleaved ectodomain of gp160. In some embodiments, the Env is a clade A Env. In some embodiments, the Env is a clade B Env. In some embodiments, the Env is a clade C Env. In some embodiments, the Env is a clade A Env from the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, the Env is a clade B Env from the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, the Env is a clade C Env from the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, the Env is the Env of a virus from the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, the Env is a BG505, 92BR020, JR-FL, YU-2, or JR-CSF Env polypeptide. In some embodiments, the Env is a BG505 Env polypeptide. UniProtKB accession number Q2N0S5-1, Q2N0S6-1, and Q2N0S7-1 provide BG505 env gp160 polypeptide sequences. In some embodiments, the Env is a well-ordered Env trimer.

[0036] The term "well-ordered Env trimer" or "well-ordered trimer" as used herein refers to an envelope glycoprotein trimer comprising three cleaved gp140 polypeptides that closely mimics the quaternary structure of the Env ectodomain on the surface of the envelope of HIV or SIV virions and the surface of the plasma membrane of HIV or SIV infected cells. In some embodiments, the gp120 and gp41 ectodomain is linked by a covalent linkage, for example, a disulfide bond. In some embodiments, the gp140 polypeptide comprises one or more mutations to promote trimer formation. In some embodiments, the gp140 polypeptide comprises one or more mutations to promote disulfide formation. In some embodiments, the well-ordered trimer is an SOSIP gp140 trimer. Well-ordered SOSIP trimers have been disclosed in US Patent Appl. Pub. No. 2014/0212458, Sanders, R. W. *et al.*, *PLoS Pathog.* 9, e1003618 (2013) and Guenaga J., et al.,

Immunity 46(5):792-803.e3 (2017), each of which is incorporated by reference herein in its entirety. In some embodiments, a well ordered trimer is formed from a clade A Env. In some embodiments, a well ordered trimer is formed from a clade B Env. In some embodiments, a well ordered trimer is formed from a clade C Env. In some embodiments, a well ordered trimer is formed from a circulating recombinant form Env. In some embodiments, a well ordered trimer is YU-2 gp140. In some embodiments, a well ordered trimer is BG505 SOSIP as disclosed in International Application No. PCT/US2018/041729, filed July 12, 2018, which is incorporated herein by reference in its entirety for all purposes. In some embodiments, a well-ordered Env trimer is a native flexibly linked (NFL) trimer as described in Sharma, et al., Cell Reports, 11(4):539-50 (2015). In some embodiments, a well-ordered Env trimer is a DS-SOSIP as described in Chuang, et al., J. Virology, 91(10) pii: e02268-16 (2017). In some embodiments, a well ordered trimer is formed from a SIV Env. In some embodiments, a well ordered trimer is an SIV Env SOSIP. In some embodiments, a well ordered trimer is formed from an Env comprising a mutation (e.g., substitution or deletion) in the CD4 binding site. In some embodiments, a well ordered trimer is YU-2 gp140 comprising the D368R substitution. In some embodiments, a well ordered trimer is formed from an Env comprising a mutation (e.g., substitution or deletion) in the CD4 binding site wherein the mutation reduces or disrupts the binding between Env and CD4. In some embodiments, a well ordered trimer is a CRF or C108 SOSIP. See, e.g., Andrabi et al, Immunity 43(5): 959–973 (2015). In some embodiments, the gp120 and gp41 ectodomain is linked by a peptide linker, for example, a Gly-Ser linker, as described in Georgiev IS, et al., J. Virology 89(10): 5318-5329 (2015). In some embodiments, the well-ordered Env trimer is stable. In some embodiments, the BG505 Env has the amino acid sequence of SEQ ID NO: 340.

[0037] The term "antibody" means an immunoglobulin molecule (or a group of immunoglobulin molecules) that recognizes and specifically binds to a target, such as a protein, polypeptide, peptide, carbohydrate, polynucleotide, lipid, or combinations of the foregoing through at least one antigen recognition site within the variable region of the immunoglobulin molecule. As used herein, the terms "antibody" and "antibodies" are terms of art and can be used interchangeably herein and refer to a molecule with an antigen-binding site that specifically binds an antigen.

[0038] Antibodies can include, for example, monoclonal antibodies, recombinantly produced antibodies, human antibodies, humanized antibodies, resurfaced antibodies, chimeric antibodies, immunoglobulins, synthetic antibodies, tetrameric antibodies comprising two heavy chain and two light chain molecules, an antibody light chain monomer, an antibody heavy chain monomer, an antibody light chain dimer, an antibody heavy chain dimer, an antibody light chain-

antibody heavy chain pair, intrabodies, heteroconjugate antibodies, single domain antibodies, monovalent antibodies, single chain antibodies or single-chain Fvs (scFv), affybodies, Fab fragments, $F(ab')_2$ fragments, disulfide-linked Fvs (sdFv), anti-idiotypic (anti-Id) antibodies (including, *e.g.*, anti-anti-Id antibodies), bispecific antibodies, and multi-specific antibodies. In certain embodiments, antibodies described herein refer to polyclonal antibody populations. Antibodies can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA, or IgY), any class (*e.g.*, IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, or IgA_2), or any subclasses (isotypes) thereof (*e.g.* IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2), of immunoglobulin molecule, based on the identity of their heavy-chain constant domains referred to as alpha, delta, epsilon, gamma, and mu, respectively. The different classes of immunoglobulins have different and well known subunit structures and three-dimensional configurations. Antibodies can be naked or conjugated or fused to other molecules such as toxins, radioisotopes, other polypeptides etc.

[0039] As used herein, the terms "antigen-binding domain," "antigen-binding region," "antigen-binding site," and similar terms refer to the portion of antibody molecules which comprises the amino acid residues that confer on the antibody molecule its specificity for the antigen (*e.g.,* HIV Env). The antigen-binding region can be derived from any animal species, such as mouse and humans.

[0040] As used herein, the terms "variable region" or "variable domain" are used interchangeably and are common in the art. The variability in sequence is concentrated in those regions called complementarity determining regions (CDRs) while the more highly conserved regions in the variable domain are called framework regions (FR). Without wishing to be bound by any particular mechanism or theory, it is believed that the CDRs of the light and heavy chains are primarily responsible for the interaction and specificity of the antibody with antigen (*e.g.,* HIV Env). In certain embodiments, the variable region is a human variable region. In certain embodiments, the variable region comprises human CDRs and human framework regions (FRs). In certain embodiments, the variable region comprises human CDRs and primate (*e.g.*, non-human primate) framework regions (FRs).

[0041] There are several approaches for determining CDRs. One approach is based on cross-species sequence variability (i.e., Kabat et al., *Sequences of Proteins of Immunological Interest*, (5th ed., 1991, National Institutes of Health, Bethesda Md.), "Kabat"). A second approach was developed by the MGT, the international ImMunoGeneTics database (imgt.cines.fr) as a high quality integrated information system specializing in immunoglobulins (IG), T cell receptors (TR) and major histocompatibility complex (MHC) of human and other vertebrates. Lefranc, M.-P., The

Immunologist, 7, 132-136 (1999). The IMGT unique numbering defined for the IG and TR variable regions and domains of all jawed vertebrates has allowed a redefinition of the limits of the framework (FR-IMGT) and complementarity determining regions (CDR-IMGT), leading to a standardized description of mutations, allelic polymorphisms, 2D representations (Colliers de Perles) and 3D structures, whatever the antigen receptor, the chain type, or the species. A third approach is based on crystallographic studies of antigen-antibody complexes (Al-lazikani et al, *J. Molec. Biol.* 273:927-948 (1997)). In addition, combinations of these approaches are sometimes used in the art to determine CDRs. In some embodiments, the CDR regions are determined according to Kabat. In some embodiments, the CDR regions are determined according to IMGT.

[0042] The Kabat numbering system is generally used when referring to a residue in the variable domain (approximately residues 1-107 of the light chain and residues 1-113 of the heavy chain) (e.g., Kabat et al., *Sequences of Immunological Interest.* (5th Ed., 1991, National Institutes of Health, Bethesda, Md.) ("Kabat").

[0043] The amino acid position numbering as in Kabat, refers to the numbering system used for heavy chain variable domains or light chain variable domains of the compilation of antibodies in Kabat et al. (*Sequences of Immunological Interest.* (5th Ed., 1991, National Institutes of Health, Bethesda, Md.), "Kabat"). Using this numbering system, the actual linear amino acid sequence can contain fewer or additional amino acids corresponding to a shortening of, or insertion into, a FR or CDR of the variable domain. For example, a heavy chain variable domain can include a single amino acid insert (residue 52a according to Kabat) after residue 52 of H2 and inserted residues (e.g. residues 82a, 82b, and 82c, etc. according to Kabat) after heavy chain FR residue 82. The Kabat numbering of residues can be determined for a given antibody by alignment at regions of homology of the sequence of the antibody with a "standard" Kabat numbered sequence. Chothia refers instead to the location of the structural loops (Chothia and Lesk, *J. Mol. Biol.* 196:901-917 (1987)). The end of the Chothia CDR-H1 loop when numbered using the Kabat numbering convention varies between H32 and H34 depending on the length of the loop (this is because the Kabat numbering scheme places the insertions at H35A and H35B; if neither 35A nor 35B is present, the loop ends at 32; if only 35A is present, the loop ends at 33; if both 35A and 35B are present, the loop ends at 34). The AbM hypervariable regions represent a compromise between the Kabat CDRs and Chothia structural loops, and are used by Oxford Molecular's AbM antibody modeling software. In some embodiments, the CDR regions are determined according to Kabat. In some embodiments, the CDR regions are determined according to IMGT. In some embodiments,

the CDR regions are determined according to Chothia. In some embodiments, the CDR regions are determined according to AbM.

Loop	Kabat	AbM	Chothia
L1	L24-L34	L24-L34	L24-L34
L2	L50-L56	L50-L56	L50-L56
L3	L89-L97	L89-L97	L89-L97
H1	H31-H35B	H26-H35B (Kabat Numbering)	H26-H32..34
H1	H31-H35	H26-H35 (Chothia Numbering)	H26-H32
H2	H50-H65	H50-H58	H52-H56
H3	H95-H102	H95-H102	H95-H102

[0044] The terms "VL" and "VL domain" are used interchangeably to refer to the light chain variable region of an antibody.

[0045] The terms "VH" and "VH domain" are used interchangeably to refer to the heavy chain variable region of an antibody.

[0046] The term "antibody fragment" refers to a portion of an intact antibody. An "antigen-binding fragment" refers to a portion of an intact antibody that binds to an antigen. An antigen-binding fragment can contain the antigenic determining variable regions of an intact antibody. Examples of antibody fragments include, but are not limited to Fab, Fab', F(ab')2, and Fv fragments, linear antibodies, and single chain antibodies.

[0047] A "monoclonal" antibody or antigen-binding fragment thereof refers to a homogeneous antibody or antigen-binding fragment population involved in the highly specific recognition and binding of a single antigenic determinant, or epitope. This is in contrast to polyclonal antibodies that typically include different antibodies directed against different antigenic determinants. The term "monoclonal" antibody or antigen-binding fragment thereof encompasses both intact and full-length monoclonal antibodies as well as antibody fragments (such as Fab, Fab', F(ab')2, Fv), single chain (scFv) mutants, fusion proteins comprising an antibody portion, and any other modified immunoglobulin molecule comprising an antigen recognition site. Furthermore, "monoclonal" antibody or antigen-binding fragment thereof refers to such antibodies and antigen-binding fragments thereof made in any number of manners including but not limited to by hybridoma, phage selection, recombinant expression, and transgenic animals.

[0048] The term "polyclonal antibody" describes a composition of different (diverse) antibody molecules which are capable of binding to or reacting with several different specific antigenic determinants on the same or on different antigens. Usually, the variability of a polyclonal antibody is located in the so-called variable regions of the polyclonal antibody, in particular in the CDR regions. In the present disclosure a mixture of two or more polyclonal antibodies (a polycomposition) is produced in one mixture from a polyclonal polycomposition cell line, which is produced from two or more parental polyclonal cell lines each expressing antibody molecules which are capable of binding to a distinct target, but it may also be a mixture of two or more polyclonal antibodies produced separately. A mixture of monoclonal antibodies providing the same antigen/epitope coverage as a polyclonal antibody described herein will be considered as an equivalent of a polyclonal antibody. When stating that a member of a polyclonal antibody binds to an antigen, it is herein meant to be binding with a binding constant below 100 nM, preferably below 10 nM, even more preferred below 1 nM.

[0049] The term "humanized" antibody or antigen-binding fragment thereof refers to forms of non-human (e.g. murine) antibodies or antigen-binding fragments that are specific immunoglobulin chains, chimeric immunoglobulins, or fragments thereof that contain minimal non-human (e.g., murine) sequences. Typically, humanized antibodies or antigen-binding fragments thereof are human immunoglobulins in which residues from the complementary determining region (CDR) are replaced by residues from the CDR of a non-human species (e.g. murine) that have the desired specificity, affinity, and capability ("CDR grafted") (Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-327 (1988); Verhoeyen et al., *Science* 239:1534-1536 (1988)). In some instances, the Fv framework region (FR) residues of a human immunoglobulin are replaced with the corresponding residues in an antibody or fragment from a non-human species (e.g., murine) that has the desired specificity, affinity, and capability. The humanized antibody or antigen-binding fragment thereof can be further modified by the substitution of additional residues either in the Fv framework region and/or within the replaced non-human residues to refine and optimize antibody or antigen-binding fragment thereof specificity, affinity, and/or capability. In general, the humanized antibody or antigen-binding fragment thereof will comprise substantially all of at least one, and typically two or three, variable domains containing all or substantially all of the CDR regions that correspond to the non-human immunoglobulin whereas all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody or antigen-binding fragment thereof can also comprise at least a portion of an immunoglobulin constant region or domain (Fc),

typically that of a human immunoglobulin. Examples of methods used to generate humanized antibodies are described in U.S. Pat. 5,225,539; Roguska et al., *Proc. Natl. Acad. Sci.,* USA, 91(3):969-973 (1994), and Roguska et al., *Protein Eng.* 9(10):895-904 (1996). In some embodiments, a "humanized antibody" is a resurfaced antibody.

[0050] The term "chimeric" antibodies or antigen-binding fragments thereof refers to antibodies or antigen-binding fragments thereof wherein the amino acid sequence is derived from two or more species. Typically, the variable region of both light and heavy chains corresponds to the variable region of antibodies or antigen-binding fragments thereof derived from one species of mammals (e.g., mouse) with the desired specificity, affinity, and capability while the constant regions are homologous to the sequences in antibodies or antigen-binding fragments thereof derived from another (usually human) to avoid eliciting an immune response in that species.

[0051] The term "epitope" or "antigenic determinant" are used interchangeably herein and refer to that portion of an antigen capable of being recognized and specifically bound by a particular antibody. When the antigen is a polypeptide, epitopes can be formed both from contiguous amino acids and noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained upon protein denaturing, whereas epitopes formed by tertiary folding are typically lost upon protein denaturing. An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation.

[0052] "Binding affinity" generally refers to the strength of the sum total of non-covalent interactions between a single binding site of a molecule (e.g., an antibody) and its binding partner (e.g., an antigen). Unless indicated otherwise, as used herein, "binding affinity" refers to intrinsic binding affinity which reflects a 1:1 interaction between members of a binding pair (e.g., antibody and antigen). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (Kd). Affinity can be measured by common methods known in the art, including those described herein. Low-affinity antibodies generally bind antigen slowly and tend to dissociate readily, whereas high-affinity antibodies generally bind antigen faster and tend to remain bound longer. A variety of methods of measuring binding affinity are known in the art, any of which can be used for purposes of the present invention. Specific illustrative embodiments are described in the following.

[0053] "Or better" when used herein to refer to binding affinity refers to a stronger binding between a molecule and its binding partner. "Or better" when used herein refers to a stronger binding, represented by a smaller numerical Kd value. For example, an antibody which has an

affinity for an antigen of "0.6 nM or better", the antibody's affinity for the antigen is <0.6 nM, i.e. 0.59 nM, 0.58 nM, 0.57 nM etc. or any value less than 0.6 nM.

[0054] As used herein, the terms "immunospecifically binds," "immunospecifically recognizes," "specifically binds," and "specifically recognizes" are analogous terms in the context of antibodies and refer to molecules that bind to an antigen (*e.g.*, epitope or immune complex) as such binding is understood by one skilled in the art. For example, a molecule that specifically binds to an antigen can bind to other peptides or polypeptides, generally with lower affinity as determined by, *e.g.*, immunoassays, BIAcore®, KinExA 3000 instrument (Sapidyne Instruments, Boise, ID), or other assays known in the art. In a specific embodiment, molecules that immunospecifically bind to an antigen bind to the antigen with a Kd that is at least 2 logs, 2.5 logs, 3 logs, or 4 logs lower than the Kd when the molecules bind non-specifically to another antigen. In one example, the antibody may specifically bind to the BG505 Env. In some embodiments, the BG505 Env has the amino acid sequence of SEQ ID NO: 340. In one example, the antibody may specifically bind to a BG505 SOSIP trimer. In one example, the antibody may specifically bind to JR-FL Env. In one example, the antibody may specifically bind to JR-FL SOSIP. In one example, the antibody may specifically bind to YU2 gp140. The antibody may bind to JR-FL SOSIP, BG505 SOSIP, or YU2 gp140 with a Kd at least 2 logs, 2.5 logs, 3 logs, or 4 logs lower than Kd of binding to other viral or non-viral polypeptides. An antibody that specifically binds to Env encompass, but are not limited to, antibodies that specifically bind to native Env, an isoform of Env, or a variant of Env (e.g., SOSIP) derived from an HIV isolate, for example, JR-FL, BG505, or YU2. In some embodiments, the antibody specifically binds to JR-FL Env. In some embodiments, the antibody specifically binds to JR-FL SOSIP. In some embodiments, the antibody specifically binds to BG505 Env. In some embodiments, the antibody specifically binds to BG505 SOSIP. In some embodiments, the antibody specifically binds to YU2 Env. In some embodiments, the antibody specifically binds to YU2 SOSIP.

[0055] By "preferentially binds," it is meant that the antibody specifically binds to an epitope more readily than it would bind to a related, similar, homologous, or analogous epitope. Thus, an antibody which "preferentially binds" to a given epitope would more likely bind to that epitope than to a related epitope, even though such an antibody may cross-react with the related epitope.

[0056] An antibody is said to "competitively inhibit" binding of a reference antibody to a given epitope if it preferentially binds to that epitope or an overlapping epitope to the extent that it blocks, to some degree, binding of the reference antibody to the epitope. Competitive inhibition

may be determined by any method known in the art, for example, competition ELISA assays. An antibody may be said to competitively inhibit binding of the reference antibody to a given epitope by at least 90%, at least 80%, at least 70%, at least 60%, or at least 50%.

[0057] The term "broadly neutralizing antibody" or "bnAb," as used herein, with respect to HIV (e.g., HIV-1), refers to an antibody that recognizes HIV Env of more than one isolate or strain of HIV and inhibits or prevents receptor binding of target cells as evaluated in an in vitro neutralization assay. In some embodiments, a broadly neutralizing antibody inhibits infection of a susceptible target cell by HIV. In some embodiments, a broadly neutralizing antibody specifically binds an HIV Env and inhibits infection of a susceptible target cell (e.g., TZM-bl) by an HIV pseudovirus comprising an Env polypeptide. HIV pseudovirus neutralization assays have been disclosed in the art, for example, in Walker, L. M. *et al.*, *Nature* **477,** 466–470 (2011), Li M., et al., J. Virol. 79:10108-10125 (2005), each of which is incorporated herein by reference in its entirety for all purposes. In some embodiments, a broadly neutralizing antibody neutralizes 2, 3, 4, 5, 6, 7, 8, 9, or more HIV strains or pseudoviruses. In some embodiments, a broadly neutralizing antibody neutralizes 2, 3, 4, 5, 6, 7, 8, 9, or more HIV strains or pseudoviruses that belong to the same or different clades. In some embodiments, a broadly neutralizing antibody is capable of neutralizing HIV strains or pseudoviruses from at least two different clades. In some embodiments, a broadly neutralizing antibody is capable of neutralizing HIV at least one clade B strain or pseudovirus and one clade C strain or pseudovirus. In some embodiments, a broadly neutralizing antibody is capable of neutralizing HIV more than one clade B strain or pseudovirus and more than one clade C strain or pseudovirus.

[0058] In some embodiments, the breadth of neutralization is tested on an indicator virus panel comprising cross-clade HIV isolates. In some embodiments, the virus panel comprises the cross-clade isolates as shown in Figure 8. In some embodiments, the virus panel comprises the cross-clade isolates as shown in Figure 9In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 50%, 60%, 70%, 80%, 90%, 95%, or 100% of cross-clade HIV isolates in the 106-member indicator virus panel. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 60% of cross-clade HIV isolates in the 106-member indicator virus panel. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 70% of cross-clade HIV isolates in the 106-member indicator virus panel. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 75% of cross-clade HIV isolates in the 106-member indicator virus panel. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 80% of cross-clade HIV

isolates in the 106-member indicator virus panel. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 90% of cross-clade HIV isolates in the 106-member indicator virus panel. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 95% of cross-clade HIV isolates in the 106-member indicator virus panel. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 40% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 50% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 60% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 70% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 75% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 80% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 90% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 95% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9.

[0059] In some embodiments, the potency of neutralization by a broadly neutralizing antibody is expressed as the median IC_{50} neutralization activity against a virus panel, for example, the indicator virus panel as shown in Figure 8 or Figure 9.

[0060] In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9 with a median IC_{50} equal to or less than about 1 μg/ml, 0.8 μg/ml, 0.5 μg/ml, 0.3 μg/ml, 0.1 μg/ml, 0.07 μg/ml, 0.06 μg/ml, 0.05 μg/ml, 0.025 μg/ml, 0.01 μg/ml or 0.005 μg/ml. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 70% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9 with a median IC_{50} equal to or less than 0.8 μg/ml. In some embodiments,

a broadly neutralizing antibody is capable of neutralizing at least about 75% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9 with a median IC_{50} equal to or less than 0.8 μg/ml. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 80% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9 with a median IC_{50} equal to or less than 0.8 μg/ml. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 70% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9 with a median IC_{50} equal to or less than 0.5 μg/ml. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 75% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9 with a median IC_{50} equal to or less than 0.5 μg/ml. In some embodiments, a broadly neutralizing antibody is capable of neutralizing at least about 80% of cross-clade HIV isolates in the indicator virus panel as shown in Figure 8 or Figure 9 with a median IC_{50} equal to or less than 0.5 μg/ml.

[0061] The term "IC_{50}" refers to the half maximal inhibitory concentration of an inhibitor, e.g., a broadly neutralizing antibody. For example, IC_{50} is the concentration of an inhibitor, e.g., a broadly neutralizing antibody, where the response, e.g., infection by virus or pseudovirus, is reduced by 50%.

[0062] The phrase "substantially similar," or "substantially the same", as used herein, denotes a sufficiently high degree of similarity between two numeric values (generally one associated with an antibody described herein and the other associated with a reference/comparator antibody) such that one of skill in the art would consider the difference between the two values to be of little or no biological and/or statistical significance within the context of the biological characteristic measured by said values (e.g., Kd values). The difference between said two values can be less than about 50%, less than about 40%, less than about 30%, less than about 20%, or less than about 10% as a function of the value for the reference/comparator antibody.

[0063] A polypeptide, antibody, polynucleotide, vector, cell, or composition which is "isolated" is a polypeptide, antibody, polynucleotide, vector, cell, or composition which is in a form not found in nature. Isolated polypeptides, antibodies, polynucleotides, vectors, cell or compositions include those which have been purified to a degree that they are no longer in a form in which they are found in nature. In some embodiments, an antibody, polynucleotide, vector, cell, or composition which is isolated is substantially pure.

[0064] As used herein, "substantially pure" refers to material which is at least 50% pure (i.e., free from contaminants), at least 90% pure, at least 95% pure, at least 98% pure, or at least 99% pure.

[0065] The terms "polypeptide," "peptide," and "protein" are used interchangeably herein to refer to polymers of amino acids of any length. The polymer can be linear or branched, it can comprise modified amino acids, and it can be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation or modification, such as conjugation with a labeling component. Also included within the definition are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, etc.), as well as other modifications known in the art. It is understood that, because the polypeptides described herein are based upon antibodies, in certain embodiments, the polypeptides can occur as single chains or associated chains.

[0066] The terms "identical" or percent "identity" in the context of two or more nucleic acids or polypeptides, refer to two or more sequences or subsequences that are the same or have a specified percentage of nucleotides or amino acid residues that are the same, when compared and aligned (introducing gaps, if necessary) for maximum correspondence, not considering any conservative amino acid substitutions as part of the sequence identity. The percent identity can be measured using sequence comparison software or algorithms or by visual inspection. Various algorithms and software are known in the art that can be used to obtain alignments of amino acid or nucleotide sequences. One such non-limiting example of a sequence alignment algorithm is the algorithm described in Karlin et al, *Proc. Natl. Acad. Sci.*, 87:2264-2268 (1990), as modified in Karlin et al., *Proc. Natl. Acad. Sci.*, 90:5873-5877 (1993), and incorporated into the NBLAST and XBLAST programs (Altschul et al., *Nucleic Acids Res.*, 25:3389-3402 (1991)). In certain embodiments, Gapped BLAST can be used as described in Altschul et al., *Nucleic Acids Res.* 25:3389-3402 (1997). BLAST-2, WU-BLAST-2 (Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)), ALIGN, ALIGN-2 (Genentech, South San Francisco, California) or Megalign (DNASTAR) are additional publicly available software programs that can be used to align sequences. In certain embodiments, the percent identity between two nucleotide sequences is determined using the GAP program in GCG software (e.g., using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 90 and a length weight of 1, 2, 3, 4, 5, or 6). In certain alternative embodiments, the GAP program in the GCG software package, which incorporates the algorithm of Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) can be used to determine the percent

identity between two amino acid sequences (e.g., using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5). Alternatively, in certain embodiments, the percent identity between nucleotide or amino acid sequences is determined using the algorithm of Myers and Miller (*CABIOS*, 4:11-17 (1989)). For example, the percent identity can be determined using the ALIGN program (version 2.0) and using a PAM120 with residue table, a gap length penalty of 12 and a gap penalty of 4. Appropriate parameters for maximal alignment by particular alignment software can be determined by one skilled in the art. In certain embodiments, the default parameters of the alignment software are used. In certain embodiments, the percentage identity "X" of a first amino acid sequence to a second sequence amino acid is calculated as 100 x (Y/Z), where Y is the number of amino acid residues scored as identical matches in the alignment of the first and second sequences (as aligned by visual inspection or a particular sequence alignment program) and Z is the total number of residues in the second sequence. If the length of a first sequence is longer than the second sequence, the percent identity of the first sequence to the second sequence will be longer than the percent identity of the second sequence to the first sequence.

[0067] As a non-limiting example, whether any particular polynucleotide has a certain percentage sequence identity (e.g., is at least 80% identical, at least 85% identical, at least 90% identical, and in some embodiments, at least 95%, 96%, 97%, 98%, or 99% identical) to a reference sequence can, in certain embodiments, be determined using the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, WI 53711). Bestfit uses the local homology algorithm of Smith and Waterman (*Advances in Applied Mathematics* 2: 482 489 (1981)) to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence described herein, the parameters are set such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

[0068] In some embodiments, two nucleic acids or polypeptides described herein are substantially identical, meaning they have at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, and in some embodiments at least 95%, 96%, 97%, 98%, 99% nucleotide or amino acid residue identity, when compared and aligned for maximum correspondence, as measured using a sequence comparison algorithm or by visual inspection. Identity can exist over a region of the sequences that is at least about 10, about 20, about 40-60 residues in length or any integral value

there between, and can be over a longer region than 60-80 residues, for example, at least about 90-100 residues, and in some embodiments, the sequences are substantially identical over the full length of the sequences being compared, such as the coding region of a nucleotide sequence for example.

[0069] A "conservative amino acid substitution" is one in which one amino acid residue is replaced with another amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art, including basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). For example, substitution of a phenylalanine for a tyrosine is a conservative substitution. In some embodiments, conservative substitutions in the sequences of the polypeptides and antibodies described herein do not abrogate the binding of the polypeptide or antibody containing the amino acid sequence, to the antigen(s). Methods of identifying nucleotide and amino acid conservative substitutions which do not eliminate antigen binding are well- known in the art (see, e.g., Brummell et al., *Biochem.* 32: 1180-1 187 (1993); Kobayashi et al., *Protein Eng.* 12(10):879-884 (1999); and Burks et al., *Proc. Natl. Acad. Sci. USA* 94:.412-417 (1997)).

[0070] Vectors that can be used include, but are not limited to, plasmids, bacterial vectors, and viral vectors. Viral vectors include cytomegalovirus (CMV) vectors. An advantage of these CMV vectors for use in therapeutic vaccine delivery is that they create a new CD8+ T cell epitope paradigm and induce more potent and enduring responses. It has been shown in animal models that vaccines based on these viral vectors can clear viral infections (Hansen, S. G. 2013. Science 340:1237874), and so these approaches have promise for a therapeutic vaccine, a setting in which tailored vaccines can be useful.

[0071] Other viral vectors can include poxvirus (vaccinia), including vaccinia Ankara and canarypox; adenoviruses, including adenovirus type 5 (Ad5); rubella; sendai virus; rhabdovirus; alphaviruses; and adeno-associated viruses. Alternatively, the vaccine antigens could be delivered as DNA, RNA or protein components of a vaccine.

[0072] As used herein, the terms "treatment" or "therapy" (as well as different forms thereof, including curative or palliative) refer to treatment of an infected person. As used herein, the term "treating" includes alleviating or reducing at least one adverse or negative effect or

symptom of a condition, disease or disorder. This condition, disease or disorder can be HIV infection.

[0073] Terms such as "treating" or "treatment" or "to treat" or "alleviating" or "to alleviate" refer to therapeutic measures that cure, slow down, lessen symptoms of, and/or halt progression of a diagnosed pathologic condition or disorder, such as HIV or AIDS. Thus, those in need of treatment include those already diagnosed with or suspected of having the disorder. In certain embodiments, a subject is successfully "treated" for the disorder according to the methods described herein if the patient shows one or more of the following: a reduction in the number of or complete absence of viral load; a reduction in the viral burden; inhibition of or an absence of the virus into peripheral organs; relief of one or more symptoms associated with the disorder; reduced morbidity and mortality; improvement in quality of life; increased progression-free survival (PFS), disease-free survival (DFS), or overall survival (OS), complete response (CR), partial response (PR), stable disease (SD), a decrease in progressive disease (PD), a reduced time to progression (TTP), or any combination thereof.

[0074] As used herein, the terms "prevention" or "prophylaxis" refer to preventing a subject from becoming infected with, or reducing the risk of a subject from becoming infected with, or halting transmission of, or the reducing the risk of transmission of a virus. Prophylactic or preventative measures refer to measures that prevent and/or slow the development of a targeted pathological condition or disorder. Thus, those in need of prophylactic or preventative measures include those prone to have the disorder and those in whom the disorder is to be prevented. In some embodiments, prevention encompasses passive immunization of a subject in need thereof comprising administering an effective amount of an antibody described herein.

[0075] As employed above and throughout the disclosure the term "effective amount" refers to an amount effective, at dosages, and for periods of time necessary, to achieve the desired result with respect to the treatment of the relevant disorder, condition, or side effect. An "effective amount" can be determined empirically and in a routine manner, in relation to the stated purpose. It will be appreciated that the effective amount of components of the present invention will vary from patient to patient not only with the particular vaccine, component or composition selected, the route of administration, and the ability of the components to elicit a desired result in the individual, but also with factors such as the disease state or severity of the condition to be alleviated, hormone levels, age, sex, weight of the individual, the state of being of the patient, and the severity of the pathological condition being treated, concurrent medication or special diets then being followed by the particular patient, and other factors which those skilled in the art will recognize, with the

appropriate dosage being at the discretion of the attending physician. Dosage regimes may be adjusted to provide the improved therapeutic response. An effective amount is also one in which any toxic or detrimental effects of the components are outweighed by the therapeutically beneficial effects.

[0076] The term "therapeutically effective amount" refers to an amount of an antibody, immunoconjugate, or other drug effective to "treat" a disease or disorder in a subject or mammal. To the extent an antibody can prevent growth and/or kill existing cells, it can be cytostatic and/or cytotoxic. A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result. Typically but not necessarily, since a prophylactic dose is used in subjects prior to or at an earlier stage of disease, the prophylactically effective amount will be less than the therapeutically effective amount.

[0077] The terms "subject," "individual," and "patient" are used interchangeably herein, and refer to an animal, for example a human, to whom treatment, including prophylactic treatment, with the antibody or pharmaceutical composition according to the present disclosure, is provided. In some embodiments, the subject, individual, or patient has been infected with HIV. In some embodiments, the subject, individual, or patient suffers from AIDS. In some embodiments, the subject, individual, or patient has been exposed to HIV. In some embodiments, the subject, individual, or patient is at risk of being exposed to HIV.

[0078] Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) or consecutive administration in any order.

[0079] The terms "pharmaceutically composition," "pharmaceutical formulation," "pharmaceutically acceptable formulation," or "pharmaceutically acceptable composition" all of which are used interchangeably, refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem complications commensurate with a reasonable benefit/risk ratio. "Pharmaceutically acceptable" or "pharmaceutical formulation" refers to a preparation which is in such form as to permit the biological activity of the active ingredient to be effective, and which contains no additional components which are unacceptably toxic to a subject to which the formulation would be administered. The formulation can be sterile.

[0080] The term "antiretroviral therapy" or "ART," as used herein, refers to any of the therapies used to manage progression of a retrovirus (e.g., HIV) infection in a subject (e.g., a human), including, for example, nucleoside reverse transcriptase inhibitors (NRTIs), non-

nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors, entry inhibitors, maturation inhibitors, cellular inhibitors, integrase strand transfer inhibitors, and multi-class combinations. Such drugs include, but are not limited to, lamivudine and zidovudine, emtricitabine (FTC), zidovudine (ZDV), azidothymidine (AZT), lamivudine (3TC), zalcitabine, dideoxycytidine (ddC), tenofovir disoproxil fumarate (TDF), didanosine (ddl), stavudine (d4T), abacavir sulfate (ABC), etravirine, delavirdine (DLV), efavirenz (EFV), nevirapine (NVP), amprenavir (APV), tipranavir (TPV), indinavir (IDV), saquinavir, saquinavir mesylate (SQV), lopinavir (LPV), ritonavir (RTV), fosamprenavir calcium (FOS-APV), ritonavir, RTV, darunavir, atazanavir sulfate (ATV), nelfinavir mesylate (NFV), enfuvirtide, T-20, maraviroc and raltegravir. ART drugs can also include antibodies that target HIV proteins or cellular proteins associated with disease progression. Also included are immune-based therapies, such as IL-2, IL-12, and alpha-epibromide. Each of these drugs can be administered alone or in combination with any other ART drug or any HIV-specific neutralizing antibody, such as a broadly neutralizing antibody, which is incorporated by reference herein in its entirety for all purposes.

[0081] The term "immunomodulator," as used herein, refers to an agent, such as an antibody or peptide, which is capable of increasing, inducing, or extending an immune response (e.g., a cell-mediated immune response and/or a humoral immune response) when administered to a subject (e.g., a human, e.g., a human infected with HIV or at risk of an HIV infection or transmission). Immunomodulators include, but are not limited to immune checkpoint inhibitors, for example, a PD-1, PD-L1, LAG-3, or TIGIT antagonist. In some embodiments, an immunomodulator used in the methods described herein comprises an anti-PD-1 antibody, anti-PD-L1 antibody, anti-LAG3 antibody, or an anti-TIGIT antibody. An immunomodulator can be administered in conjunction with (e.g., prior to, concurrently with, or subsequent to, or within the context of a treatment regimen that includes the administration of a broadly neutralizing antibody described herein.

[0082] As used in this specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the content clearly dictates otherwise. Thus, for example, reference to "a cell" includes a combination of two or more cells, and the like.

[0083] The term "and/or" as used in a phrase such as "A and/or B" herein is intended to include both "A and B," "A or B," "A," and "B." Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following embodiments: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[0084] The term "about" as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of up to ±20% from the specified value, as such variations are appropriate to perform the disclosed methods. Unless otherwise indicated, all numbers expressing quantities of ingredients, properties such as molecular weight, reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth in the following specification and attached claims are approximations that may vary depending upon the desired properties sought to be obtained by the present invention. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

[0085] Notwithstanding that the numerical ranges and parameters setting forth the broad scope described herein are approximations, the numerical values set forth in the specific examples are reported as precisely as possible. Any numerical value, however, inherently contain certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

[0086] It is understood that wherever embodiments are described herein with the language "comprising," otherwise analogous embodiments described in terms of "consisting of" and/or "consisting essentially of" are also provided.

II. Anti-HIV antibodies

[0087] In one aspect, provided herein are anti-HIV antibodies that bind to Env. In some embodiments, an antibody described herein is a monoclonal antibody. In some embodiments, an antibody described herein is a human antibody. In some embodiments, an antibody described herein is a broadly neutralizing antibody. In some embodiments, an antibody described herein specifically binds the Env of at least one HIV isolate in the indicator virus panels of Figure 8 and 9. In some embodiments, an antibody described herein specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 8 and 9. In some embodiments, an antibody described herein is a VRC01 class antibody. In some embodiments, an antibody described herein binds Env at the CD4 receptor binding site (CD4bs) epitope region. In some embodiments, an antibody described herein binds to wild type Env, but does not bind a mutant variant of Env comprising a substitution or deletion in the CD4 receptor binding site. In some embodiments, the Env is a clade A Env. In some embodiments, the Env is a clade B Env. In some

embodiments, the Env is a clade C Env. In some embodiments, the Env is a clade A Env from the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, the Env is a clade B Env from the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, the Env is a clade C Env from the indicator virus panel as shown in Figure 8 or Figure 9. In some embodiments, the Env is the Env of a virus from the indicator virus panel as shown in Figure 8 or Figure 9.In some embodiments, the Env is BG505, JR-FL, YU-2, or JR-CSF r92RW020, BG505, or JR-FL Env.

[0088] In some embodiments, an isolated monoclonal antibody described herein comprises a VH, a VL, or a VH and VL as shown in the section titled "SEQUENCES."

[0089] In some embodiments, an isolated monoclonal antibody described herein comprises one, two, three, four, five or six of the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 sequences as shown in the section titled "SEQUENCES."

[0090] In some embodiments, an isolated monoclonal antibody described herein comprises a VH CDR3 sequence as shown in the section titled "SEQUENCES."

[0091] In some embodiments, an isolated monoclonal antibody described herein comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 sequence as shown in the section titled "SEQUENCES."

[0092] Also provided herein are polypeptides that comprise an amino acid sequence having at least about 80% sequence identity, at least about 85% sequence identity, at least about 90% sequence identity, at least about 95% sequence identity, at least about 96% sequence identity, at least about 97% sequence identity, at least about 98% sequence identity, or at least about 99% sequence, or is identical to the sequences listed in the section titled "SEQUENCES."

[0093] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H,

PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0094] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

[0095] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0096] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37-54. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0097] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37, 39, 40, 42-48, or 50-53. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0098] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 44 or 47. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0099] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L,

PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0100] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0101] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0102] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody

comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0103] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0104] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0105] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a,

PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; (b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and (c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0106] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; (b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and (c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-

71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0107] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-71I1a, or PCIN63-71L; (b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-71I1a, or PCIN63-71L; and (c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0108] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 1-18; (b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 19-36; and (c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37-54. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0109] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 1, 3, 4, 6-12, or 14-17; (b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 19, 21, 22, 24-30, or 32-35; and (c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37, 39, 40, 42-48, or 50-53. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0110] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 8 or 11; (b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 26 or 29; and (c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 44 or 47. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0111] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a,

PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0112] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C,

PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0113] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the VH CDR1 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VH CDR2 comprises the VH CDR2 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0114] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0115] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1, 3, 4, 6-12, or 14-17 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19, 21, 22, 24-30, or 32-35 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0116] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 8 or 11 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 26 or 29 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0117] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a,

PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; (b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and (c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0118] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; (b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and (c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0119] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the VH CDR1 of PCIN63-71I1a, or PCIN63-71L; (b) the VH CDR2 comprises the VH CDR2 of PCIN63-71I1a, or PCIN63-71L; and (c) the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0120] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18; (b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36; and (c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0121] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1, 3, 4, 6-12, or 14-17; (b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19, 21, 22, 24-30, or 32-35; and (c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-

71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0122] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 8 or 11; (b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 26 or 29; and (c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0123] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; (b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and (c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH

CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0124] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; (b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and (c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0125] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-71I1a, or PCIN63-71L; (b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-71I1a, or PCIN63-71L; and (c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL

CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0126] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0127] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-

71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0128] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the VL CDR1 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VL CDR2 comprises the VL CDR2 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VL CDR3 comprises the VL CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0129] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3,

wherein (a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; (b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and (c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0130] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; (b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and (c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some

embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0131] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the VL CDR1 of PCIN63-71I1a, or PCIN63-71L; (b) the VL CDR2 comprises the VL CDR2 of PCIN63-71I1a, or PCIN63-71L; and (c) the VL CDR3 comprises the VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0132] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 55-72; (b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 73-90; and (c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 91-108. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0133] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 55, 57, 58, 60-66, or 68-71; (b) the VL CDR2

comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 73, 75, 76, 78-84, or 86-89; and (c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 91, 93, 94, 96-102, or 104-107. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0134] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 62 or 65; (b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 80 or 83; and (c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 98 or 101. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0135] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments,

the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0136] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55, 57, 58, 60-66, or 68-71 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73, 75, 76, 78-84, or 86-89 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91, 93, 94, 96-102, or 104-107 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0137] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 62 or 65 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; (b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 80 or 83 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and (c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 98 or 101 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0138] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72; (b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90; and (c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0139] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55, 57, 58, 60-66, or 68-71; (b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73, 75, 76, 78-84, or 86-89; and (c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91, 93, 94, 96-102, or 104-107. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0140] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein (a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 62 or 65; (b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 80 or 83; and (c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 98 or 101. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a,

PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, and VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0141] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively.

[0142] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively.

[0143] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-71I1a, or PCIN63-71L VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively.

[0144] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of (a) SEQ ID NO: 1, 19, 37, 55, 73, and 91, respectively; (b) SEQ ID NO: 2, 20, 38, 56, 74, and 92, respectively; (c) SEQ ID NO: 3, 21, 39, 57, 75, and 93, respectively; (d) SEQ ID NO: 4, 22, 40, 58, 76, and 94, respectively; (e) SEQ ID NO: 5, 23, 41, 59, 77, and 95,

respectively; (f) SEQ ID NO: 6, 24, 42, 60, 78, and 96, respectively; (g) SEQ ID NO: 7, 25, 43, 61, 79, and 97, respectively; (h) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively; (i) SEQ ID NO: 9, 27, 45, 63, 81, and 99, respectively; (j) SEQ ID NO: 10, 28, 46, 64, 82, and 100, respectively; (k) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively; (l) SEQ ID NO: 12, 30, 48, 66, 84, and 102, respectively; (m) SEQ ID NO: 13, 31, 49, 67, 85, and 103, respectively; (n) SEQ ID NO: 14, 32, 50, 68, 86, and 104, respectively; (o) SEQ ID NO: 15, 33, 51, 69, 87, and 105, respectively; (p) SEQ ID NO: 16, 34, 52, 70, 88, and 106, respectively; (q) SEQ ID NO: 17, 35, 53, 71, 89, and 107, respectively; or (r) SEQ ID NO: 18, 36, 54, 72, 90, and 108, respectively.

[0145] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of (a) SEQ ID NO: 1, 19, 37, 55, 73, and 91, respectively; (b) SEQ ID NO: 3, 21, 39, 57, 75, and 93, respectively; (c) SEQ ID NO: 4, 22, 40, 58, 76, and 94, respectively; (d) SEQ ID NO: 6, 24, 42, 60, 78, and 96, respectively; (e) SEQ ID NO: 7, 25, 43, 61, 79, and 97, respectively; (f) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively; (g) SEQ ID NO: 9, 27, 45, 63, 81, and 99, respectively; (h) SEQ ID NO: 10, 28, 46, 64, 82, and 100, respectively; (i) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively; (j) SEQ ID NO: 12, 30, 48, 66, 84, and 102, respectively; (k) SEQ ID NO: 14, 32, 50, 68, 86, and 104, respectively; (l) SEQ ID NO: 15, 33, 51, 69, 87, and 105, respectively; (m) SEQ ID NO: 16, 34, 52, 70, 88, and 106, respectively; or (n) SEQ ID NO: 17, 35, 53, 71, 89, and 107, respectively.

[0146] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of (a) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively; or (b) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively.

[0147] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b,

PCIN63-77C, or PCIN63-77D. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL of an antibody described herein. In some embodiments, the antibody comprises the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL of PCIN63-71I1a, or PCIN63-71L.

[0148] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL of an antibody described herein. In some embodiments, the antibody comprises the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL of PCIN63-71I1a, or PCIN63-71L.

[0149] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%,

98%, 99% or 100% identical to the VH of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL of an antibody described herein. In some embodiments, the antibody comprises the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL of PCIN63-71I1a, or PCIN63-71L.

[0150] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235-252. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL of an antibody described herein. In some embodiments, the antibody comprises the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL of PCIN63-71I1a, or PCIN63-71L.

[0151] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235, 237, 238, 240-246, or 248-251. In some

embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL of an antibody described herein. In some embodiments, the antibody comprises the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL of PCIN63-71I1a, or PCIN63-71L.

[0152] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 242 or245. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VL of an antibody described herein. In some embodiments, the antibody comprises the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VL of PCIN63-71I1a, or PCIN63-71L.

[0153] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K,

PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH of an antibody described herein. In some embodiments, the antibody comprises the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH of PCIN63-71I1a, or PCIN63-71L.

[0154] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH of an antibody described herein. In some embodiments, the antibody comprises the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH of PCIN63-71I1a, or PCIN63-71L.

[0155] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region

(VL), wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH of an antibody described herein. In some embodiments, the antibody comprises the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH of PCIN63-71I1a, or PCIN63-71L.

[0156] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253-270. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH of an antibody described herein. In some embodiments, the antibody comprises the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH of PCIN63-71I1a, or PCIN63-71L.

[0157] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), , wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%,

98%, 99% or 100% identical to SEQ ID NO: 253, 255, 256, 258-264, or 266-269. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH of an antibody described herein. In some embodiments, the antibody comprises the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH of PCIN63-71I1a, or PCIN63-71L.

[0158] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 260 or 263. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH of an antibody described herein. In some embodiments, the antibody comprises the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH of PCIN63-71I1a, or PCIN63-71L.

[0159] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-

71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH and VL, respectively. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0160] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C VH and VL, respectively. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0161] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL),), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-71I1a, or PCIN63-71L VH and VL, respectively. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or

PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0162] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235-252 and the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253-270. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0163] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to (a) SEQ ID NO: 235 and 253, respectively; (b) SEQ ID NO: 236 and 254, respectively; (c) SEQ ID NO: 237 and 255, respectively; (d) SEQ ID NO: 238 and 256, respectively; (e) SEQ ID NO: 239 and 257, respectively; (f) SEQ ID NO: 240 and 258, respectively; (g) SEQ ID NO: 241 and 259, respectively; (h) SEQ ID NO: 242 and 260, respectively; (i) SEQ ID NO: 243 and 261, respectively; (j) SEQ ID NO: 244 and 262, respectively; (k) SEQ ID NO: 245 and 263, respectively; (l) SEQ ID NO: 246 and 264, respectively; (m) SEQ ID NO: 247 and 265, respectively; (n) SEQ ID NO: 248 and 266, respectively; (o) SEQ ID NO: 249 and 267, respectively; (p) SEQ ID NO: 250 and 268, respectively; (q) SEQ ID NO: 251 and 269, respectively; or (r) SEQ ID NO: 252 and 270, respectively. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

[0164] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising one or more of Motif #1, Motif #2, and Motif #3. In some embodiments, the VH comprises an amino acid sequence comprising Motif #1, Motif #2, and Motif #3. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 109-126 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 310-315 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 310 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 311 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 312 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 313 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 314 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 315 at Kabat positions H31-H37. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 127-144 at Kabat positions H52-H56. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 316-318 at Kabat positions H52-H56. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 316 at Kabat positions H52-H56. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 317 at Kabat positions H52-H56. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 318 at Kabat positions H52-H56. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 145 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 146 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 147 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 149 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 150 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 151 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 156 at Kabat positions

H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 157 at Kabat positions H61-H62. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 161 at Kabat positions H61-H62. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from the same antibody described herein. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) Motif #1, Motif #2, and Motif #3, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from the same antibody described herein. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0165] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising one or more of (a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37; (b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62. In some embodiments, an isolated

monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37; (b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from the same antibody described herein. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) Motif #1, Motif #2, and Motif #3, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from the same antibody described herein. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from PCIN63-71I1a, or PCIN63-71L.In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0166] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising one or more of (a) the amino acid sequence of SEQ ID NO: 310-315 at Kabat positions H31-H37; (b) the amino acid sequence

of SEQ ID NO: 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 310-315 at Kabat positions H31-H37; (b) the amino acid sequence of SEQ ID NO: 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from the same antibody described herein. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) Motif #1, Motif #2, and Motif #3, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from the same antibody described herein. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, Motif #1, Motif #2, and Motif #3 is derived from PCIN63-71I1a, or PCIN63-71L.In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0167] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region

(VL), wherein the VL comprises an amino acid sequence comprising one or more of Motif #4, Motif #5, Motif #6, and Motif #7. In some embodiments, the VL comprises an amino acid sequence comprising of Motif #4, Motif #5, Motif #6, and Motif #7. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 163-180 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 319-324 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 319 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 320 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 321 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 322 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 323 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 323 at Kabat positions H26-H34. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 181-198 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 325-334 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 325 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 326 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 327 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 328 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 329 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 330 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 331 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 332 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 333 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 334 at Kabat positions H49-H56. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 199-216 at Kabat positions H67-H70. In some embodiments, Motif #6

comprises the amino acid sequence of SEQ ID NO: 335-339 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 335 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 336 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 337 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 338 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 339 at Kabat positions H67-H70. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 217 at Kabat positions H89-H97. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 218 at Kabat positions H89-H97. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 222 at Kabat positions H89-H97. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 224 at Kabat positions H89-H97. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 229 at Kabat positions H89-H97. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 234 at Kabat positions H89-H97. In some embodiments, the VL comprises an amino acid sequence comprising (a) VL CDR1, VL CDR2, and VL CDR3, and (b) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the VL comprises an amino acid sequence comprising (a) VL CDR1, VL CDR2, and VL CDR3, and (b) Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or

PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0168] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence comprising one or more of (a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34; (b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56; (c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and (d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34; (b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56; (c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and (d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, the VL comprises an amino acid sequence comprising (a) VL CDR1, VL CDR2, and VL CDR3, and (b) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the VL comprises an amino acid sequence comprising (a) VL CDR1, VL CDR2, and VL CDR3, and (b) Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH

CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0169] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence comprising one or more of (a) the amino acid sequence of SEQ ID NO: 319-324 at Kabat positions H26-H34; (b) the amino acid sequence of SEQ ID NO: 325-334 at Kabat positions H49-H56; (c) the amino acid sequence of SEQ ID NO: 335-339 at Kabat positions H67-H70; and (d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 319-324 at Kabat positions H26-H34; (b) the amino acid sequence of SEQ ID NO: 325-334 at Kabat positions H49-H56; (c) the amino acid sequence of SEQ ID NO: 335-339 at Kabat positions H67-H70; and (d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, the VL comprises an amino acid sequence comprising (a) VL CDR1, VL CDR2, and VL CDR3, and (b) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the VL comprises an amino acid sequence comprising (a) VL CDR1, VL CDR2, and VL CDR3, and (b) Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-66B, PCIN63-71C,

PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VL CDR1, VL CDR2, VL CDR3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0170] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein (a) the VH comprises an amino acid sequence comprising one or more of Motif #1, Motif #2, and Motif #3, and/or (b) the VL comprises an amino acid sequence comprising one or more of Motif #4, Motif #5, Motif #6, and Motif #7. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein (a) the VH comprises an amino acid sequence comprising Motif #2 and (b) the VL comprises an amino acid sequence comprising Motif #4, and Motif #6. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein (a) the VH comprises an amino acid sequence comprising Motif #1, Motif #2, and Motif #3, and (b) the VL comprises an amino acid sequence comprising Motif #4, Motif #5, Motif #6, and Motif #7. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of SEQ ID NO: 109-126 at Kabat positions H31-H37. In some embodiments, Motif #1 comprises the amino acid sequence of 310-315 at Kabat positions H31-H37. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 127-144

or 316-318 at Kabat positions H52-H56. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 127-144 at Kabat positions H52-H56. In some embodiments, Motif #2 comprises the amino acid sequence of SEQ ID NO: 316-318 at Kabat positions H52-H56. In some embodiments, Motif #3 comprises the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 163-180 at Kabat positions H26-H34. In some embodiments, Motif #4 comprises the amino acid sequence of SEQ ID NO: 319-324 at Kabat positions H26-H34. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 181-198 at Kabat positions H49-H56. In some embodiments, Motif #5 comprises the amino acid sequence of SEQ ID NO: 325-334 at Kabat positions H49-H56. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 199-216 at Kabat positions H67-H70. In some embodiments, Motif #6 comprises the amino acid sequence of SEQ ID NO: 335-339 at Kabat positions H67-H70. In some embodiments, Motif #7 comprises the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3 and the VL comprises an amino acid sequence comprising (d) VL CDR1, VL CDR2, and VL CDR3, and (e) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3 and the VL comprises an amino acid sequence comprising (d) VL CDR1, VL CDR2, and VL CDR3, and (e) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O,

PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0171] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising one or more of (a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37; (b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62 and/or the VL comprises an amino acid sequence comprising one or more of (d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34; (e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56; (f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and (g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and the VL comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34 and (b) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region

(VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37; (b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62, and the VL comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34; (b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56; (c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and (d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3 and the VL comprises an amino acid sequence comprising (d) VL CDR1, VL CDR2, and VL CDR3, and (e) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3 and the VL comprises an amino acid sequence comprising (d) VL CDR1, VL CDR2, and VL CDR3, and (e) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL

CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0172] In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising one or more of (a) the amino acid sequence of SEQ ID NO: 310-315 at Kabat positions H31-H37; (b) the amino acid sequence of SEQ ID NO: 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62 and/or the VL comprises an amino acid sequence comprising one or more of (d) the amino acid sequence of SEQ ID NO: 319-324 at Kabat positions H26-H34; (e) the amino acid sequence of SEQ ID NO: 325-334 at Kabat positions H49-H56; (f) the amino acid sequence of SEQ ID NO: 335-339 at Kabat positions H67-H70; and (g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising the amino acid sequence of SEQ ID NO: 316-318 at Kabat positions H52-H56; and the VL comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 319-324 at Kabat positions H26-H34 and (b) the amino acid sequence of SEQ ID NO: 335-339 at Kabat positions H67-H70. In some embodiments, an isolated monoclonal antibody described herein specifically binds to Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence comprising (a) the amino acid sequence of SEQ ID NO: 310-315 at Kabat positions H31-H37; (b) the amino acid sequence of SEQ ID NO: 316-318 at Kabat positions H52-H56; and (c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62, and the VL comprises an amino acid sequence comprising (d) the amino acid sequence of SEQ ID NO: 319-324 at Kabat positions H26-H34; (e) the amino acid sequence of SEQ ID NO: 325-334 at Kabat positions H49-H56; (f) the amino acid sequence of SEQ ID NO: 335-339 at Kabat positions H67-H70; and (g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3 and the VL comprises an amino acid

sequence comprising (d) VL CDR1, VL CDR2, and VL CDR3, and (e) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the VH comprises an amino acid sequence comprising (a) VH CDR1, VH CDR2, and VH CDR3, and (b) one or more of Motif #1, Motif #2, and Motif #3 and the VL comprises an amino acid sequence comprising (d) VL CDR1, VL CDR2, and VL CDR3, and (e) one or more of Motif #4, Motif #5, Motif #6, and Motif #7, wherein the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from the same antibody described herein. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the sequence of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, VL CDR3, Motif #1, Motif #2, Motif #3, Motif #4, Motif #5, Motif #6, and Motif #7 is derived from PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody described herein. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of PCIN63-71I1a, or PCIN63-71L. In some embodiments, the antibody comprises the VH and VL of an antibody described herein. In some embodiments, the antibody comprises the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the antibody comprises the VH and VL of PCIN63-71I1a, or PCIN63-71L.

[0173] In some embodiments, an antibody described herein is not identical to PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0174] In some embodiments, an antibody described herein is markedly different from PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0175] In some embodiments, an antibody described herein comprises a VH CDR3 comprising a sequence that is not identical to the VHCDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0176] In some embodiments, an antibody described herein comprises a VH CDR1, VH CDR2, or VH CDR3 comprising an amino acid sequence that is not identical to the amino acid sequence of VH CDR1, VH CDR2, or VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0177] In some embodiments, an antibody described herein comprises a VL CDR1, VL CDR2, or VL CDR3 comprising an amino acid sequence that is not identical to the amino acid sequence of VL CDR1, VL CDR2, or VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0178] In some embodiments, an antibody described herein comprises a VH comprising an amino acid sequence that is not identical to the amino acid sequence of VH PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0179] In some embodiments, an antibody described herein comprises a VL comprising an amino acid sequence that is not identical to the amino acid sequence of VL PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0180] In some embodiments, an antibody described herein comprises at least one substitution, insertion, or deletion compared to the corresponding amino acid sequence of PCIN63-

66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

[0181] In some embodiments, an isolated monoclonal antibody described herein further comprises heavy and/or light chain constant regions.

[0182] In some embodiments, an isolated monoclonal antibody described herein further comprises human heavy and/or light chain constant regions.

[0183] In some embodiments, the heavy chain constant region is selected from the group consisting of human immunoglobulins IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

[0184] In some embodiments, the heavy chain constant region comprises a native amino acid sequence.

[0185] In some embodiments, the heavy chain constant region comprises a variant amino acid sequence.

[0186] In some embodiments, the antibody is a recombinant antibody, a chimeric antibody, a human antibody, an antibody fragment, a bispecific antibody, a trispecific antibody, or a multispecific antibody.

[0187] In some embodiments, an antibody described herein is a multispecific antibody, e.g. a bispecific antibody. Multispecific antibodies are monoclonal antibodies that have binding specificities for at least two different sites. In some embodiments, one of the binding specificities is for HIV Env and the other is for any other antigen. In some embodiments, bispecific antibodies bind to two different epitopes of HIV Env. Bispecific antibodies can be prepared as full length antibodies or antibody fragments.

[0188] Techniques for making multispecific antibodies, e.g., bispecific antibodies include, but are not limited to, recombinant co-expression of two immunoglobulin heavy chain-light chain pairs having different specificities (see Milstein and Cuello, Nature 305: 537 (1983)), WO 93/08829, and Traunecker et al., EMBO J. 10: 3655 (1991)), and "knob-in-hole" engineering (see, e.g., U.S. Patent No. 5,731,168). Multi-specific antibodies may also be made by engineering electrostatic steering effects for making antibody Fc-heterodimeric molecules (WO 2009/089004A1); cross-linking two or more antibodies or fragments (see, e.g., US Patent No. 4,676,980, and Brennan et al., Science, 229: 81 (1985)); using leucine zippers to produce bi-specific antibodies (see, e.g., Kostelny et al., J. Immunol., 148(5):1547-1553 (1992)); using "diabody" technology for making bispecific antibody fragments (see, e.g., Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993)); and using single-chain Fv (scFv) dimers (see,e.g. Gruber et al., J. Immunol., 152:5368

(1994)); and preparing trispecific antibodies as described, e.g., in Tutt et al. J. Immunol. 147: 60 (1991). Engineered antibodies with three or more functional antigen binding sites, including "Octopus antibodies" and dual variable domain (DVD) immunoglobulins are also included herein (see, e.g. US 2006/0025576A1 and US Patent 10,093,733). The antibody or fragment disclosed herein also includes a "Dual Acting Fab" or "DAF" comprising an antigen binding site that binds to different epitopes, e.g., two different HIV Env epitopes (see, US 2008/0069820, for example).

[0189] In some embodiments, an antibody described herein is a multispecific antibody, e.g. a bispecific antibody comprising a first antigen binding domain comprising a VH domain or VH and VL domains disclosed herein, and a second antigen binding region capable of binding an HIV Env epitope. In one embodiment, the second antigen binding region binds to an HIV Env epitope region different from the HIV Env epitope region bound by an antibody disclosed herein. In one embodiment, the second antigen binding region binds to the high-mannose patch epitope region, V1/V2-glycan site (V2g) epitope region, or gp41 MPER epitope region. In some embodiments, the second antigen binding region binds to the high-mannose patch epitope region (e.g., PGT-121 or an engineered variant thereof). In some embodiments, the second antigen binding region binds to the high-mannose patch epitope region disclosed in International Appl. No. PCT/US2019/43578, filed on July 26, 2016, which is incorporated herein by reference in its entirety for all purposes. In some embodiments, the second antigen binding region binds to the V1/V2-glycan site (V2g) epitope region. In some embodiments, the second antigen binding region binds to the gp41 MPER epitope region.

[0190] In some embodiments, the antibody fragment comprises a single-chain Fv (scFv), F(ab) fragment, F(ab')2 fragment, or an isolated VH domain.

[0191] In some embodiments, the antibody is capable of neutralizing at least two cross-clade isolates of HIV.

[0192] In some embodiments, an antibody described herein specifically binds the Env of at least one HIV isolate in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein specifically binds the Env of 1, 2, 3, 4, 5, 10, 15, 20, or 25 HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein specifically binds the Env of at least 50%, 60%, 70%, 80%, 90%, or 95% of the HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein specifically binds the Env of the 100% of HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an

antibody described herein binds Env at the CD4 receptor binding site (CD4bs) epitope region. In some embodiments, an antibody described herein binds to wild type Env, but does not bind a mutant variant of Env comprising a substitution or deletion in the CD4 receptor binding site.

[0193] In some embodiments, an antibody described herein specifically binds the Env of at least one HIV isolate in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein specifically binds the Env of 1, 2, 3, 4, 5, 10, 15, 20, or 25 HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein specifically binds the Env of at least 50%, 60%, 70%, 80%, 90%, or 95% of the HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein specifically binds the Env of the 100% of HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein binds Env at the CD4 receptor binding site (CD4bs) epitope region. In some embodiments, an antibody described herein binds to wild type Env, but does not bind a mutant variant of Env comprising a substitution or deletion in the CD4 receptor binding site.

[0194] In some embodiments, an antibody described herein is capable of neutralizing at least one HIV isolate in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein is capable of neutralizing at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein is capable of neutralizing 1, 2, 3, 4, 5, 10, 15, 20, or 25 HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein is capable of neutralizing at least 50%, 60%, 70%, 80%, 90%, or 95% of the HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein is capable of neutralizing the 100% of HIV isolates in the indicator virus panel of Figure 8. In some embodiments, the IC50 for neutralizing an HIV isolate is higher than the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution. In some embodiments, the IC50 for neutralizing an HIV isolate is the same as the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution. In some embodiments, the IC50 for neutralizing an HIV isolate is lower than the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution.

[0195] In some embodiments, an antibody described herein is capable of neutralizing at least one HIV isolate in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein is capable of neutralizing at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described

herein is capable of neutralizing 1, 2, 3, 4, 5, 10, 15, 20, or 25 HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein is capable of neutralizing at least 50%, 60%, 70%, 80%, 90%, or 95% of the HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein is capable of neutralizing the 100% of HIV isolates in the indicator virus panel of Figure 9. In some embodiments, the IC50 for neutralizing an HIV isolate is higher than the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution. In some embodiments, the IC50 for neutralizing an HIV isolate is the same as the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution. In some embodiments, the IC50 for neutralizing an HIV isolate is lower than the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution.

[0196] In some embodiments, an antibody described herein specifically binds to Env and is capable of neutralizing at least two isolates of HIV. In some embodiments, an antibody described herein is a broadly neutralizing antibody. In some embodiments, the two isolates are two cross-clade isolates. In some embodiments, an antibody described herein is capable of neutralizing at least one clade A HIV isolate, at least one clade B HIV isolate, and at least one clade C HIV isolate. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 8. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 9. In some embodiments, an antibody described herein is capable of neutralizing the cross-clade HIV isolates with a median IC50 equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing the cross-clade HIV isolates with a mean IC50 equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 8 with a mean IC50 equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 8 with a mean IC50 equal to or less than about 0.8 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 8 with a mean IC50 equal to or less than 0.5 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 80% of cross-clade HIV isolates

in the indicator virus panel of Figure 8 with a mean IC50 equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 9 with a mean IC50 equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 9 with a mean IC50 equal to or less than about 0.8 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 9 with a mean IC50 equal to or less than about 0.5 μg/ml. In some embodiments, an antibody described herein is capable of neutralizing at least about 80% of cross-clade HIV isolates in the indicator virus panel of Figure 9 with a mean IC50 equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml.

[0197] In some embodiments, the IC50 for neutralizing an HIV isolate is higher than the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution. In some embodiments, the IC50 for neutralizing an HIV isolate is the same as the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution. In some embodiments, the IC50 for neutralizing an HIV isolate is lower than the IC50 of neutralizing a corresponding HIV isolate comprising the N276A substitution.

[0198] In another aspect, provided herein are antibodies that bind the same or an overlapping epitope of Env (*e.g.*, an epitope of BG505, JR-FL, YU-2, and JR-CSF Env) as an antibody described herein (*e.g.*, PCIN63-71I1a, or PCIN63-71L). In certain embodiments, the epitope of an antibody can be determined by, *e.g.*, NMR spectroscopy, X-ray diffraction crystallography studies, ELISA assays, hydrogen/deuterium exchange coupled with mass spectrometry (*e.g.*, liquid chromatography electrospray mass spectrometry), array-based oligo-peptide scanning assays, and/or mutagenesis mapping (*e.g.*, site-directed mutagenesis mapping). For X-ray crystallography, crystallization may be accomplished using any of the known methods in the art (*e.g.*, Giegé R *et al.*, (1994) Acta Crystallogr D Biol Crystallogr 50(Pt 4): 339-350; McPherson A (1990) Eur J Biochem 189: 1-23; Chayen NE (1997) Structure 5: 1269-1274; McPherson A (1976) J Biol Chem 251: 6300-6303). Antibody:antigen crystals may be studied using well known X-ray diffraction techniques and may be refined using computer software such as X-PLOR (Yale University, 1992, distributed by Molecular Simulations, Inc.; *see*, e.g., Meth Enzymol (1985) volumes 114 & 115, eds Wyckoff HW *et al.*; U.S. Patent Application No. 2004/0014194), and BUSTER (Bricogne G

(1993) Acta Crystallogr D Biol Crystallogr 49(Pt 1): 37-60; Bricogne G (1997) Meth Enzymol 276A: 361-423, ed Carter CW; Roversi P *et al.*, (2000) Acta Crystallogr D Biol Crystallogr 56(Pt 10): 1316-1323). Mutagenesis mapping studies may be accomplished using any method known to one of skill in the art. *See*, *e.g.*, Champe M *et al.*, (1995) *supra* and Cunningham BC & Wells JA (1989) *supra* for a description of mutagenesis techniques, including alanine scanning mutagenesis techniques. In a specific embodiment, the epitope of an antibody is determined using alanine scanning mutagenesis studies. Usually, binding to the antigen is reduced or disrupted when a residue within the epitope is substituted to alanine. In some embodiments, the Kd of binding to the antigen is increased by about 5-fold, 10-fold, 20-fold, 10-fold or more when a residue within the epitope is substituted for alanine. In some embodiments, binding affinity is determined by ELISA. In addition, antibodies that recognize and bind to the same or overlapping epitopes of Env (*e.g.*, an epitope of BG505, YU-2, JR-FL, and JR-CSF Env) can be identified using routine techniques such as an immunoassay, for example, by showing the ability of one antibody to block the binding of another antibody to a target antigen, *i.e.*, a competitive binding assay.

[0199] In some embodiments, provided herein is an antibody, which immunospecifically binds to the same epitope as an antibody comprising a heavy chain variable region (VH) and light chain variable region (VL) of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, provided herein is an antibody, which immunospecifically binds to the same epitope as an antibody comprising a VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, provided herein is an antibody, which immunospecifically binds to the same epitope as an antibody comprising a VH and VL of PCIN63-71I1a, or PCIN63-71L. In some embodiments, provided herein is an antibody, which immunospecifically binds to the same epitope as an antibody comprising the VH and VL of SEQ ID NO 242 and 260, respectively. In some embodiments, provided herein is an antibody, which immunospecifically binds to the same epitope as an antibody comprising the VH and VL of 245 and 263, respectively. In some embodiments, provided herein is an antibody, which immunospecifically binds to the same epitope as an antibody comprising a VH and VL of PCIN63-71I1a, or PCIN63-71L for specific binding to Env. Assays known to one of skill in the art or described herein (*e.g.*, X-ray crystallography, hydrogen/deuterium exchange coupled with mass spectrometry (e.g., liquid chromatography

electrospray mass spectrometry), alanine scanning, ELISA assays, etc.) can be used to determine if two antibodies bind to the same epitope.

[0200] In another aspect, provided herein are antibodies that compete (*e.g.*, in a dose dependent manner) for binding to Env (*e.g.*, an epitope of BG505, YU-2, JR-FL, and JR-CSF Env) with an antibody described herein (*e.g.*, PCIN63-71I1a, or PCIN63-71L), as determined using assays known to one of skill in the art or described herein (*e.g.*, ELISA competitive assays or surface plasmon resonance). In another aspect, provided herein are antibodies that competitively inhibit (*e.g.*, in a dose dependent manner) an antibody described herein (*e.g.*, PCIN63-71I1a, or PCIN63-71L) from binding to Env (*e.g.*, an epitope of BG505, YU-2, JR-FL, and JR-CSF Env), as determined using assays known to one of skill in the art or described herein (*e.g.*, ELISA competitive assays, or suspension array or surface plasmon resonance assay).

[0201] In some embodiments, an antibody described herein competes for binding to Env with an antibody disclosed herein. In some embodiments, an antibody described herein competes for binding to Env with an antibody comprising the VH and VL of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, an antibody described herein competes for binding to Env with an antibody comprising the VH and VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, an antibody described herein competes for binding to Env with an antibody comprising the VH and VL of PCIN63-71I1a, or PCIN63-71L. In some embodiments, an antibody described herein competes for binding to Env with an antibody comprising the VH and VL of SEQ ID NO 242 and 260, respectively. In some embodiments, an antibody described herein competes for binding to Env with an antibody comprising the VH and VL of 245 and 263, respectively. In some embodiments, the Env is BG505 Env. In some embodiments, the Env is YU-2 Env. In some embodiments, the Env is JR-FL Env. In some embodiments, the Env is JR-CSF Env.

[0202] In certain embodiments, the epitope of an antibody described herein is used as an immunogen to produce antibodies.

[0203] In one aspect, provided herein are methods for producing an engineered variant of an antibody described herein. In some embodiments, a method for producing an engineered variant comprises directed-evolution and yeast display. Methods for producing an engineered antibody are

known to those skilled in the art, for example, as described in International Appl. No. PCT/US2019/43578, filed on July 26, 2016, which is incorporated herein by reference in its entirety for all purposes. In some embodiments, an engineered antibody possesses one or more improved properties, for example, higher binding affinity to target antigen, higher binding affinity to target antigen at low pH, increased median neutralization IC_{50} potency, and increased breadth of neutralization compared to the parent antibody.

[0204] In some embodiments, a method of producing an engineered variant of a parent antibody comprises substituting one or more amino acid residues of the VH; and/or substituting one or more amino acid residues of the VL to create an engineered variant antibody, and producing the engineered variant antibody. In some embodiments, the parent antibody is an antibody described herein. In some embodiments, the parent antibody is PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D. In some embodiments, the parent antibody is PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C. In some embodiments, the parent antibody is PCIN63-71I1a, or PCIN63-71L. In some embodiments, the method further comprises determining that the engineered variant antibody has improved properties, for example, by determining the engineered variant antibody's binding affinity to target antigen, binding affinity to target antigen at low pH, median neutralization IC_{50} potency, or breadth of neutralization compared to the parent antibody.

[0205] The affinity or avidity of an antibody or fusion polypeptide for an antigen can be determined experimentally using any suitable method well known in the art, e.g., flow cytometry, enzyme-linked immunoabsorbent assay (ELISA), or radioimmunoassay (RIA), or kinetics (e.g., BIACORE™ analysis). Direct binding assays as well as competitive binding assay formats can be readily employed. (See, for example, Berzofsky, et al., "Antibody-Antigen Interactions," In Fundamental Immunology, Paul, W. E., Ed., Raven Press: New York, N.Y. (1984); Kuby, Janis Immunology, W. H. Freeman and Company: New York, N.Y. (1992); and methods described herein. The measured affinity of a particular antibody-antigen interaction can vary if measured under different conditions (e.g., salt concentration, pH, temperature). Thus, measurements of affinity and other antigen-binding parameters (e.g., Kd, Kon, Koff) are made with standardized solutions of antibody and antigen, and a standardized buffer, as known in the art and such as the buffer described herein.

[0206] In some embodiments, the broadly neutralizing anti-Env antibody described herein is a monoclonal antibody. Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein (1975) Nature 256:495. Using the hybridoma method, a bovine host (e.g., cow) is immunized to elicit the production by lymphocytes of antibodies that will specifically bind to an immunizing antigen. Lymphocytes can also be immunized *in vitro*. Following immunization, the lymphocytes are isolated and fused with a suitable myeloma cell line using, for example, polyethylene glycol, to form hybridoma cells that can then be selected away from unfused lymphocytes and myeloma cells. Hybridomas that produce monoclonal antibodies directed specifically against a chosen antigen as determined by immunoprecipitation, immunoblotting, or by an *in vitro* binding assay (e.g., radioimmunoassay (RIA); enzyme-linked immunosorbent assay (ELISA)) can then be propagated either *in vitro* culture using standard methods (Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, 1986) or in vivo as ascites tumors in an animal. The monoclonal antibodies can then be purified from the culture medium or ascites fluid using any method known in the art.

[0207] Alternatively monoclonal antibodies can also be made using recombinant DNA methods as described in U.S. Patent 4,816,567. The polynucleotides encoding a monoclonal antibody are isolated from mature B-cells or hybridoma cells, such as by RT-PCR using oligonucleotide primers that specifically amplify the genes encoding the heavy and light chains of the antibody, and their sequence is determined using conventional procedures. The isolated polynucleotides encoding the heavy and light chains are then cloned into suitable expression vectors, which when transfected into host cells such as *E. coli* cells, simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, monoclonal antibodies are generated by the host cells. Also, recombinant monoclonal antibodies or fragments thereof of the desired species can be isolated from phage display libraries expressing CDRs of the desired species as described (McCafferty et al., 1990, Nature, 348:552-554; Clackson et al., 1991, Nature, 352:624-628; and Marks et al., 1991, J. Mol. Biol., 222:581-597).

[0208] The polynucleotide(s) encoding a monoclonal antibody can further be modified in a number of different manners using recombinant DNA technology to generate alternative antibodies. In some embodiments, the constant domains of the light and heavy chains of, for example, a mouse monoclonal antibody can be substituted 1) for those regions of, for example, a human antibody to generate a chimeric antibody or 2) for a non-immunoglobulin polypeptide to generate a fusion antibody. In some embodiments, the constant regions are truncated or removed

to generate the desired antibody fragment of a monoclonal antibody. Site-directed or high-density mutagenesis of the variable region can be used to optimize specificity, affinity, etc. of a monoclonal antibody.

[0209] Methods for engineering, humanizing or resurfacing non-human or human antibodies can also be used and are well known in the art. A humanized, resurfaced or similarly engineered antibody can have one or more amino acid residues from a source that is non-human, e.g., but not limited to, mouse, rat, rabbit, non-human primate or other mammal. These non-human amino acid residues are replaced by residues that are often referred to as "import" residues, which are typically taken from an "import" variable, constant or other domain of a known human sequence.

[0210] Such imported sequences can be used to reduce immunogenicity or reduce, enhance or modify binding, affinity, on-rate, off-rate, avidity, specificity, half-life, or any other suitable characteristic, as known in the art. In general, the CDR residues are directly and most substantially involved in influencing antibody binding. Accordingly, part or all of the non-human or human CDR sequences are maintained while the non-human sequences of the variable and constant regions can be replaced with human or other amino acids.

[0211] Antibodies can also optionally be humanized, resurfaced, engineered or human antibodies engineered with retention of high affinity for the antigen and other favorable biological properties. To achieve this goal, humanized (or human) or engineered antibodies and resurfaced antibodies can be optionally prepared by a process of analysis of the parental sequences and various conceptual humanized and engineered products using three-dimensional models of the parental, engineered, and humanized sequences. Three-dimensional immunoglobulin models are commonly available and are familiar to those skilled in the art. Computer programs are available which illustrate and display probable three-dimensional conformational structures of selected candidate immunoglobulin sequences. Inspection of these displays permits analysis of the likely role of the residues in the functioning of the candidate immunoglobulin sequence, i.e., the analysis of residues that influence the ability of the candidate immunoglobulin to bind its antigen. In this way, framework (FR) residues can be selected and combined from the consensus and import sequences so that the desired antibody characteristic, such as increased affinity for the target antigen(s), is achieved.

[0212] Humanization, resurfacing or engineering of antibodies described herein can be performed using any known method, such as but not limited to those described in, Winter (Jones et al., Nature 321:522 (1986); Riechmann et al., Nature 332:323 (1988); Verhoeyen et al., Science 239:1534

(1988)), Sims et al., J. Immunol. 151: 2296 (1993); Chothia and Lesk, J. Mol. Biol. 196:901 (1987), Carter et al., Proc. Natl. Acad. Sci. U.S.A. 89:4285 (1992); Presta et al., J. Immunol. 151:2623 (1993), U.S. Pat. Nos. 5,639,641, 5,723,323; 5,976,862; 5,824,514; 5,817,483; 5,814,476; 5,763,192; 5,723,323; 5,766,886; 5,714,352; 6,204,023; 6,180,370; 5,693,762; 5,530,101; 5,585,089; 5,225,539; 4,816,567; PCT/: US98/16280; US96/18978; US91/09630; US91/05939; US94/01234; GB89/01334; GB91/01134; GB92/01755; WO90/14443; WO90/14424; WO90/14430; EP 229246; 7,557,189; 7,538,195; and 7,342,110, each of which is entirely incorporated herein by reference, including the references cited therein.

[0213] In certain alternative embodiments, the antibody is a human antibody. Human antibodies can be directly prepared using various techniques known in the art. Human antibodies can be isolated from suitable donors following the methods described herein. Immortalized human B lymphocytes immunized *in vitro* or isolated from an immunized individual that produce an antibody directed against a target antigen can be generated (*See*, *e.g.*, Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, p. 77 (1985); Boemer et al., 1991, J. Immunol., 147 (1):86-95; and U.S. Patent 5,750,373). Also, the human antibody can be selected from a phage library, where that phage library expresses human antibodies, as described, for example, in Vaughan et al., 1996, Nat. Biotech., 14:309-314, Sheets et al., 1998, Proc. Nat'l. Acad. Sci., 95:6157-6162, Hoogenboom and Winter, 1991, J. Mol. Biol., 227:381, and Marks et al., 1991, J. Mol. Biol., 222:581). Techniques for the generation and use of antibody phage libraries are also described in U.S. Patent Nos. 5,969,108, 6,172,197, 5,885,793, 6,521,404; 6,544,731; 6,555,313; 6,582,915; 6,593,081; 6,300,064; 6,653,068; 6,706,484; and 7,264,963; and Rothe et al., 2007, J. Mol. Bio., doi:10.1016/j.jmb.2007.12.018 (each of which is incorporated by reference in its entirety). Affinity maturation strategies and chain shuffling strategies (Marks et al., 1992, Bio/Technology 10:779-783, incorporated by reference in its entirety) are known in the art and can be employed to generate high affinity human antibodies.

[0214] In certain embodiments an antibody fragment is provided. Various techniques are known for the production of antibody fragments. Traditionally, these fragments are derived via proteolytic digestion of intact antibodies (for example Morimoto et al., 1993, Journal of Biochemical and Biophysical Methods 24:107-117; Brennan et al., 1985, Science, 229:81). In certain embodiments, antibody fragments are produced recombinantly. Fab, Fv, and scFv antibody fragments can all be expressed in and secreted from *E. coli* or other host cells, thus allowing the production of large amounts of these fragments. Such antibody fragments can also be isolated from antibody phage libraries. The antibody fragment can also be linear antibodies as described in U.S.

Patent 5,641,870, for example, and can be monospecific or bispecific. Other techniques for the production of antibody fragments will be apparent to the skilled practitioner.

[0215] In certain embodiments, the variable domains in both the heavy and light chains are altered by at least partial replacement of one or more CDRs and, if necessary, by partial framework region replacement and sequence changing. Although the CDRs can be derived from an antibody of the same class or even subclass as the antibody from which the framework regions are derived, it is envisaged that the CDRs will be derived from an antibody of different class and in certain embodiments from an antibody from a different species. It may not be necessary to replace all of the CDRs with the complete CDRs from the donor variable region to transfer the antigen-binding capacity of one variable domain to another. Rather, it may only be necessary to transfer those residues that are necessary to maintain the activity of the antigen-binding site. Given the explanations set forth in U.S. Pat. Nos. 5,585,089, 5,693,761 and 5,693,762, it will be well within the competence of those skilled in the art, either by carrying out routine experimentation or by trial and error testing to obtain a functional antibody with reduced immunogenicity.

[0216] Alterations to the variable region notwithstanding, those skilled in the art will appreciate that the modified antibodies described herein will comprise antibodies (e.g., full-length antibodies or immunoreactive fragments thereof) in which at least a fraction of one or more of the constant region domains has been deleted or otherwise altered so as to provide desired biochemical characteristics such as increased serum half-life when compared with an antibody of approximately the same immunogenicity comprising a native or unaltered constant region. In some embodiments, the constant region of the modified antibodies will comprise a human constant region. Modifications to the constant region compatible with this invention comprise additions, deletions or substitutions of one or more amino acids in one or more domains. That is, the modified antibodies described herein can comprise alterations or modifications to one or more of the three heavy chain constant domains (CH1, CH2 or CH3) and/or to the light chain constant domain (CL). In some embodiments, modified constant regions wherein one or more domains are partially or entirely deleted are contemplated. In some embodiments, the modified antibodies will comprise domain deleted constructs or variants wherein the entire CH2 domain has been removed (ΔCH2 constructs). In some embodiments, the omitted constant region domain will be replaced by a short amino acid spacer (e.g., 10 residues) that provides some of the molecular flexibility typically imparted by the absent constant region.

[0217] It will be noted that in certain embodiments, the modified antibodies can be engineered to fuse the CH3 domain directly to the hinge region of the respective modified

antibodies. In other constructs it may be desirable to provide a peptide spacer between the hinge region and the modified CH2 and/or CH3 domains. For example, compatible constructs could be expressed wherein the CH2 domain has been deleted and the remaining CH3 domain (modified or unmodified) is joined to the hinge region with a 5-20 amino acid spacer. Such a spacer can be added, for instance, to ensure that the regulatory elements of the constant domain remain free and accessible or that the hinge region remains flexible. However, it should be noted that amino acid spacers can, in some cases, prove to be immunogenic and elicit an unwanted immune response against the construct. Accordingly, in certain embodiments, any spacer added to the construct will be relatively non-immunogenic, or even omitted altogether, so as to maintain the desired biochemical qualities of the modified antibodies.

[0218] Besides the deletion of whole constant region domains, it will be appreciated that the antibodies described herein can be provided by the partial deletion or substitution of a few or even a single amino acid. For example, it may be desirable to simply delete that part of one or more constant region domains that control the effector function (e.g., complement C1Q binding) to be modulated. Such partial deletions of the constant regions can improve selected characteristics of the antibody (serum half-life) while leaving other desirable functions associated with the subject constant region domain intact. Moreover, as alluded to above, the constant regions of the disclosed antibodies can be modified through the mutation or substitution of one or more amino acids that enhances the profile of the resulting construct. In this respect it may be possible to disrupt the activity provided by a conserved binding site (e.g., Fc binding) while substantially maintaining the configuration and immunogenic profile of the modified antibody. Certain embodiments can comprise the addition of one or more amino acids to the constant region to enhance desirable characteristics such as decreasing or increasing effector function or provide for more cytotoxin or carbohydrate attachment. In such embodiments it can be desirable to insert or replicate specific sequences derived from selected constant region domains.

[0219] The half-life of an IgG is mediated by its pH-dependent binding to the neonatal receptor FcRn. In some embodiments, an antibody described herein comprises a variant Fc region that has been modified to enhance binding to FcRn (see, e.g., Petkova et al., Int. Immunol. 18: 1759-1769 (2006); Dall'Acqua et al., J. Immunol.169: 5171-5180 (2002); Oganesyan et al., Mol. Immunol. 46: 1750-1755 (2009); Dall'Acqua et al., J. Biol. Chem. 281: 23514-23524 (2006), Hinton et al., J. Immunol. 176: 346-356 (2006); Datta-Mannan et al., Drug Metab. Dispos. 35: 86-94 (2007); Datta-Mannan et al., J. Biol. Chem. 282: 1709-1717 (2007); WO 06/130834; Strohl,

Curr. Op. Biotechnol. 20: 685-691 (2009); and Yeung et al., J. Immunol. 182: 7663-7671 (2009), the contents of each of which is herein incorporated by reference in its entirety).

[0220] In some embodiments, an antibody described herein comprises a variant Fc region that has been modified to have a selective affinity for FcRn at pH 6.0, but not pH 7.4. By way of example, the variant Fc region contains one or more of the following modifications that increase half-life: IgG1-M252Y, S254T, T256E; IgG1-T250Q, M428L; IgG1-M428L and N434S (the "LS" mutation); IgG1-H433K, N434Y; IgG1-N434A; and IgG1-T307A, E380A, N434A; wherein the numbering of the residues is that of the EU index of Kabat et al. (Kabat et al., Sequences of Proteins of Immunological Interest, 1991 Fifth edition, herein incorporated by reference).

[0221] In some embodiments, an antibody described herein comprises a variant Fc region that has been modified to reduce its effector functions. In some embodiments, the variant Fc region comprises the L234A, L235A hinge region substitutions, wherein the numbering of the residues is that of the EU index of Kabat et al.

[0222] In some embodiments, an antibody described herein comprises an Fc region having a carbohydrate structure that lacks fucose attached (directly or indirectly) to the Fc region or has a reduced level of fucosylation. In some embodiments, a fucosylation variant antibody has improved ADCC function. See, e.g., US Patent Publication Nos. US 2003/0157108; US 2004/0093621, each of which is incorporated by reference herein in its entirety. Examples of publications related to "defucosylated" or "fucose-deficient" antibody variants include: US 2003/0157108; WO 2000/61739; WO 2001/29246; US 2003/0115614; US 2002/0164328; US 2004/0093621; US 2004/0132140; US 2004/0110704; US 2004/0110282; US 2004/0109865; WO 2003/085119; WO 2003/084570; WO 2005/035586; WO 2005/035778; WO2005/053742; WO2002/031140; Okazaki et al. J. Mol. Biol. 336:1239-1249 (2004); Yamane-Ohnuki et al. Biotech. Bioeng. 87: 614 (2004), each of which is incorporated by reference herein in its entirety. Examples of cell lines capable of producing defucosylated antibodies include Lec 13 CHO cells deficient in protein fucosylation (Ripka et al. Arch. Biochem. Biophys. 249:533-545 (1986); US Pat Appl No US 2003/0157108 A1; and WO 2004/056312), and knockout cell lines, such as alpha-1,6-fucosyltransferase gene, FUT8, knockout CHO cells (see, e.g., Yamane-Ohnuki et al. Biotech. Bioeng. 87: 614 (2004); Kanda, Y. et al., Biotechnol. Bioeng., 94(4):680-688 (2006); and WO2003/085107), each of which is incorporated by reference herein in its entirety.

[0223] In some embodiment, an antibody described herein comprises bisected oligosaccharides, in which a biantennary oligosaccharide attached to the Fc region of the antibody is bisected by GlcNAc. In some embodiment, an antibody comprising bisected oligosaccharides

has reduced fucosylation and/or improved ADCC function. See, e.g., WO 2003/011878; U.S. Pat. No. 6,602,684; and US 2005/0123546, each of which is incorporated by reference herein in its entirety. In some embodiment, an antibody described herein comprises at least one galactose residue in the oligosaccharide attached to the Fc region. Such antibody variants may have improved CDC function. See, e.g., in WO 1997/30087; WO 1998/58964; and WO 1999/22764, each of which is incorporated by reference herein in its entirety.

[0224] In some embodiments, an antibody described herein comprises a variant Fc region comprising a combination of substitutions with increased binding to FcRn and Fc gamma RIIIa. The combinations increase antibody half-life and ADCC. For example, such combination include antibodies with the following amino acid substitution in the Fc region: (1) S239D/I332E and T250Q/M428L; (2) S239D/I332E and M428L/N434S; (3) S239D/I332E and N434A; (4) S239D/I332E and T307A/E380A/N434A; (5) S239D/I332E and M252Y/S254T/T256E; (6) S239D/A330L/I332E and 250Q/M428L; (7) S239D/A330L/I332E and M428L/N434S; (8) S239D/A330L/I332E and N434A; (9) S239D/A330L/I332E and T307A/E380A/N434A; or (10) S239D/A330L/I332E and M252Y/S254T/T256E, wherein the numbering of the residues is that of the EU index of Kabat et al. In some embodiments, an antibody comprising the variant Fc region is directly cytotoxic to infected cells, or uses natural defenses such as complement, antibody dependent cellular cytotoxicity (ADCC), or phagocytosis by macrophages.

[0225] The present invention further embraces variants and equivalents which are substantially homologous to the chimeric, humanized and human antibodies, or antibody fragments thereof, set forth herein. These can contain, for example, conservative substitution mutations, i.e., the substitution of one or more amino acids by similar amino acids. For example, conservative substitution refers to the substitution of an amino acid with another within the same general class such as, for example, one acidic amino acid with another acidic amino acid, one basic amino acid with another basic amino acid or one neutral amino acid by another neutral amino acid. What is intended by a conservative amino acid substitution is well known in the art.

[0226] The polypeptides provided herein can be recombinant polypeptides, natural polypeptides, or synthetic polypeptides comprising an antibody, or fragment thereof. It will be recognized in the art that some amino acid sequences described herein can be varied without significant effect of the structure or function of the protein. Thus, the invention further includes variations of the polypeptides which show substantial activity or which include regions of an antibody, or fragment thereof, against a human folate receptor protein. Such mutants include deletions, insertions, inversions, repeats, and type substitutions.

[0227] The polypeptides and analogs can be further modified to contain additional chemical moieties not normally part of the protein. Those derivatized moieties can improve the solubility, the biological half-life or absorption of the protein. The moieties can also reduce or eliminate any desirable side effects of the proteins and the like. An overview for those moieties can be found in REMINGTON'S PHARMACEUTICAL SCIENCES, 21th ed., Mack Publishing Co., Easton, PA (2005).

III. Polynucleotides

[0228] In certain aspects, provided herein are polynucleotides comprising a nucleotide sequence or nucleotide sequences encoding a broadly neutralizing anti-Env antibody described herein or a fragment thereof and vectors, *e.g.*, vectors comprising such polynucleotides. In some embodiments, the vectors can be used for recombinant expression of an antibody described herein in host cells (*e.g.*, *E. coli* and mammalian cells). In some embodiments, the vectors can be used for administration of an antibody described herein to a patient in need thereof.

[0229] In one aspect, provided herein are isolated polynucleotides encoding the heavy chain variable region or heavy chain of an antibody described herein.

[0230] In one aspect, provided herein are isolated polynucleotides encoding the light chain variable region or light chain of an antibody described herein.

[0231] In one aspect, provided herein are isolated polynucleotides encoding the heavy chain variable region or heavy chain of an antibody described herein and the light chain variable region or light chain of an antibody described herein.

[0232] In some embodiments, the polynucleotide encodes a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 235-252.

[0233] In some embodiments, the polynucleotide encodes a light chain variable region comprising the amino acid sequence of SEQ ID NO: 253-270.

[0234] In some embodiments, an isolated polynucleotide described herein encodes a broadly neutralizing antibody described herein and comprises an mRNA. In some embodiments, the mRNA comprises at least one modified nucleotide. In some embodiments, a modified mRNA encoding an antibody described herein is for administering to a subject to treat or prevent HIV infection.

[0235] As used herein, an "isolated" polynucleotide or nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source (*e.g.*, in a mouse or a human) of the nucleic acid molecule. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium

when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. For example, the language "substantially free" includes preparations of polynucleotide or nucleic acid molecule having less than about 15%, 10%, 5%, 2%, 1%, 0.5%, or 0.1% (in particular less than about 10%) of other material, *e.g.*, cellular material, culture medium, other nucleic acid molecules, chemical precursors and/or other chemicals. In a specific embodiment, a nucleic acid molecule(s) encoding an antibody or fusion polypeptide described herein is isolated or purified.

[0236] In particular aspects, provided herein are polynucleotides comprising nucleotide sequences encoding antibodies described herein, as well as antibodies that compete with such antibodies for binding to HIV, or which binds to the same epitope as that of such antibodies.

[0237] In certain aspects, provided herein are polynucleotides comprising a nucleotide sequence encoding the light chain or heavy chain of an antibody described herein. The polynucleotides can comprise nucleotide sequences encoding a light chain comprising the VL of antibodies described herein. The polynucleotides can comprise nucleotide sequences encoding a heavy chain comprising the VH of antibodies described herein. In specific embodiments, a polynucleotide described herein encodes a VH domain comprising the amino acid sequence set forth in SEQ ID NO: 235-252. In specific embodiments, a polynucleotide described herein encodes a VL domain comprising the amino acid sequence set forth in SEQ ID NO: 253-270. In some embodiments, the antibody is a human antibody. In some embodiments, the antibody is a chimeric antibody.

[0238] In particular embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding a broadly neutralizing anti-Env antibody comprising three VL chain CDRs, *e.g.*, containing VL CDR1, VL CDR2, and VL CDR3 of any one of antibodies described herein. In specific embodiments, provided herein are polynucleotides comprising three VH chain CDRs, *e.g.*, containing VH CDR1, VH CDR2, and VH CDR3 of any one of antibodies described herein. In specific embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding an anti-Env antibody comprising three VL CDRs, *e.g.*, containing VL CDR1, VL CDR2, and VL CDR3 of any one of antibodies described herein and three VH chain CDRs, *e.g.*, containing VH CDR1, VH CDR2, and VH CDR3 of any one of antibodies described herein. In some embodiments, the antibody is a human antibody.

[0239] In particular embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding a broadly neutralizing anti-Env antibody comprising three VL chain CDRs, *e.g.*, containing VL CDR1, VL CDR2, and VL CDR3 of any one of antibodies described

herein. In some embodiment, the antibody comprises a VL, wherein the VL comprises an amino acid sequence comprising one or more of Motifs #4, #5, #6, and #7 (comprising the amino acid sequence of SEQ ID NO: 163-180 or 319-324, 181-198 or 325-334, 199-216 or 335-339, and 217-234, respectively). In some embodiment, the antibody comprises a VL, wherein the VL comprises an amino acid sequence comprising Motifs #4, #5, #6, and #7.

[0240] In particular embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding a broadly neutralizing anti-Env antibody comprising three VH chain CDRs, *e.g.*, containing VH CDR1, VH CDR2, and VH CDR3 of any one of antibodies described herein. In some embodiment, the antibody comprises a VH, wherein the VH comprises an amino acid sequence comprising one or more of Motifs #1, #2, and #3 (comprising the amino acid sequence of SEQ ID NO: 109-126 or 310-315, 127-144 or 316-318, and 145-162, respectively). In some embodiment, the antibody comprises a VH, wherein the VH comprises an amino acid sequence comprising Motifs #1, #2, and #3.

[0241] In particular embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding a broadly neutralizing anti-Env antibody comprising three VL CDRs, *e.g.*, containing VL CDR1, VL CDR2, and VL CDR3 of any one of antibodies described herein and three VH chain CDRs, *e.g.*, containing VH CDR1, VH CDR2, and VH CDR3 of any one of antibodies described herein. In some embodiment, the antibody comprises a VL and a VH, wherein the VL comprises an amino acid sequence comprising one or more of Motifs #4, #5, #6, and #7 (comprising the amino acid sequence of SEQ ID NO: 163-180 or 319-324, 181-198 or 325-334, 199-216 or 335-339, and 217-234, respectively), and/or the VH comprises an amino acid sequence comprising one or more of Motifs #1, #2, and #3 (comprising the amino acid sequence of SEQ ID NO: 109-126 or 310-315, 127-144 or 316-318, and 145-162, respectively). In some embodiment, the antibody comprises a VL and a VH, wherein the VL comprises an amino acid sequence comprising Motifs #4, and #6, and the VH comprises an amino acid sequence comprising Motifs #2. In some embodiment, the antibody comprises a VL and a VH, wherein the VL comprises an amino acid sequence comprising Motifs #4, #5, #6, and #7 (comprising the amino acid sequence of SEQ ID NO: 163-180 or 319-324, 181-198 or 325-334, 199-216 or 335-339, and 217-234, respectively), and the VH comprises an amino acid sequence comprising Motifs #1, #2, and #3 (comprising the amino acid sequence of SEQ ID NO: 109-126 or 310-315, 127-144 or 316-318, and 145-162, respectively).

[0242] In some embodiments, provided herein are polynucleotides comprising a nucleotide sequence encoding a broadly neutralizing anti-Env antibody comprising the VH CDR3

of an antibody described herein. In some embodiments, the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54. In some embodiments, the antibody is a human antibody.

[0243] In specific embodiments, a polynucleotide provided herein comprises a nucleotide sequence encoding an antibody or fragment thereof described herein comprising: framework regions (*e.g.*, framework regions of the VL domain and VH domain) that are human framework regions, wherein the antibody immunospecifically binds Env. In certain embodiments, a polynucleotide provided herein comprises a nucleotide sequence encoding an antibody or fragment thereof (*e.g.*, CDRs or variable domain) described herein.

[0244] In specific aspects, provided herein is a polynucleotide comprising a nucleotide sequence encoding an antibody comprising a light chain and a heavy chain, *e.g.*, a separate light chain and heavy chain. With respect to the light chain, in a specific embodiment, a polynucleotide provided herein comprises a nucleotide sequence encoding a kappa light chain. In another specific embodiment, a polynucleotide provided herein comprises a nucleotide sequence encoding a lambda light chain. In yet another specific embodiment, a polynucleotide provided herein comprises a nucleotide sequence encoding an antibody described herein comprising a human kappa light chain or a human lambda light chain. In a particular embodiment, a polynucleotide provided herein comprises a nucleotide sequence encoding an antibody, which immunospecifically binds to Env, wherein the antibody comprises a light chain, and wherein the amino acid sequence of the VL domain can comprise the amino acid sequence set forth herein, and wherein the constant region of the light chain comprises the amino acid sequence of a human kappa light chain constant region. In another particular embodiment, a polynucleotide provided herein comprises a nucleotide sequence encoding an antibody, which immunospecifically binds to Env, and comprises a light chain, wherein the amino acid sequence of the VL domain can comprise the amino acid sequence set forth herein, and wherein the constant region of the light chain comprises the amino acid sequence of a human lambda light chain constant region. For example, human constant region sequences can be those described in U.S. Patent No. 5,693,780.

[0245] In a particular embodiment, a polynucleotide provided herein comprises a nucleotide sequence encoding an antibody described herein, which immunospecifically binds to Env, wherein the antibody comprises a heavy chain, wherein the amino acid sequence of the VH domain can comprise the amino acid sequence of SEQ I DNO: 235-252, and wherein the constant region of the heavy chain comprises the amino acid sequence of a human alpha or gamma heavy chain constant region.

[0246] In yet another specific embodiment, a polynucleotide provided herein comprises a nucleotide sequence encoding an antibody described herein, which immunospecifically binds Env, wherein the antibody comprises a VL domain and a VH domain comprising any amino acid sequences described herein, and wherein the constant regions comprise the amino acid sequences of the constant regions of a human IgA_1, human IgA_2 ' human IgG_1 (*e.g.*, allotype 1, 17, or 3), human IgG_2, or human IgG_4.

[0247] In yet another specific embodiment, a polynucleotide provided herein comprises a nucleotide sequences encoding an anti-Env antibody or a fragment thereof that are optimized, *e.g.*, by codon/RNA optimization, replacement with heterologous signal sequences, and elimination of mRNA instability elements. Methods to generate optimized nucleic acids encoding an anti-Env antibody or a fragment thereof (*e.g.*, light chain, heavy chain, VH domain, or VL domain) for recombinant expression by introducing codon changes and/or eliminating inhibitory regions in the mRNA can be carried out by adapting the optimization methods described in, *e.g.*, U.S. Patent Nos. 5,965,726; 6,174,666; 6,291,664; 6,414,132; and 6,794,498, accordingly. For example, potential splice sites and instability elements (*e.g.*, A/T or A/U rich elements) within the RNA can be mutated without altering the amino acids encoded by the nucleic acid sequences to increase stability of the RNA for recombinant expression. The alterations utilize the degeneracy of the genetic code, *e.g.*, using an alternative codon for an identical amino acid. In some embodiments, it can be desirable to alter one or more codons to encode a conservative mutation, *e.g.*, a similar amino acid with similar chemical structure and properties and/or function as the original amino acid.

[0248] In certain embodiments, an optimized polynucleotide sequence encoding an anti-Env antibody described herein or a fragment thereof (*e.g.*, VL domain or VH domain) can hybridize to an antisense (*e.g.*, complementary) polynucleotide of an unoptimized polynucleotide sequence encoding an anti-Env antibody described herein or a fragment thereof (*e.g.*, VL domain or VH domain). In specific embodiments, an optimized nucleotide sequence encoding an anti-Env antibody described herein or a fragment hybridizes under high stringency conditions to antisense polynucleotide of an unoptimized polynucleotide sequence encoding an anti-Env antibody described herein or a fragment thereof. In a specific embodiment, an optimized nucleotide sequence encoding an anti-Env antibody described herein or a fragment thereof hybridizes under high stringency, intermediate or lower stringency hybridization conditions to an antisense polynucleotide of an unoptimized nucleotide sequence encoding an anti-Env antibody described herein or a fragment thereof. Information regarding hybridization conditions has been described,

see, *e.g.*, U.S. Patent Application Publication No. US 2005/0048549 (*e.g.*, paragraphs 72-73), which is incorporated herein by reference.

[0249] The polynucleotides can be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. Nucleotide sequences encoding antibodies described herein, and modified versions of these antibodies can be determined using methods well known in the art, *i.e.*, nucleotide codons known to encode particular amino acids are assembled in such a way to generate a nucleic acid that encodes the antibody. Such a polynucleotide encoding the antibody can be assembled from chemically synthesized oligonucleotides (*e.g.*, as described in Kutmeier G *et al.*, (1994), BioTechniques 17: 242-246), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

[0250] Alternatively, a polynucleotide encoding an antibody or fragment thereof described herein can be generated from nucleic acid from a suitable source (*e.g.*, PBMCs) using methods well known in the art (*e.g.*, PCR and other molecular cloning methods). For example, PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of a known sequence can be performed using genomic DNA obtained from hybridoma cells producing the antibody of interest. Such PCR amplification methods can be used to obtain nucleic acids comprising the sequence encoding the light chain and/or heavy chain of an antibody. Such PCR amplification methods can be used to obtain nucleic acids comprising the sequence encoding the variable light chain region and/or the variable heavy chain region of an antibody. The amplified nucleic acids can be cloned into vectors for expression in host cells and for further cloning, for example, to generate chimeric and humanized antibodies.

[0251] If a clone containing a nucleic acid encoding a particular antibody or fragment thereof is not available, but the sequence of the antibody molecule or fragment thereof is known, a nucleic acid encoding the immunoglobulin or fragment can be chemically synthesized or obtained from a suitable source (*e.g.*, an antibody cDNA library or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody described herein) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, *e.g.*, a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR can then be cloned into replicable cloning vectors using any method well known in the art.

[0252] DNA encoding anti-Env antibodies described herein can be readily isolated and sequenced using conventional procedures (*e.g.*, by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of the anti-Env antibodies). PBMCs can serve as a source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as *E. coli* cells, simian COS cells, Chinese hamster ovary (CHO) cells (*e.g.*, CHO cells from the CHO GS System™ (Lonza)), or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of anti-Env antibodies in the recombinant host cells.

[0253] The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains with a coding sequence for a non-immunoglobulin polypeptide, or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide.

[0254] Also provided are polynucleotides that hybridize under high stringency, intermediate or lower stringency hybridization conditions to polynucleotides that encode an antibody described herein. In specific embodiments, polynucleotides described herein hybridize under high stringency, intermediate or lower stringency hybridization conditions to polynucleotides encoding a VH domain and/or VL domain provided herein.

[0255] Hybridization conditions have been described in the art and are known to one of skill in the art. For example, hybridization under stringent conditions can involve hybridization to filter-bound DNA in 6x sodium chloride/sodium citrate (SSC) at about 45°C followed by one or more washes in 0.2xSSC/0.1% SDS at about 50-65°C; hybridization under highly stringent conditions can involve hybridization to filter-bound nucleic acid in 6xSSC at about 45°C followed by one or more washes in 0.1xSSC/0.2% SDS at about 68°C. Hybridization under other stringent hybridization conditions are known to those of skill in the art and have been described, see, for example, Ausubel FM *et al.*, eds., (1989) Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc. and John Wiley & Sons, Inc., New York at pages 6.3.1-6.3.6 and 2.10.3.

IV. Vectors, Cells, and Methods of Producing a Broadly Neutralizing Agent

[0256] In certain aspects, provided herein are cells (*e.g.*, host cells) expressing (*e.g.*, recombinantly) antibodies described herein which specifically bind to Env and related polynucleotides and expression vectors. Provided herein are vectors (*e.g.*, expression vectors) comprising polynucleotides comprising nucleotide sequences encoding anti-Env antibodies or a fragment thereof described herein. In some embodiments, the vectors can be used for recombinant

expression of an antibody described herein in host cells (*e.g.*, mammalian cells). In some embodiments, the vectors can be used for administration of an antibody described herein to a patient in need thereof. Also provided herein are host cells comprising such vectors for recombinantly expressing anti-Env antibodies described herein. In a particular aspect, provided herein are methods for producing an antibody described herein, comprising expressing such antibody in a host cell. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0257] In certain aspects, provided herein is an isolated vector comprising a polynucleotide described herein. In some embodiments, the vector is a viral vector.

[0258] In certain aspects, provided herein is a recombinant virus comprising a polynucleotide described herein. In some embodiments, the recombinant virus encodes an antibody described herein. In one embodiment, the recombinant virus encodes a bispecific antibody described herein. In one embodiment, the recombinant virus is a replication defective virus. Suitable replication defective viral vectors are known to those skilled in the art, for example, as disclosed in U.S. Pat. Nos. 7198784, 9408905, 9862931, 8067156, U.S. Pat. Appl. Pub. Nos. 20150291935, 20120220492, 20180291351, and 20170175137, each of which is incorporated herein by reference in its entirety. In one embodiment, the recombinant virus is a retrovirus or retroviral vector, for example, a lentivirus or lentiviral vector. In one embodiment, the recombinant virus is an adenovirus or adenoviral vector, HSV or HSV vector, or influenza virus or viral vector. In one embodiment, the recombinant virus is an adeno-associated virus (AAV). In one embodiment, the recombinant virus is for administration to a subject to prevent or treat HIV infection. In one embodiment, the recombinant virus is an adeno-associated virus (AAV) for administration to a subject to prevent or treat HIV infection. Recombinant AAV particles encoding an antibody that binds to HIV Env and methods for producing thereof are known to one skilled in the art, for example, as disclosed in US Patent 8,865,881 and US20190031740, each of which is incorporated by reference herein in its entirety for all purposes. See also, Lin and Balazs, Retrovirology 15:66 (2018) and van den berg et al., Molecular Therapy: methods & Clinical Development 14:100-112 (2019), each of which is incorporated by reference herein in its entirety for all purposes. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0259] In certain aspects, provided herein is a host cell comprising a polynucleotide described herein, or a vector described herein. In some embodiments, the vector encodes an antibody described herein. In some embodiments, a vector described herein comprises a first vector encoding

a VH described herein and a second vector encoding a VL described herein. In some embodiments, a vector described herein comprises a first nucleotide sequence encoding a VH described herein and a second nucleotide sequence encoding a VL described herein.

[0260] In some embodiments, the host cell is selected from the group consisting of E. coli, Pseudomonas, Bacillus, Streptomyces, yeast, CHO, YB/20, NS0, PER-C6, HEK-293T, NIH-3T3, Helga, BHK, Hep G2, SP2/0, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, BMT10 cell, plant cell, insect cell, and human cell in tissue culture. In some embodiments, the host cell is CHO.

[0261] In certain aspects, provided herein is a method of producing an antibody that binds to HIV comprising culturing a host cell described herein so that the polynucleotide is expressed and the antibody is produced. In some embodiments, the method further comprises recovering the antibody.

[0262] The isolated polypeptides, i.e., anti-HIV Env antibodies described herein can be produced by any suitable method known in the art. Such methods range from direct protein synthetic methods to constructing a DNA sequence encoding isolated polypeptide sequences and expressing those sequences in a suitable transformed host. In some embodiments, a DNA sequence is constructed using recombinant technology by isolating or synthesizing a DNA sequence encoding a wild-type protein of interest. Optionally, the sequence can be mutagenized by site-specific mutagenesis to provide functional analogs thereof. See, e.g., Zoeller et al., Proc. Nat'l. Acad. Sci. USA 81:5662-5066 (1984) and U.S. Pat. No. 4,588,585.

[0263] In some embodiments a DNA sequence encoding a polypeptide of interest would be constructed by chemical synthesis using an oligonucleotide synthesizer. Such oligonucleotides can be designed based on the amino acid sequence of the desired polypeptide and selecting those codons that are favored in the host cell in which the recombinant polypeptide of interest will be produced. Standard methods can be applied to synthesize an isolated polynucleotide sequence encoding an isolated polypeptide of interest. For example, a complete amino acid sequence can be used to construct a back-translated gene. Further, a DNA oligomer containing a nucleotide sequence coding for the particular isolated polypeptide can be synthesized. For example, several small oligonucleotides coding for portions of the desired polypeptide can be synthesized and then ligated. The individual oligonucleotides typically contain 5' or 3' overhangs for complementary assembly.

[0264] Once assembled (by synthesis, site-directed mutagenesis or another method), the polynucleotide sequences encoding a particular isolated polypeptide of interest will be inserted into an expression vector and operatively linked to an expression control sequence appropriate for

expression of the protein in a desired host. Proper assembly can be confirmed by nucleotide sequencing, restriction mapping, and expression of a biologically active polypeptide in a suitable host. As is well known in the art, in order to obtain high expression levels of a transfected gene in a host, the gene must be operatively linked to transcriptional and translational expression control sequences that are functional in the chosen expression host.

[0265] In certain embodiments, recombinant expression vectors are used to amplify and express DNA encoding antibodies or fragments thereof. Recombinant expression vectors are replicable DNA constructs which have synthetic or cDNA-derived DNA fragments encoding a polypeptide chain of an antibody or fragment thereof operatively linked to suitable transcriptional or translational regulatory elements derived from mammalian, microbial, viral or insect genes. A transcriptional unit generally comprises an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, transcriptional promoters or enhancers, (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate transcription and translation initiation and termination sequences. Such regulatory elements can include an operator sequence to control transcription. The ability to replicate in a host, usually conferred by an origin of replication, and a selection gene to facilitate recognition of transformants can additionally be incorporated. DNA regions are operatively linked when they are functionally related to each other. For example, DNA for a signal peptide (secretory leader) is operatively linked to DNA for a polypeptide if it is expressed as a precursor which participates in the secretion of the polypeptide; a promoter is operatively linked to a coding sequence if it controls the transcription of the sequence; or a ribosome binding site is operatively linked to a coding sequence if it is positioned so as to permit translation. Structural elements intended for use in yeast expression systems include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it can include an N-terminal methionine residue. This residue can optionally be subsequently cleaved from the expressed recombinant protein to provide a final product.

[0266] The choice of expression control sequence and expression vector will depend upon the choice of host. A variety of host-expression vector systems can be utilized to express antibody molecules described herein (see, *e.g.,* U.S. Patent No. 5,807,715). Such host-expression systems represent vehicles by which the coding sequences of interest can be produced and subsequently purified, but also represent cells which can, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule described herein *in situ*. These include but are not limited to microorganisms such as bacteria (*e.g., E. coli* and *B. subtilis*) transformed

with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (*e.g., Saccharomyces Pichia*) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (*e.g.,* baculovirus) containing antibody coding sequences; plant cell systems (*e.g.,* green algae such as *Chlamydomonas reinhardtii*) infected with recombinant virus expression vectors (*e.g.,* cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (*e.g.,* Ti plasmid) containing antibody coding sequences; or mammalian cell systems (*e.g.,* COS (*e.g.*, COS1 or COS), CHO, BHK, MDCK, HEK 293, NS0, PER.C6, VERO, CRL7O3O, HsS78Bst, Helga, and NIH 3T3, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20 and BMT10 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (*e.g.,* metallothionein promoter) or from mammalian viruses (*e.g.,* the adenovirus late promoter; the vaccinia virus 7.5K promoter). In a specific embodiment, cells for expressing antibodies described herein are CHO cells, for example CHO cells from the CHO GS System™ (Lonza). In a particular embodiment, cells for expressing antibodies described herein are human cells, *e.g.*, human cell lines. In a specific embodiment, a mammalian expression vector is pOptiVEC™ or pcDNA3.3. In a particular embodiment, bacterial cells such as *Escherichia coli*, or eukaryotic cells (*e.g.*, mammalian cells), especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary (CHO) cells in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking MK & Hofstetter H (1986) Gene 45: 101-105; and Cockett MI *et al.,* (1990) Biotechnology 8: 662-667). In certain embodiments, antibodies described herein are produced by CHO cells or NS0 cells. In a specific embodiment, the expression of nucleotide sequences encoding antibodies described herein which immunospecifically bind Env is regulated by a constitutive promoter, inducible promoter or tissue specific promoter.

[0267] For applications where it is desired that the antibodies described herein be expressed in vivo, for example in a subject in need of treatment with an antibody described herein, any vector that allows for the expression of the antibodies and is safe for use in vivo may be used. In some embodiments, the vector is a viral vector. Viral vectors can include poxvirus (vaccinia), including vaccinia Ankara and canarypox; adenoviruses, including adenovirus type 5 (Ad5); rubella; Sendai virus; rhabdovirus; alphaviruses; and adeno-associated viruses. In some embodiments, the viral

vector is an adeno-associated virus. Alternatively, a polynucleotide encoding the antibody could be delivered as DNA or RNA to the subject for in vivo expression of the antibody.

[0268] Suitable host cells for expression of a polypeptide of interest such as an antibody described herein include prokaryotes, yeast, insect or higher eukaryotic cells under the control of appropriate promoters. Prokaryotes include gram negative or gram positive organisms, for example *E. coli* or bacilli. Higher eukaryotic cells include established cell lines of mammalian origin. Cell-free translation systems could also be employed. Appropriate cloning and expression vectors for use with bacterial, fungal, yeast, and mammalian cellular hosts are described by Pouwels et al. (Cloning Vectors: A Laboratory Manual, Elsevier, N.Y., 1985), the relevant disclosure of which is hereby incorporated by reference. Additional information regarding methods of protein production, including antibody production, can be found, e.g., in U.S. Patent Publication No. 2008/0187954, U.S. Patent Nos. 6,413,746 and 6,660,501, and International Patent Publication No. WO 04009823, each of which is hereby incorporated by reference herein in its entirety.

[0269] Various mammalian or insect cell culture systems are also advantageously employed to express a recombinant protein such as an antibody described herein. Expression of recombinant proteins in mammalian cells can be performed because such proteins are generally correctly folded, appropriately modified and completely functional. Examples of suitable mammalian host cell lines include but are not limited to CHO, VERO, BHK, Hela, MDCK, HEK 293, NIH 3T3, W138, BT483, Hs578T, HTB2, BT2O and T47D, NS0 (a murine myeloma cell line that does not endogenously produce any immunoglobulin chains), CRL7O3O, COS (*e.g.*, COS1 or COS), PER.C6, VERO, HsS78Bst, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20, BMT10 and HsS78Bst cells. Mammalian expression vectors can comprise nontranscribed elements such as an origin of replication, a suitable promoter and enhancer linked to the gene to be expressed, and other 5' or 3' flanking nontranscribed sequences, and 5' or 3' nontranslated sequences, such as necessary ribosome binding sites, a polyadenylation site, splice donor and acceptor sites, and transcriptional termination sequences. Baculovirus systems for production of heterologous proteins in insect cells are reviewed by Luckow and Summers, Bio/Technology 6:47 (1988).

[0270] The proteins produced by a transformed host can be purified according to any suitable method. Such standard methods include chromatography (e.g., ion exchange, affinity and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for protein purification. Affinity tags such as hexahistidine, maltose binding domain, influenza coat sequence and glutathione-S-transferase can be attached to the protein to allow easy

purification by passage over an appropriate affinity column. Isolated proteins can also be physically characterized using such techniques as proteolysis, nuclear magnetic resonance and x-ray crystallography.

[0271] For example, supernatants from systems which secrete recombinant protein, e.g., an antibody, into culture media can be first concentrated using a commercially available protein concentration filter, for example, an Amicon or Millipore Pellicon ultrafiltration unit. Following the concentration step, the concentrate can be applied to a suitable purification matrix. Alternatively, an anion exchange resin can be employed, for example, a matrix or substrate having pendant diethylaminoethyl (DEAE) groups. The matrices can be acrylamide, agarose, dextran, cellulose or other types commonly employed in protein purification. Alternatively, a cation exchange step can be employed. Suitable cation exchangers include various insoluble matrices comprising sulfopropyl or carboxymethyl groups. Finally, one or more reversed-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further an agent. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a homogeneous recombinant protein.

[0272] Recombinant protein produced in bacterial culture can be isolated, for example, by initial extraction from cell pellets, followed by one or more concentration, salting-out, aqueous ion exchange or size exclusion chromatography steps. High performance liquid chromatography (HPLC) can be employed for final purification steps. Microbial cells employed in expression of a recombinant protein can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents.

[0273] Methods known in the art for purifying antibodies and other proteins also include, for example, those described in U.S. Patent Publication Nos. 2008/0312425, 2008/0177048, and 2009/0187005, each of which is hereby incorporated by reference herein in its entirety.

[0274] In specific embodiments, an antibody described herein is isolated or purified. Generally, an isolated antibody is one that is substantially free of other antibodies with different antigenic specificities than the isolated antibody. For example, in a particular embodiment, a preparation of an antibody described herein is substantially free of cellular material and/or chemical precursors. The language "substantially free of cellular material" includes preparations of an antibody in which the antibody is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, an antibody that is substantially free of cellular material includes preparations of antibody having less than about 30%, 20%, 10%, 5%, 2%, 1%, 0.5%, or

0.1% (by dry weight) of heterologous protein (also referred to herein as a "contaminating protein") and/or variants of an antibody, for example, different post-translational modified forms of an antibody. When the polypeptide (e.g., antibody described herein) is recombinantly produced, it is also generally substantially free of culture medium, *i.e.,* culture medium represents less than about 20%, 10%, 2%, 1%, 0.5%, or 0.1% of the volume of the protein preparation. When the polypeptide (e.g., antibody described herein) is produced by chemical synthesis, it is generally substantially free of chemical precursors or other chemicals, *i.e.,* it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly, such preparations of the polypeptide (e.g., antibody described herein) have less than about 30%, 20%, 10%, or 5% (by dry weight) of chemical precursors or compounds other than the polypeptide of interest. In some embodiments, antibodies described herein are isolated or purified.

V. Pharmaceutical Compositions

[0275] Compositions comprising the antibodies or antigen-binding fragments described herein are also provided. Further provided herein are compositions comprising a polynucleotide or polynucleotides encoding the antibodies or antigen-binding fragments described herein. In some embodiments, the polynucleotide comprises mRNA. In some embodiments, the composition is a pharmaceutical composition.

[0276] In some embodiments, the composition is a lyophilized composition. In some embodiments, the composition is formulated for topical administration, and in certain embodiments the composition is formulated for vaginal or rectal administration.

[0277] In certain aspects, provided herein is a pharmaceutical composition comprising an antibody described herein and a pharmaceutically acceptable excipient. In some embodiments, the antibody is an intact antibody. In some embodiments, the antibody is an antigen binding antibody fragment. In some embodiments, the composition is formulated for topical administration, and in certain embodiments the composition is formulated for vaginal or rectal administration.

[0278] In another embodiment, the disclosure provides a pharmaceutical composition comprising an antibody described herein. Such compositions are intended for prevention and treatment of HIV infection.

[0279] In further embodiments of the present disclosure, a composition comprising the antibody described herein can additionally be combined with other compositions for the treatment of HIV infection or the prevention of HIV transmission.

[0280] In some embodiments, an antibody described herein may be administered within a pharmaceutically-acceptable diluent, carrier, or excipient, in unit dose form. Conventional

pharmaceutical practice may be employed to provide suitable formulations or compositions to administer to individuals being treated for HIV infection. In some embodiments, the administration is prophylactic. Any appropriate route of administration may be employed, for example, administration may be parenteral, intravenous, intra-arterial, subcutaneous, intramuscular, intraperitoneal, intranasal, aerosol, suppository, oral administration, vaginal, or anal.

[0281] The pharmaceutical compositions described herein are prepared in a manner known *per se*, for example, by means of conventional dissolving, lyophilizing, mixing, granulating or confectioning processes. The pharmaceutical compositions may be formulated according to conventional pharmaceutical practice (see for example, in Remington: The Science and Practice of Pharmacy (21st ed.), ed. A.R. Gennaro, 2005, Lippincott Williams & Wilkins, Philadelphia, PA, and Encyclopedia of Pharmaceutical Technology, eds. J. Swarbrick and J. C. Boylan, 2013, Marcel Dekker, New York, NY).

[0282] The injection compositions are prepared in customary manner under sterile conditions; the same applies also to introducing the compositions into ampoules or vials and sealing the containers.

[0283] Pharmaceutical compositions according to the invention may be, for example, in unit dose form, such as in the form of ampoules, vials, suppositories, tablets, pills, or capsules. The formulations can be administered to human individuals in therapeutically or prophylactic effective amounts (e.g., amounts which prevent, eliminate, or reduce a pathological condition) to provide therapy for a disease or condition. The preferred dosage of therapeutic agent to be administered is likely to depend on such variables as the type and extent of the disorder, the overall health status of the particular patient, the formulation of the compound excipients, and its route of administration.

[0284] In certain embodiments, the compositions described herein can be formulated for topical administration, and in certain embodiments the composition is formulated for vaginal or rectal administration. The composition may be formulated as a gel, or formulated as a topical cream, ointment, lotion or foam formulation. Useful formulations are known in the art, for example, as disclosed in U.S. Patent Appl. Pub. No. 20130022619, which is incorporated by reference herein in its entirety for all purposes.

[0285] In certain embodiments, the composition may further comprise a pharmaceutically acceptable excipient, a lubricant, or an antiviral agent.

[0286] The topical formulations of the present invention can be used to prevent HIV infection in a human, or to inhibit transmission of the HIV virus from an infected human to another human.

The topical formulations of the present invention can inhibit the growth or replication of HIV. The topical formulations are useful in the prophylactic treatment of humans who are at risk for HIV infection. The topical formulations also can be used to treat objects or materials, such as contraceptive devices (for example condoms or intrauterine devices), medical equipment, supplies, or fluids, including biological fluids, such as blood, blood products, and tissues, to prevent or inhibit viral infection of a human. Such topical formulations also are useful to prevent transmission, such as sexual transmission of viral infections, e.g., HIV, which is the primary way in which HIV is transmitted globally. The methods of prevention or inhibition or retardation of transmission of viral infection, e.g., HIV infection, in accordance with the present invention, comprise vaginal, rectal, penile or other topical treatment with an antiviral effective amount of a topical preparation of the present invention, alone or in combination with another antiviral compound as described herein.

[0287] In some embodiments the composition is in the form of a cream, lotion, gel, or foam that is applied to the affected skin or epithelial cavity, and preferably spread over the entire skin or epithelial surface which is at risk of contact with bodily fluids. Such formulations, which are suitable for vaginal or rectal administration, may be present as aqueous or oily suspensions, solutions or emulsions (liquid formulations) containing in addition to the active ingredient, such carriers as are known in the art to be appropriate. These formulations are useful to protect not only against sexual transmission of HIV, but also to prevent infection of a baby during passage through the birth canal. Thus the vaginal administration can take place prior to sexual intercourse, during sexual intercourse, and immediately prior to childbirth.

[0288] As a vaginal formulation, the active ingredient may be used in conjunction with a spermicide and may be employed with a condom, diaphragm, sponge or other contraceptive device. Examples of suitable spermicides include nonylphenoxypolyoxyethylene glycol (nonoxynol 9), benzethonium chloride, and chlorindanol. Suitably, the pH of the composition is 4.5 to 8.5. Vaginal compositions preferably have a pH of 4.5 to 6, most preferably about 5.

[0289] Vaginal formulations include suppositories (for example, gel-covered creams), tablets and films. The suppositories can be administered by insertion with an applicator using methods well known in the art.

[0290] Vaginal formulations further include vaginal ring devices formulated for sustained release. See, e.g., Morrow et al., Eur J Pharm Biopharm. 77(1):3-10 (2011), Zhao et al., Antimicrob Agents Chemother. 61(7) pii: e02465-16 (2017).

[0291] Buccal formulations include creams, ointments, gels, tablets or films that comprise ingredients that are safe when administered via the mouth cavity. Buccal formulations can also comprise a taste-masking or flavoring agent.

[0292] The present compositions may be associated with a contraceptive device or article, such as a vaginal ring device, an intrauterine device (IUD), vaginal diaphragm, vaginal sponge, pessary, condom, etc.

[0293] In some embodiments the compositions described herein are used in conjunction with condoms, to enhance the risk-reducing effectiveness of condoms and provide maximum protection for users. The composition can either be coated onto condoms during manufacture, and enclosed within conventional watertight plastic or foil packages that contain one condom per package, or it can be manually applied by a user to either the inside or the outside of a condom, immediately before use. As used herein, "condom" refers to a barrier device which is used to provide a watertight physical barrier between male and female genitalia during sexual intercourse, and which is removed after intercourse. This term includes conventional condoms that cover the penis; it also includes so-called "female condoms" which are inserted into the vaginal cavity prior to intercourse.

[0294] In another embodiment a composition described herein is in the form of an intra-vaginal pill, an intra-rectal pill, or a suppository. The suppository or pill should be inserted into the vaginal or rectal cavity in a manner that permits the suppository or pill, as it dissolves or erodes, to coat the vaginal or rectal walls with a prophylactic layer of an antibody described herein.

[0295] In certain embodiments, the composition may further comprise a pharmaceutically acceptable excipient, a lubricant, or an antiviral agent.

[0296] Compositions used in the methods of this invention may also comprise other active agents, such as another agent to prevent HIV infection, and agents that protect individuals from conception and other sexually transmitted diseases. Thus, in another embodiment the compositions used in this invention further comprise a second anti-HIV agent, a virucide effective against viral infections other than HIV, and/or a spermicide.

[0297] The compositions used in this invention may also contain a lubricant that facilitates application of the composition to the desired areas of skin and epithelial tissue, and reduces friction during sexual intercourse. In the case of a pill or suppository, the lubricant can be applied to the exterior of the dosage form to facilitate insertion.

[0298] In the cream or ointment embodiments of the present invention, the topical formulation comprises one or more lubricants. The gels and foams of the present invention optionally can include one or more lubricants.

[0299] Non-limiting examples of useful lubricants include cetyl esters wax, hydrogenated vegetable oil, magnesium stearate, methyl stearate, mineral oil, polyoxyethylene-polyoxypropylene copolymer, polyethylene glycol, polyvinyl alcohol, sodium lauryl sulfate, white wax, or mixtures of two or more of the above.

[0300] The gel formulations of the present invention comprise one or more gelling agents. Non-limiting examples of useful gelling agents include carboxylic acid polymers including acrylic acid polymers crosslinked with cross links such as allyl ethers of sucrose (e.g. carbomer brand thickeners), cetostearyl alcohol, hydroxymethyl cellulose, polyoxyethylene-polyoxypropylene copolymer, sodium carboxymethylcellulose, polyvinyl pyrrolidone, or mixtures of two or more thereof.

VI. Uses and Methods

Therapeutic Uses and Methods:

[0301] In one aspect, provided herein is a method of treating HIV or inhibiting transmission of HIV. In some embodiments, the method of inhibiting transmission of HIV comprises administering to a subject in need thereof an effective amount of an antibody described herein (e.g., a bispecific or multispecific antibody), a pharmaceutical composition described herein, an isolated polynucleotide described herein, or a recombinant virus described herein (e.g., recombinant AAV). In some embodiments, the method of inhibiting transmission of HIV comprises administering to a subject in need thereof an effective amount of an antibody described herein. In some embodiments, the subject has been exposed to HIV. In some embodiments, the subject is at risk of being exposed to HIV. In some embodiments, the subject at risk of being exposed to HIV is a health care worker, a sexual partner of an HIV infected individual, or a sex worker. In some embodiments, the subject that has been exposed to HIV or is at risk of being exposed to HIV is a newborn. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0302] In one aspect, provided herein is a method of reducing the risk of a subject becoming infected with HIV comprising administering to the subject in need thereof an effective amount of an antibody described herein, a pharmaceutical composition described herein, an isolated polynucleotide described herein, or a recombinant virus described herein. In some embodiments, the subject is administered an antibody described herein. In some embodiments, the subject has been exposed to HIV. In some embodiments, the subject is at risk of being exposed to HIV. In some embodiments, the subject at risk of being exposed to HIV is a health care worker, a sexual partner

of an HIV infected individual, or a sex worker. In some embodiments, the subject that has been exposed to HIV or is at risk of being exposed to HIV is a newborn. In one aspect, provided herein is an antibody, a pharmaceutical composition, an isolated polynucleotide, or a recombinant virus for reducing the risk of a subject becoming infected with HIV. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0303] In one aspect, provided herein is a method for passively immunizing a subject comprising administering to the subject in need thereof an effective amount of an antibody described herein, a pharmaceutical composition described herein, an isolated polynucleotide described herein, or a recombinant virus described herein. In some embodiments, the subject is administered an antibody described herein. In some embodiments, the subject has been exposed to HIV. In some embodiments, the subject is at risk of being exposed to HIV. In some embodiments, the subject at risk of being exposed to HIV is a health care worker, a sexual partner of an HIV infected individual, or a sex worker. In some embodiments, the subject that has been exposed to HIV or is at risk of being exposed to HIV is a newborn. In one aspect, provided herein is provided herein is an antibody, a pharmaceutical composition, an isolated polynucleotide, or a recombinant virus for passively immunizing a subject. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0304] Further provided herein is a method of neutralizing an HIV virus comprising contacting the virus with an effective amount of an antibody described herein. In some embodiments, the virus is comprised by a composition, for example, a fluid, including a biological fluid, such as blood or blood product. In certain embodiments, the method comprises adding an antibody described herein to a composition comprising HIV in a sufficient amount or concentration to neutralize the HIV. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0305] Further provided herein is a method of reducing viral load comprising administering to a subject in need thereof an effective amount of an antibody (e.g., bispecific antibody) described herein, a pharmaceutical composition described herein, an isolated polynucleotide described herein, or a recombinant virus described herein. In one embodiment, the method comprises administering to a subject in need thereof an effective amount of an antibody (e.g., a bispecific antibody) described herein. In one embodiment, the method comprises administering to a subject

in need thereof an effective amount of a recombinant AAV encoding an antibody (e.g., a bispecific antibody) described herein. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0306] In some embodiments of a method described herein, the antibody can be a chimeric antibody, engineered antibody, recombinant antibody, or a monoclonal antibody described herein. In some embodiments, the antibody is a full antibody, an F(ab) fragment, or an F(ab)2 fragment described herein. In a specific embodiment, the antibody is an engineered monoclonal antibody described herein. In a specific embodiment, the antibody is a recombinant monoclonal antibody described herein. In a specific embodiment, the antibody is a chimeric monoclonal antibody described herein. In a specific embodiment, the antibody is a F(ab) described herein. In a specific embodiment, the antibody is a F(ab')2 fragment described herein.

[0307] In some embodiments, a method of preventing HIV infection provided herein comprises administering to a subject in need thereof a therapeutically sufficient amount of an antibody described herein, a pharmaceutical composition described herein, an isolated polynucleotide described herein, or a recombinant virus described herein. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0308] In some embodiments, a method of treating HIV/AIDS provided herein comprises administering to a subject in need thereof a therapeutically sufficient amount of an antibody described herein, a pharmaceutical composition described herein, an isolated polynucleotide described herein, or a recombinant virus described herein. In some embodiments, a method of treating HIV/AIDS comprises administering an antibody described herein. In some embodiments, a method of treating HIV/AIDS comprises administering a pharmaceutical composition described herein. In some embodiments, a method of treating HIV/AIDS comprises administering an isolated polynucleotide described herein. In some embodiments, a method of treating HIV/AIDS comprises administering a recombinant virus described herein. In one aspect, provided herein is an antibody, a pharmaceutical composition, an isolated polynucleotide, or a recombinant virus for treating HIV/AIDS. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0309] In some embodiments, the administering to the subject is by at least one mode selected from oral, parenteral, subcutaneous, intramuscular, intravenous, vaginal, rectal, buccal, sublingual, and transdermal

[0310] In some embodiments, a method of treatment described herein further comprises administering at least one additional therapeutic agent. In some embodiments, the additional therapeutic agent comprises an antiretroviral therapy (ART) agent, a reservoir activator, an immunomodulator, a second antibody, or a second and third antibody. In some embodiments, the additional therapeutic agent comprises a second antibody. In some embodiments, the additional therapeutic agent comprises a second and third antibody. In some embodiments, the additional therapeutic agent comprises a second and optionally third antibody which is an anti-HIV antibody. In some embodiments, the additional therapeutic agent comprises a second and optionally third antibody which is an anti-HIV Env antibody. In some embodiments, the additional therapeutic agent comprises a second and optionally third anti-HIV Env antibody which binds to an HIV Env epitope region different from the HIV Env epitope region bound by an antibody described herein. In some embodiments, the additional therapeutic agent comprises a second and optionally third anti-HIV Env antibody which binds to the high-mannose patch epitope region, V1/V2-glycan site (V2g) epitope region, or gp41 MPER epitope region. In some embodiments, the additional therapeutic agent comprises a second anti-HIV Env antibody which binds to the high-mannose patch epitope region (e.g., PGT-121 or an engineered variant thereof). In some embodiments, the additional therapeutic agent comprises a second anti-HIV Env antibody which binds to the high-mannose patch epitope region disclosed in International Appl. No. PCT/US2019/43578, filed on July 26, 2016, which is incorporated herein by reference in its entirety for all purposes. In some embodiments, the additional therapeutic agent comprises a second anti-HIV Env antibody which binds to the V1/V2-glycan site (V2g) epitope region. In some embodiments, the additional therapeutic agent comprises a second anti-HIV Env antibody which binds to the gp41 MPER epitope region.

[0311] In certain embodiments, the subject is at risk for exposure to HIV. In some embodiments, the subject is infected with HIV. In some embodiments, the subject is diagnosed with AIDS. In certain embodiments, the subject at risk for exposure to HIV is a health care worker. In certain embodiments, the subject at risk for exposure to HIV is a sex worker. In certain embodiments, the subject at risk for exposure to HIV is a sexual partner of an HIV infected individual. In certain embodiments, the subject at risk for exposure to HIV is a newborn.

[0312] The invention also features methods of blocking HIV infection in a subject (e.g., a human) at risk of HIV transmission. For example, in one aspect, the subject may be a fetus of an HIV-infected pregnant female and the method includes administering to the HIV-infected pregnant female an antibody described herein, thereby blocking the HIV infection in the fetus. In other instances, the subject is a newborn having an HIV-infected mother, a subject at risk of HIV transmission following a needle stick injury, or a subject at risk of HIV transmission following a sexual exposure to an HIV-infected individual.

[0313] In instances when the subject is a newborn having an HIV-infected mother, the newborn can be administered an antibody described herein peripartum and/or postpartum, for example, prior to, during, and/or following breastfeeding from the HIV-infected mother, in order to block an HIV infection in the newborn. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0314] In instances when the subject is at risk of HIV transmission following a sexual exposure to an HIV-infected individual, the subject can be administered an antibody described herein following the sexual exposure in order to block an HIV infection in the subject. In one embodiment, the antibody is a multispecific, such as bispecific antibody. In one embodiment, the antibody comprises PCIN63-71I1a. In one embodiment, the antibody comprises or PCIN63-71L.

[0315] In some embodiments, an antibody described herein can be used as a microbicides to prevent mucosal HIV acquisition. In some embodiments, an antibody described herein is used to prevent vaginal or rectal acquisition of HIV. In some embodiments, an antibody described herein can be used as a microbicides to reduce the likelihood of mucosal HIV acquisition. In some embodiments, an antibody described herein is used to reduce the likelihood of vaginal or rectal acquisition of HIV.

[0316] In any of the methods described above, further administration of ART and/or an immunomodulator and/or a second antibody is contemplated. For example, the ART and/or immunomodulator and/or a second antibody can be administered in conjunction with, prior to, concurrently with, subsequent to, or within the context of a treatment regimen that includes administration of an antibody described herein.

[0317] An antibody described herein, or a pharmaceutical composition described herein can be delivered to a subject by a variety of routes, such as oral, parenteral, subcutaneous, intravenous, intradermal, transdermal, intranasal, vaginal, or anal. In some embodiments, the antibody or pharmaceutical composition is administered intravenously, vaginally, or anally.

[0318] The amount of an antibody described herein, or a pharmaceutical composition described herein which will be effective in the treatment and/or prevention of a condition will depend on the nature of the disease, and can be determined by standard clinical techniques.

[0319] The precise dose to be employed in a pharmaceutical composition will also depend on the route of administration, and the seriousness of the disease, and should be decided according to the judgment of the practitioner and each subject's circumstances. For example, effective doses may also vary depending upon means of administration, target site, physiological state of the patient (including age, body weight and health), whether the patient is human or an animal, other medications administered, or whether treatment is prophylactic or therapeutic. Usually, the patient is a human but non-human mammals including transgenic mammals can also be treated. Treatment dosages are optimally titrated to optimize safety and efficacy.

[0320] In certain embodiments, an *in vitro* assay is employed to help identify optimal dosage ranges. Effective doses may be extrapolated from dose response curves derived from *in vitro* or animal model test systems.

Detection & Diagnostic Uses

[0321] An antibody described herein can be used to detect HIV and/or assay HIV levels in a biological sample using classical immunohistological methods known to those of skill in the art, including immunoassays, such as the enzyme linked immunosorbent assay (ELISA), immunoprecipitation, or Western blotting. An antibody described herein can also be used as an imaging agent, for example, a tissue-penetrating imaging agent. In some embodiments, an antibody described herein is conjugated with a detectable label. Suitable assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (^{125}I, ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^{3}H), indium (^{121}In), and technetium (^{99}Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin. Such labels can be used to label an antibody or fusion polypeptide described herein. Alternatively, a second antibody that recognizes an antibody described herein can be labeled and used in combination with the antibody described herein to detect HIV levels.

[0322] As used herein, the term "biological sample" refers to any biological sample obtained from a subject, cell line, tissue, or other source potentially comprising HIV. Methods for obtaining tissue biopsies and body fluids from animals (*e.g.*, humans) are well known in the art.

[0323] In another embodiment, an antibody described herein can be used to detect levels of HIV, which levels can then be linked to certain disease symptoms. An antibody described herein

may carry a detectable or functional label. An antibody described herein can carry a fluorescence label. Exemplary fluorescence labels include, for example, reactive and conjugated probes, *e.g.*, Aminocoumarin, Fluorescein and Texas red, Alexa Fluor dyes, Cy dyes and DyLight dyes. An antibody described herein can carry a radioactive label, such as the isotopes ^{3}H, ^{14}C, ^{32}P, ^{35}S, ^{36}Cl, ^{51}Cr, ^{57}Co, ^{58}Co, ^{59}Fe, ^{67}Cu, ^{90}Y, ^{99}Tc, ^{111}In, ^{117}Lu, ^{121}I, ^{124}I, ^{125}I, ^{131}I, ^{198}Au, ^{211}At, ^{213}Bi, ^{225}Ac and ^{186}Re. When radioactive labels are used, currently available counting procedures known in the art may be utilized to identify and quantitate the specific binding of an antibody described herein to HIV. In the instance where the label is an enzyme, detection may be accomplished by any of the presently utilized colorimetric, spectrophotometric, fluorospectrophotometric, amperometric or gasometric techniques as known in the art. This can be achieved by contacting a sample or a control sample with an antibody described herein under conditions that allow for the formation of a complex between the antibody and HIV. Any complexes formed between the antibody and HIV are detected and compared in the sample and the control. An antibody described herein can also be used to purify HIV via immunoaffinity purification.

[0324] In some aspects, provided herein are methods for *in vitro* detecting HIV in a sample, comprising contacting said sample with an antibody described herein. In some aspects, provided herein is the use of an antibody described herein, for *in vitro* detecting HIV in a sample. In one aspect, provided herein is an antibody or pharmaceutical composition described herein for use in the detection of HIV in a subject. In one aspect, provided herein is an antibody or pharmaceutical composition described herein for use as a diagnostic. In one preferred embodiment, the antibody comprises a detectable label. In some embodiments, the subject is a human. In some embodiments, the method of detecting HIV in a sample comprises contacting the sample with an antibody described herein.

[0325] In some embodiments, the present disclosure provides methods of purifying HIV from a sample. In some embodiments, the method of purifying HIV from a sample comprises contacting the sample with an antibody described herein under conditions that allow the antibody to bind to HIV. In some embodiments, the antibody comprises a tag, for example, hexa-histidine tag or FLAG-tag to facilitate the purification of HIV.

VII. Kits

[0326] Provided herein are kits comprising one or more antibodies described herein. In some embodiments, a pharmaceutical pack or kit described herein comprises one or more containers filled with one or more of the ingredients of the pharmaceutical compositions described herein,

such as one or more antibodies described herein. In some embodiments, a kit contains an antibody described herein or a pharmaceutical composition described herein, and a second prophylactic or therapeutic agent used in the treatment or prevention of HIV. In some embodiments, the second agent is an antiretroviral agent. In some embodiments, the second agent is an immunomodulator. In some embodiments, the second agent is one or more anti-HIV antibody. In some embodiments, the second agent is one or more anti-HIV Env antibody that binds to an HIV Env epitope region different from the HIV Env epitope region bound by an antibody described herein. In some embodiments, the second agent is one or more anti-HIV Env antibody that binds to the high-mannose patch epitope region, V1/V2-glycan site (V2g) epitope region, or gp41 MPER epitope region. In some embodiments, a kit contains an antibody described herein or a pharmaceutical composition described herein, and a reagent used in the detection of HIV. In some embodiments, the detection reagent comprises DNA primers for the detection of HIV. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

[0327] In some embodiments, a kit described herein comprises an antibody described herein or a pharmaceutical composition described herein and a) a detection reagent, b) an HIV antigen, c) a notice that reflects approval for use or sale for human administration, or d) any combination thereof.

[0328] In some embodiments, a kit described herein comprises a fusion polypeptide described herein or a pharmaceutical composition described herein and a) a detection reagent, b) an HIV antigen, c) a notice that reflects approval for use or sale for human administration, or d) any combination thereof.

[0329] Embodiments of the present disclosure can be further defined by reference to the following non-limiting examples, which describe in detail preparation of certain antibodies of the present disclosure and methods for using antibodies of the present disclosure. It will be apparent to those skilled in the art that many modifications, both to materials and methods, can be practiced without departing from the scope of the present disclosure.

[0330] All documents, patent, and patent applications cited herein are hereby incorporated by reference, and may be employed in the practice described herein.

EXAMPLES

Example 1. Fast and Focused Maturation of a VH1-2-Restricted HIV-Env CD4 Binding Site Targeting bnAb lineage involves direct binding to the N276-glycan.

[0331] The VH1-2 restricted VRC01-class antibodies targeting the HIV Env CD4 binding-site (CD4bs) is a major focus of HIV vaccine strategies. While enormous progress has been made in the elicitation VRC01-class antibody precursors by immunization, challenges remain in understanding how to drive such responses towards the neutralization profile characteristic to this family of antibodies. To inform these strategies, described here is the rapid development of a VRC01-class antibody lineage in the subtype C infected IAVI-Protocol C neutralizer PC063. PCIN63 antibodies have the hallmark VRC01-class features and demonstrates similar neutralization breath to the prototype VRC01 antibody, but are 3 to 4-fold less mutated. Maturation occurred rapidly within ~24 months of emergence and was focused on key contact residues. This first longitudinal study of broadly neutralizing VRC01-class Abs reveals compelling nuances in the recognition of the CD4bs in the context of the surrounding glycan fence.

[0332] Elicitation of broadly neutralizing antibodies (bnAbs) targeting the HIV envelope glycoprotein (Env) is thought be a key component of a successful HIV-1 vaccine (Fauci, 2017). VRC01-class antibodies, which target the highly conserved CD4 receptor binding site (CD4bs), are among the broadest neutralizing antibodies. However, these bnAbs typically display exceptionally high level of somatic hypermutation (SHM) (Falkowska et al., 2012; Huang et al., 2016; Scheid et al., 2011; Wu et al., 2010; Zhou et al., 2015) and often require years to develop during natural infection (Landais et al., 2016; Lynch et al., 2012). These features suggest that VRC01-class antibodies not only undergo a long and complex affinity maturation process (Wu et al., 2015) and may be highly difficult to elicit by immunization.

[0333] VRC01-like antibodies have been isolated from several chronically HIV infected individuals and display up to 42% nucleotide difference in sequence but share common features (Wu et al., 2010; Zhou et al., 2015) (Huang et al., 2016, Sajadi et al., 2018) including being derived from a VH1-2 variable gene, having a 5-amino acid LCDR3 and a short/flexible LCDR1. These shared features can serve as targets to elicit by vaccination, making such bnAbs amenable for rationally designed germline-targeting immunogens (Jardine et al., 2013; McGuire et al., 2013). Such immunogens have succeeded in eliciting narrowly neutralizing antibody responses with VRC01-like characteristics in transgenic mice models (Briney et al., 2016b; Dosenovic et al., 2015; Jardine et al., 2015; McGuire et al., 2016; Sok et al., 2016; Tian et al., 2016). Comparison of mature

VRC01-class antibodies has also highlighted the functional role of key "patches" of SHM that contribute to neutralization breadth and potency (Briney et al., 2016b; Jardine et al., 2013; McGuire et al., 2013). The importance of these mutations was confirmed by the narrowly neutralizing DRVI07 antibody lineage which harbored all the distinguishing features of VRC01-class antibodies except for the SHM mutations in the light chain needed to accommodate of the N276- and N462-glycans (Kong et al., 2016). These data indicate that adaptation to the glycans surrounding the CD4bs is the major hurdle for acquiring neutralization breadth for this class of antibodies.

[0334] A detailed analysis of VRC01-like antibody development during infection has been limited by the rare nature of these responses during natural infection and the lack of longitudinal sampling. Furthermore, although germline-targeting immunogens have enabled isolation and characterization of naïve precursors B-cells with VRC01-like features (Jardine et al., 2016a, Havenar-Daughton et al., 2018), whether these precursors are representative of naïve B-cells that will eventually lead to bnAbs is not known. Moreover, there is no clear pathway for how VRC01-like-class precursors might quickly acquire breadth and/or whether key mutations should be acquired in a particular order.

[0335] Described herein is the rapid development of VRC01-like bnAbs in a subtype-C infected Protocol C participant, PC063, with clear CD4bs-targeting broadly neutralizing plasma activity (Landais et al., 2016).

PCIN63 antibodies define a minimally mutated VRC01-like bnAb lineage.

[0336] Broadly neutralizing antibody activity was first detected in PC063 plasma at 54 months post infection (mpi), approximately two years later than observed for most Protocol C broad neutralizers, and reached a peak at 72 mpi (Figure 1A). To isolate the antibodies contributing to the plasma neutralization breadth in this donor, we used the previously described recombinant HIV Env (rgp140F) WT and D368R (CD4bs epitope knock-out) proteins for antibody isolation (Li et al., 2012). These proteins differentially adsorbed the broad neutralizing activity from the plasma (Figure S1A) and were used as fluorescent baits to sort CD4bs-specific memory B-cells from peripheral blood mononuclear cells (PMBCs) samples collected at 66, 71 and 77 mpi (Figure 1A).

[0337] A dominant IGHV1-2*02/IGHJ5*02 + IGKV1-5*03/IGKJ1*01 subset of 18 mAbs, which defined the PCIN63 lineage, was identified from the rpg140 WT^{pos} $D368R^{neg}$ B cells (Figure 6B). PCIN63 Abs exhibited characteristic features of VRC01-class bnAbs, including a 5-amino acid LCDR3 QxxEx Motif, a flexible Gly-rich LCRD1 and a 15-aa HCDR3 containing a WxxxDx Motif upstream of HFR4 (Figure 1B, 6C, 6D, 7). Notably, the frequency of 5-aa LCDR3 B cells in

the naïve repertoire of PC063, although higher than what was found in normal blood donors from the United States (California), was comparable to HIV negative individuals screened at African Protocol C sites (Figure 6E).

[0338] The SHM frequency of the PCIN63 lineage, ranging from 9.6% to 16.0% (V_H+J_H) and 10.0% to 13.7% (V_K+J_K) nucleotide mutation for the heavy (HC) and light (LC) chains, respectively, is notably 3-4-fold lower compared to other VRC01-class bnAbs (Figure 1B, Figure 6C). Alignment of PCIN63 mAbs amino-acid sequences showed that the SHMs were enriched at positions previously shown to be key epitope contact residues for this class of bNAbs. These include the HCDR1 and HCDR2 mutations important for high affinity binding to the gp120-Loop D and CD4bs-loop, and light chain mutations in LCDR1 and LFR3 that reduce the clash with the N276- and N462 glycans on Env (Figure 7). Moreover, select PCIN63 bnAbs levels of neutralization breadth and potency are equivalent to VRC01 on a large cross-clade panel of pseudoviruses (N=134) despite being 3 to 4-fold less mutated (Figure 1C, Figure 8, 9). In fact, PCIN63 mAbs have striking similarities to mAb min12A12, a minimally mutated but broad version of the CD4bs 12A21 bnAb designed by Schief and colleagues (Figure 7, 8) (Jardine et al., 2016b).

Fast maturation of the PCIN63 bnAb lineage

[0339] To better understand the focused maturation of the PCIN63 lineage, next-generation sequencing (NGS) of the circulating IgG^+ B-cell repertoire was performed at 17 time points between 4 and 77 mpi. PCIN63 lineage HC and KC sequences were first detected at 40mpi, followed by two waves of expansion at 44 and 61 mpi (Figure 10A-C), with a transient decline in frequency at 50 and 55mpi, during which the lineage appeared to affinity mature at a constant rate (Figure 10B). Interestingly, while the emergence of the PCIN63 bnAb lineage was substantially delayed compared to bnAb lineages, the affinity maturation time needed to achieve neutralization breadth was overall equivalent (Figure 1D). The fast and focused maturation of PCIN63 Abs did not appear to be associated with a particular enrichment in AID hotspots that might have rapidly favored such selection (not shown).

[0340] The PCIN63 unmutated common ancestor (UCA) was defined next. For the HC, an unmutated common ancestor (PCIN63-UCA-HC) was identified from the 40mpi timepoint. However, for the light chain, lineage assignment solely based on V_K+J_K gene usage and 5-aa LCDR3 criteria identified 18 possible germline (GL) light chains, among which PCIN63-UCA-KC1 with a QQSEA LCDR3 was the most frequent (Figure 10D). While none of the PCIN63 LC sequences detected at 40mpi were 100% identical to VK1-5 and JK1-1 germline genes, all had an

identical LCDR3 (QLYET) which was the second most frequent GL light chain sequence identified (PCIN63-UCA-KC2) (Figure 10D). To functionally characterize these putative UCAs, all 18 light chain variants were subsequently paired with the HC UCA and first evaluated for binding to eOD-GT8, a VRC01-class germline targeting immunogen (Figure 10E). Only three, including UCA-KC2 bound to eOG-GT8 with affinities similar to recently described putative VRC01-like bnAb precursors (Havenar-Daughton et al., 2018). All putative PCIN63-UCAs were tested against representative autologous Env sequences identified by NGS and SGA at all time points before 40mpi, including one rare viral variant lacking both the N276- and N462- glycans (M28-H1) (Figure 11A). None of the putative PCIN63-UCA Abs neutralized any of the autologous Env clones tested and no binding could be detected to the corresponding pseudoviruses lysates derived gp120s or recombinant gp120 from selected representative Env clones (Figure 11B), although gp120s from Env variants isolated at 28 and 33 mpi did not expressed sufficiently well to be evaluated.

[0341] Delineating the order in which SHM Motifs are selected may inform the elicitation of similar antibodies by vaccination. Accordingly, the emergence and frequency of up to 7 SHM Motifs were tracked over the course of infection to qualitatively determine the contributions of each to the expansion of the antibody lineage (Figure 2A). Longitudinal analysis revealed early selection of the HCDR2-Motif #2, typically a key contact with the CD4bs-loop, and LCDR2-Motif#5 (Figure 2B, 2C). It was followed by HCDR1-Motif#1 (stabilizing HCDR2) at 42 mpi, HFWR3-Motif#3 (V5 loop contact), LCDR2-Motif#5 and LCDR1-Motif#4 (adaptation to N276-glycan) at 44 mpi and HFWR3-Motif#6 (adaptation to N276-glycan), and finally LCDR3-Motif#7 (contact with Loop D) at 49 mpi (Figure 2A). Notably, LC Motifs, especially the LCDR1, appeared to be fixed in sequence almost immediately after selection was initiated while HC Motifs (#1 and #2 in particular), sampled a greater diversity. Although PCIN63 lineage maturation later selected an additional Gly residue, the sudden selection of the triple Gly + $D32_{LC}$ mutations, altogether at once, in LCDR1-Motif#4 at 44mpi was most striking. Concomitantly, HFWR3-Motif#3 and LCDR2-Motif#5 reached equilibrium of two dominant Motif variations, followed by fixation of HCDR2-Motif #2 and HFWR3-Motif#3 at 55mpi and finally HCDR1-Motif#1 and LCDR3-Motif#7 at 66mpi. Overall, the results highlight that less diversity is permissible in the light chain for epitope recognition whereas the heavy chain may be more "tunable" to further drive affinity maturation.

Dependence of SHM Motifs in the PCIN63 bnAb lineage for neutralization

[0342] Next assessed was the functional relevance of each SHM Motif to antibody neutralization. Antibody variants were generated by introducing individual SHM Motifs to the

UCA HC + KC pair and evaluated each variant for neutralization against autologous virus with and without the N276 glycan (Figure 3A). Pairing of the UCA-HC variants with affinity mature 71I-KC results in cross-neutralization of WT and N276A viruses, particularly when Motifs #2 is introduced to the UCA-HC. Interestingly, the combined LC SHMs alone allowed weak neutralization of all N276-glycan bearing autologous Env but not their N276-glycan lacking counterparts. In contrast, the UCA-KC paired with the affinity-matured 71I-HC predominantly neutralized viruses lacking the N276 glycan site except with the introduction of Motifs #4 and #6 to the UCA-KC, with a critical role of $D32_{LC}$ (Figure 11C). These observations not only confirm the critical role of the LC mutations in adaptation to the N276-glycan but also suggest direct engagement between the LC and this glycan.

[0343] Additionally, antibody variants were created where individual SHM Motifs on the affinity mature antibody PCIN63-71I were reverted back to germline and subsequently evaluated for neutralization on the same viruses (Figure 3B). Overall, individual reversions of SHM Motifs in either the HC or the KC had minimal effects the variants were paired with affinity-mature KC or HC, indicating a level of redundancy across the SHM Motifs for epitope recognition and that single SHM Motifs are not essential for neutralization. Overall, it is apparent that HCDR2-Motif#2, LCDR1-Motif4 and LFWR3-Motif#6 are sufficient but not necessary for autologous neutralization by PCIN63 Ab.

PCIN63 bnAbs engage the N276-glycan of some Env strains

[0344] To better understand how this antibody lineage might interact with the N276 and other surrounding glycans, neutralization against WT and corresponding N276A viruses were tested. The data revealed a glycan hierarchy of importance for neutralization by PCIN63 Abs, with N276 $\geq$ N197 > N262 $\approx$ N301 > N462/N463 > N448 (Figure 12). This trend is overall consistent with effect on neutralization by other VRC01-class bnAbs, particularly 12A21 and other Abs bearing a glycine-rich LCDR1 loop (VRC23, VRC27, VRC-CH31) with the exception of VRC-N6 (Figure 12, 13). Important variations were observed between viral strains for PCIN63 Abs neutralization as well as among PCIN63 bnAbs variants for neutralization of the same viral strain (Figure 4A). These variations were still apparent, although to a lesser extent, when pseudoviruses were produced in GnT I-/- cells (293-S) yielding predominant Man5 glycans on HIV Env (Figure 4A). The negative effect of N276-glycan removal was particularly striking and suggests that PCIN63 Abs may directly contact the N276-glycan in the context of some Env strain such as JR-CSF (Figure 4A). Other components of the epitope including surrounding glycans as well as key contact residues

on Env evaluated, and a general trend in dependency on the N276 glycan was observed when other obstructive features are present (JR-CSF) and tolerance of the N276 glycan when surrounding obstructive features are missing (JR-FL), such as a N461-glycan closer to the Ab and the lack of N197- and N234-glycans (Figure 4A). Comparably, an alignment of PCIN63 antibody sequences that are N276 glycan-tolerant revealed similar features with the glycan-tolerant 12A21 sequence that are not present among the PCIN63 glycan-dependent sequences (Figure 4B). In fact, these two categories of PCIN63 Abs appeared to segregate into separate branches of the lineage phylogenetic tree (Figure 10D).

Modelling PCIN63 maturation

[0345] To better understand the putative interactions between PCIN63 Abs and the Env trimer, an *in silico* model of 12A21 bound to BG505 SOSIP.664 was constructed using the published structures of 12A21 bound to gp120 (PDB ID: 4JPW) (Klein et al, 2013) and glycosylated BG505 SOSIP.664 bound to 35O22 and PGT122 (PDB ID: 6DE7) (Zhang et al, 2018) (Figure 5). We evaluated this model in the context of PCIN63 maturation (Figures 2 and 3). This model suggests contacts between E62 and HCDR2-$N57_{HC}$, and N279 and LCDR3-$E96_{LC}$ consistent with the strain-specific N276-glycan dependent variations observed in Figure 4A. Similarly, the N276-glycan dependent PCIN63 Abs carried SHM Motifs possibly sub-optimal for high affinity contacts with the CD4bs loop (non-aromatic residue $N54_{HC}$) and V5 loop ($Y61_{HC}$), while N276-glycan tolerant PCIN63 mAbs carried a fourth Gly in LCDR1-Motif#4 ($G34_{LC}$) and a more canonical LCDR3-Motif#7 with aromatic residues at position 91 and 97 optimal for loop D and V5 loop binding (Figure 4B). Interestingly, all PCIN63 mAbs also carried $R/W19_{HC}$ and $E/D76_{HC}$ mutations possibly involved in N197-glycan interactions. Overall, these data support a critical role for direct contact of the N276-glycan when the CD4bs loop is less accessible and Env protein contacts sub-optimal.

[0346] The late onset of plasma neutralization breadth in PC063 is consistent with previous studies reporting that CD4bs-specifc bnAbs appear to require more time to develop than bnAbs targeting other Env epitopes, a hypothesis also supported by the high levels of SHMs typically found among VRC01-class antibodies. In contrast, PCIN63 bnAbs appeared to have acquired neutralization breadth in less than two years and with minimal levels of SHM. While DRVIA7 narrowly neutralizing Abs also derived from the VK1-5 variable gene (Kong et al., 2016) the neutralization breadth of this lineage was limited compared to typical VRC01-class antibodies.

Accordingly, the PCIN63 lineage is the first case where a VRC01-class antibody lineage with high levels of neutralization breadth and potency was followed longitudinally from germline to affinity-mature antibody (Figure 1B) (Wu et al., 2010, Jardine et al., 2015, Zhou et al., 2015). Together with the recent finding that VK1-5+ subclass of VRC01-class precursors were nearly as common as the most frequent VK3-20+ precursors in naïve donor repertoires, (Havenar-Daughton et al., 2018), the isolation of the first VK1-5+ VRC01-class bnAb lineage suggests i) that the naive B-cells isolated using germline targeting immunogens may indeed represent true bnAbs precursors and ii) that this particular subclass of bnAbs serve as favorable targets for vaccine design because of their relatively higher frequency. Furthermore, the absence of enrichment in AID hotspots for this lineage suggests that the rapid affinity maturation of the PCIN63 lineage is not unique and might therefore be similarly recapitulated by vaccination.

[0347] The heavy chain of the PCIN63 lineage, particularly HC Motifs #1 and #2, appears to sample a higher level of diversity compared to the "all or nothing" SHM pattern of the LC Motifs, especially the LCDR1. These data suggest a highly stringent selection pressure on adapt to the V5 loop, loop D, and associated glycans, and a rather fine-tuned affinity maturation to the CD4bs loop. While our data confirms previous findings on the critical SHM needed on the LC to accommodate the N276-glycan, we also observed dependence on the N276-glycan by earlier PCIN63 intermediates (LCDR1-Motif#4 GGGD). This dependence on the N276-glycan was more pronounced when interactions with the CDabs-loop and loop D are suboptimal, suggesting that immunization strategies should not focus on glycan-deleted immunogens alone to drive affinity maturation of this lineage.

[0348] Altogether, these data suggest that PCIN63 Abs maturation pathway required a fine balance between glycan avoidance to better access the CD4bs and Loop D contact residues, and direct glycan binding to counter lower affinity of early intermediates as Env evolved to escape autologous Ab responses. While acquiring a deletion in LCDR1 to avoid the N276-glycan, as seen in the majority of VRC01-like Abs, might be more difficult to reproduce by vaccination, our data support a vaccine strategy selecting intermediates with N276 glycan dependence to begin followed by affinity maturation to eventually accommodate this key glycan. While follow-up studies will be critical to fully understand the complex evolution of Ab/Env interaction in the PCIN63 lineage, this detailed maturation pathway of a natural minimally mutated VRC01-like bnAb already provide valuable information for immunogen and vaccine design.

Experimental model and subject details

[0349] Ethics Statement, Study Participant and Samples Donor PC064 was part of the IAVI sponsored Protocol C cohort in sub-Saharan Africa that involved rapid screening of 613 individuals with a recent history of HIV exposure for HIV antibodies in sub-Saharan Africa (Landais et al., 2016). Samples were collected with written, informed consent, and the study was reviewed and approved by the relevant Ethics and Research Committees.

[0350] Donor PC063 was enrolled in the Protocol C longitudinal primary infection cohort approximately 19 weeks (4 months) after infection by a subtype C HIV-1 virus, and was identified as one of the top 20% neutralizers, neutralizing up to 85% of viruses on a 37-virus panel (Landais et al., 2016). The neutralizing activity was first detected in the plasma after 5 year of infection (61 months, 80 weeks) and steadily increased to reach a plateau at 2 years (24 months, 266 weeks), neutralizing 79% of viruses from a large panel (Seaman et al., 2010, Landais et al., 2016). The plasma broadly neutralizing activity was mapped to the CD4 binding site as it was competed by RSC3 and its absorption with rgp120 monomers was competed by b6 and sensitive to the D168R mutation (Landais et al., 2016).

[0351] Cell lines. Human embryonic kidney (HEK)-derived 293T, HEK293S N-acetylglucosaminyltransferase I-negative (GnTI-/-), and HeLa-derived TZM-bl cells were maintained in complete Dulbecco's Modified Eagle Medium (herein referred to as cDMEM) containing high- glucose Dulbecco's Modified Eagle Medium (DMEM, Thermo Fisher), 1X Penicillin-Streptomycin (Pen Strep, Thermo Fisher) and 10% fetal bovine serum (FBS, Gemini Bio Products) at 37°C and 5% CO_2. FreeStyle® 293F cells (Thermo Fisher) were maintained in Freestyle 293 Expression Medium at 37°C and 10% CO_2 with shaking at 120 RPM.

Methods details

[0352] Single memory B-cell sorting and isolation of PCIN63 monoclonal antibodies. Sorting of antigen- and epitope-specific memory B cells was performed as previously described (Choi et al., 2016; Sok et al., 2014; Tiller et al., 2008; Wu et al., 2010).

[0353] Fluorescent-labeled antibodies recognizing cell surface markers were purchased from BD Biosciences. AVI-tagged WT and D368R YU2-gp140-Foldon proteins (plasmid generously provided by Y. Li) were produced, purified, labeled with biotin (Avidity), and coupled to streptavidin-PE, streptavidin-APC (Life Technologies), and streptavidin-BV421 (BD Biosciences), as previously described (Sok et al., 2014). Cells were stained with the Live/Dead Fixable Near-IR Dead Cell Stain Kit (Life Technologies) for 30 minutes on ice according to the manufacturer's

instructions. Cells were then labeled with antibodies for surface markers together with probes for 1 hour in Brilliant Stain buffer (BD Biosciences) on ice. Cells were sorted into individual wells of a 96 well plate containing First Strand buffer containing DTT and RNAseOUT® (Life Technologies) using a BD FACSAria III sorter, and were immediately sealed and stored at-80°C after sorting each plate.

[0354] cDNA was generated from cells sorted into lysis buffer using Superscript® III Reverse Transcriptase (Life Technologies) and random hexamers (Gene Link). Nested PCR amplification of heavy- and light-chain variable regions was performed using Multiplex PCR Kit (Qiagen) and previously described primer sets (Tiller et al., 2008). Amplified heavy- and light-chain variable regions were sequenced and subsequently analyzed using IMGT (the International ImMunoGeneTics Information System, www.imgt.org) V-quest (Lefranc et al., 2009).

[0355] Antibodies of interest were cloned into expression vectors (Tiller et al., 2008) by re-amplification of sequences using the same primers but modified to introduce homology to the cut ends of the vector, and cloning was performed using the Seamless Cloning and Assembly Enzyme mix (Life Technologies) in expression vectors with the appropriate IgG1, Ig kappa or Ig lambda constant domain. Antibodies incorporating targeted amino acid mutations were generated by Quickchange® mutagenesis (Stratagene). Monoclonal antibodies were reconstituted by transient transfection in HEK293 cells followed by purification from serum-free culture supernatants.

[0356] PCIN63 antibody expression and purification. Antibodies HC and LC constructs were transiently expressed with the FreeStyle® 293 Expression System (Invitrogen). Supernatant was collected after 4-5 days of culture and whole IgGs were purified with Protein A sepharose (GE Healthcare). Purified proteins purity and integrity checked by SDS–PAGE.

[0357] B-cell repertoire next generation sequencing and computational analysis. RNA was prepared (RNEasy® kit, Qiagen) from total PBMCs and was subjected to reverse transcription using barcoding primers that contain unique Ab identifiers as previously described (Briney et al., 2016a). The cDNA was then amplified using a mix of gene specific primers containing unique identifiers. Illumina sequencing adapters and sample-specific indexes were added during a second round of PCR. Samples were quantified using fluorometry (Qubit; Life Technologies), pooled at approximately equimolar concentrations, and the sample pool was re-quantified before loading onto an Illumina MiSeq. Paired-end MiSeq reads were merged with PANDAseq (Masella et al., 2012). GL assignment, junction identification, and other basic Ab information was determined using AbStar (www.github.com/briney/abstar). Sequences were assigned to clonal lineages using Clonify (Briney et al., 2016a). PCIN63 lineage sequences were clustered at 97.5% identity with

USEARCH (Edgar, et al., 2010), and the size of each cluster was recorded. Cluster centroids were used to generate a multiple sequence alignment with MAFFT (Katoh et al., 2005), and a tree file was calculated with FastTree using default settings (Price et al., 2010). The phylogenetic tree was drawn in Python using the ETE Toolkit (Huerta-Cepas et al., 2010).

[0358] Single genome amplification (SGA), sequencing and cloning. HIV-1 RNA was isolated from plasma using the Qiagen QIAamp® Viral RNA kit, and reverse transcribed to cDNA using SuperScript® III Reverse Transcriptase (Invitrogen, CA). The envelope genes were amplified from single genome templates (Salazar-Gonzalez et al., 2008) and amplicons were directly sequenced using the ABI PRISM Big Dye Terminator Cycle Sequencing Ready Reaction kit (Applied Biosystems, Foster City, CA) and resolved on an ABI 3100 automated genetic analyser. The full-length env sequences were assembled and edited using Sequencher v.4.5 software (Genecodes, Ann Arbor, MI). Multiple sequence alignments were performed using Clustal X (ver. 1.83) and edited with BioEdit (ver. 7.0.9). Sequence alignments were visualized using Highlighter for Amino Acid Sequences v1.1.0 (beta). The phylogeny was reconstructed using FastTree (Price et al., 2010) with a GTR1CAT model, and rooted on the PI/SU. Signals of selective pressure were detected with MEME (episodic diversifying selection) (Murrell et al., 2012) and DEPS (directional selection) (Kosakovsky-Pond et al., 2008) using the FastTree-generated trees, implemented in Hyphy (Pond et al., 2005).

[0359] Selected envelope amplicons were cloned into the expression vector pcDNA 3.1 (directional) (Invitrogen) by re-amplification of SGA first-round products using Pfu Ultra II enzyme (Stratagene) with the EnvM primer, 59-TAGCCCTTCCAGT CCCCCCTTTTCTTTTA-39 (Gao et al., 1996) and directional primer, EnvAstop, 59-CAC CGGCTTAGGCATCTCCTATGGCAGGAAGAA-39 (Kraus et al., 2010). Cloned env genes were sequenced to confirm that they exactly matched the sequenced amplicon. Autologous clones were mutated at key residues within the C-strand using the Stratagene QuickChange II kit (Stratagene) as described by the manufacturer. Mutations were confirmed by sequencing. Envelope clones were used to generate single round of replication Env-pseudoviruses as described below.

[0360] Full-length *env* amplification sequencing and computational analysis. HIV-1 envelope genes were amplified and sequenced as described in Laird-Smith *et. al.* (2016) (Laird Smith et al., 2016). Briefly, virions were purified from plasma using a sucrose cushion and ultracentrifugation. Viral RNA was extracted (Viral RNA Mini Kit, Qiagen) and subjected to RT-PCR (SuperScript III First Strand, Thermo Fisher). The cDNA was used as template to generate HIV-1 *env* amplificons, which were then purified (QIAquick, Qiagen). Replicate PCR reactions for each sample were

visualized, quantitated (2100 Bioanalyzer System, Agilent Biosciences) and pooled by sample. Preparation and sequencing of SMRTbell template libraries of ~2.6-kb insert size were performed according to the manufacturer's instructions (Pacific Biosciences). Additional details are provided in Supplemental Information.

[0361] CCS sequences were constructed using the PacBio SMRTportal software (version 2.3). The Full-Length Envelope Analysis (FLEA) pipeline was used to error correct these CCS reads, and cluster them into near-identical clusters, inferring High Quality Consensus Sequences (HQCSs) for each cluster. Envelope phylogenies, as well as the dynamics of amino acid frequency evolution, were inferred from these HQCSs. MAFFT (v7.164b (Katoh and Standley, 2013), with manual curation, was used to create a multiple sequence alignment. Gappy regions were manually removed when reconstructing phylogenies, since their alignment is uncertain. Phylogenies were reconstructed with FastTree v2.1 (Price et al., 2010), and visualized with FigTree (http://tree.bio.ed.ac.uk/software/figtree/). Frequency kinetic plots and similar analyses were created with custom Mathematica scripts.

[0362] Selected full-length autologous *env* gene sequences were synthesized for representative clones of each time point using GeneArt® gene synthesis services (Life Technologies), then cloned into pcDNA3.1 vector (Life Technologies) for pseudovirus production. Mutagenesis was performed using Quickchange site-directed mutagenesis kit (Agilent Technologies).

[0363] Neutralization assay. Plasma and monoclonal antibodies neutralizing activity was assessed using single round of replication in TZM-bl target cells, as described previously (Landais et al., 2016) and in absence of DEAE-dextran. Briefly, wild-type (WT) and mutant pseudoviruses were generated by co-transfection of 293T cells with an Env-expressing plasmid and an Env-deficient genomic backbone plasmid (pSG3ΔEnv). Pseudoviruses were harvested 72h post transfection for use in neutralization assays. Pseudoviruses incorporating single amino acid mutations were generated by Quickchange mutagenesis (Stratagene). Plasma samples were heat-inactivated at 56 C for 45min prior to use in neutralization assays.

[0364] Serum adsorptions. Serum adsorptions with antigen-coupled beads were performed using tosyl-activated magnetic beads (Life Technologies), as described previously (Li et al., 2008). Beads coupling was performed at a ratio of 1mg gp140 per 25mg of beads. Plasma samples were depleted of Abs binding to these proteins through multiple rounds of immunoprecipitation. The depletion of Abs of the desired specificity was confirmed by ELISA prior to using depleted serum in pseudovirus neutralization assays.

[0365] Surface plasmon resonance (SPR) SPR experiments were performed on a Proteon XPR36 instrument (Bio-Rad) using GLC sensor chips (Bio-Rad) and 1x HBS buffer (Teknova) supplemented with 1 mg/mL BSA). Chips were prepared using the Human Antibody Capture Kit (GE Healthcare) according to manufacturer's instructions. For kinetic measurements, approximately 100 RUs of the indicated mAbs were captured onto the sensor surface. 4-fold dilution series of the indicated analytes were flowed over the captured mAbs for 120 seconds, followed by buffer injections for 600 seconds. After each cycle, surfaces were regenerated by four injections of 3 M magnesium chloride with 180 second contact times. Data were analyzed using the ProteOn Manager software (Bio-Rad). Following interspot and column double referencing, data were fitted to a Langmuir 1:1 binding model or equilibrium binding model as appropriate.

[0366] ELISA assays Half-area 96-well ELISA plates were coated overnight at 4C with 50 μL PBS containing 250 ng of compound per well. The D7324 polyclonal sheep Ab (Aalto Bioreagents) targeting the C5 domain of gp120 was also used to capture autologous gp120 from pseudovirus stocks lysed by adding 1% NP40 for 30 minutes at room temperature. The wells were washed four times with PBS containing 0.05% Tween 20 and blocked with 3% BSA at room temperature for 1h. Serial dilutions of sera were then added to the wells, and the plates were incubated at room temperature for 1 hour. After washing four times, goat anti-human IgG F(ab')2 conjugated to alkaline phosphatase (Pierce), diluted 1:1000 in PBS containing 1% BSA and 0.025% Tween 20, was added to the wells. The plates were incubated at room temperature for 1 h, washed four times, and the plates were developed by adding alkaline phosphatase substrate (Sigma) diluted in alkaline phosphatase staining buffer (pH 9.8), according to the manufacturer's instructions. The optical density at 405 nm was read on a microplate reader (Molecular Devices). EC50 values were calculated using Prism6 (GraphPad).

[0367] Quantification and Statistical Analysis For all mAb/serum pseudovirus neutralization and ELISA assays (Figures 1C, 3A, 3B, 4A, 6A, 8, 9, 11C, 11D, 12) the IC_{50}, or concentration of mAb/ dilution of serum needed to obtain 50% neutralization against a given pseudovirus, was calculated from the non-linear regression of the neutralization curve. For neutralization assays in which a fold-change in IC_{50} imparted by a particular virus mutant or virus treatment was reported (Figures 4A, 12), the IC50 obtained for one virus/assay condition was divided by the IC_{50} obtained for the other virus/assay condition, as indicated in the figure legends. All neutralization and ELISA assays were repeated at least twice, and data shown are from representative experiments.

[0368] SPR measurements (Figures 10E) were taken over two independent experiments, and data shown are from representative experiments.

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[0414] While the invention has been described in connection with what is presently considered to be the most practical and preferred embodiments, it is to be understood that the invention is not to be limited to the disclosed embodiments, but on the contrary, is intended to cover various modifications and equivalent arrangements included within the spirit and scope of the appended claims.

[0415] All publications, patents, patent applications, internet sites, and accession numbers/database sequences including both polynucleotide and polypeptide sequences cited herein are hereby incorporated by reference herein in their entirety for all purposes to the same extent as if each individual publication, patent, patent application, internet site, or accession number/database sequence were specifically and individually indicated to be so incorporated by reference.

SEQUENCES

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SEQ ID NO: 134; PCIN63-71I1a; Motif #2
NLHAVNY

SEQ ID NO: 135; PCIN63-71J2a; Motif #2
NLHAVNY

SEQ ID NO: 136; PCIN63-71K; Motif #2
NINARNN

SEQ ID NO: 137; PCIN63-71L; Motif #2
NINARNN

SEQ ID NO: 138; PCIN63-71M1a; Motif #2

NINARNQ

SEQ ID NO: 139; PCIN63-71N1a; Motif #2
NLHAVNY

SEQ ID NO: 140; PCIN63-71O; Motif #2
NLHAVNY

SEQ ID NO: 141; PCIN63-71P; Motif #2
NLHAVNY

SEQ ID NO: 142; PCIN63-77B1b; Motif #2
NINARNQ

SEQ ID NO: 143; PCIN63-77C; Motif #2
NINARNN

SEQ ID NO: 144; PCIN63-77D; Motif #2
NINARNH

SEQ ID NO: 145; PCIN63-66B; Motif #3
PRK

SEQ ID NO: 146; PCIN63-71B; Motif #3
AHK

SEQ ID NO: 147; PCIN63-71C; Motif #3
PHK

SEQ ID NO: 148; PCIN63-71D2b; Motif #3
PHK

SEQ ID NO: 149; PCIN63-71F; Motif #3
APN

SEQ ID NO: 150; PCIN63-71G; Motif #3
AHQ

SEQ ID NO: 151; PCIN63-71H; Motif #3
PYQ

SEQ ID NO: 152; PCIN63-71I1a; Motif #3
AHQ

SEQ ID NO: 153; PCIN63-71J2a; Motif #3
AHQ

SEQ ID NO: 154; PCIN63-71K; Motif #3
PYQ

SEQ ID NO: 155; PCIN63-71L; Motif #3
PYQ

SEQ ID NO: 156; PCIN63-71M1a; Motif #3
AYQ

SEQ ID NO: 157; PCIN63-71N1a; Motif #3
AHN

SEQ ID NO: 158; PCIN63-71O; Motif #3
AHQ

SEQ ID NO: 159; PCIN63-71P; Motif #3
AHQ

SEQ ID NO: 160; PCIN63-77B1b; Motif #3
AYQ

SEQ ID NO: 161; PCIN63-77C; Motif #3
PQT

SEQ ID NO: 162; PCIN63-77D; Motif #3
AYQ

SEQ ID NO: 163; PCIN63-66B; Motif #4
SGGDG

SEQ ID NO: 164; PCIN63-71B; Motif #4
SGGKG

SEQ ID NO: 165; PCIN63-71C; Motif #4
GGGDA

SEQ ID NO: 166; PCIN63-71D2b; Motif #4
GGGDA

SEQ ID NO: 167; PCIN63-71F; Motif #4
GHGDA

SEQ ID NO: 168; PCIN63-71G; Motif #4
GGGDG

SEQ ID NO: 169; PCIN63-71H; Motif #4
GGGDA

SEQ ID NO: 170; PCIN63-71I1a; Motif #4
GGGDG

SEQ ID NO: 171; PCIN63-71J2a; Motif #4
GGGDA

SEQ ID NO: 172; PCIN63-71K; Motif #4
GGGDA

SEQ ID NO: 173; PCIN63-71L; Motif #4
GGGDA

SEQ ID NO: 174; PCIN63-71M1a; Motif #4
GGGDA

SEQ ID NO: 175; PCIN63-71N1a; Motif #4
SGGNG

SEQ ID NO: 176; PCIN63-71O; Motif #4
GGGDG

SEQ ID NO: 177; PCIN63-71P; Motif #4
GGGDG

SEQ ID NO: 178; PCIN63-77B1b; Motif #4
GGGDA

SEQ ID NO: 179; PCIN63-77C; Motif #4
GGGDA

SEQ ID NO: 180; PCIN63-77D; Motif #4
SGGDG

SEQ ID NO: 181; PCIN63-66B; Motif #5
FNKD

SEQ ID NO: 182; PCIN63-71B; Motif #5
FTKD

SEQ ID NO: 183; PCIN63-71C; Motif #5
FNKN

SEQ ID NO: 184; PCIN63-71D2b; Motif #5
FNKN

SEQ ID NO: 185; PCIN63-71F; Motif #5
YNKS

SEQ ID NO: 186; PCIN63-71G; Motif #5
HNIN

SEQ ID NO: 187; PCIN63-71H; Motif #5
FNKN

SEQ ID NO: 188; PCIN63-71I1a; Motif #5
HNIN

SEQ ID NO: 189; PCIN63-71J2a; Motif #5
FNKN

SEQ ID NO: 190; PCIN63-71K; Motif #5

FRKN

SEQ ID NO: 191; PCIN63-71L; Motif #5
FRKN

SEQ ID NO: 192; PCIN63-71M1a; Motif #5
FNKN

SEQ ID NO: 193; PCIN63-71N1a; Motif #5
FSKD

SEQ ID NO: 194; PCIN63-71O; Motif #5
HNLN

SEQ ID NO: 195; PCIN63-71P; Motif #5
HNAN

SEQ ID NO: 196; PCIN63-77B1b; Motif #5
FNKN

SEQ ID NO: 197; PCIN63-77C; Motif #5
FNKK

SEQ ID NO: 198; PCIN63-77D; Motif #5
FNKD

SEQ ID NO: 199; PCIN63-66B; Motif #6
FHE

SEQ ID NO: 200; PCIN63-71B; Motif #6
FGD

SEQ ID NO: 201; PCIN63-71C; Motif #6
FHD

SEQ ID NO: 202; PCIN63-71D2b; Motif #6
FHD

SEQ ID NO: 203; PCIN63-71F; Motif #6
SGE

SEQ ID NO: 204; PCIN63-71G; Motif #6
FHE

SEQ ID NO: 205; PCIN63-71H; Motif #6
FHD

SEQ ID NO: 206; PCIN63-71I1a; Motif #6
FHE

SEQ ID NO: 207; PCIN63-71J2a; Motif #6
FHD

SEQ ID NO: 208; PCIN63-71K; Motif #6
FHE

SEQ ID NO: 209; PCIN63-71L; Motif #6
FHE

SEQ ID NO: 210; PCIN63-71M1a; Motif #6
FHD

SEQ ID NO: 211; PCIN63-71N1a; Motif #6
SHE

SEQ ID NO: 212; PCIN63-71O; Motif #6
FHE

SEQ ID NO: 213; PCIN63-71P; Motif #6
FHE

SEQ ID NO: 214; PCIN63-77B1b; Motif #6
FHD

SEQ ID NO: 215; PCIN63-77C; Motif #6
FHD

SEQ ID NO: 216; PCIN63-77D; Motif #6
FGD

SEQ ID NO: 217; PCIN63-66B; Motif #7
QVLET

SEQ ID NO: 218; PCIN63-71B; Motif #7
QVYES

SEQ ID NO: 219; PCIN63-71C; Motif #7
QVLET

SEQ ID NO: 220; PCIN63-71D2b; Motif #7
QVLET

SEQ ID NO: 221; PCIN63-71F; Motif #7
QVYES

SEQ ID NO: 222; PCIN63-71G; Motif #7
QVVEW

SEQ ID NO: 223; PCIN63-71H; Motif #7
QVLET

SEQ ID NO: 224; PCIN63-71I1a; Motif #7
QVFEW

SEQ ID NO: 225; PCIN63-71J2a; Motif #7
QVLET

SEQ ID NO: 226; PCIN63-71K; Motif #7
QVLET

SEQ ID NO: 227; PCIN63-71L; Motif #7
QVLET

SEQ ID NO: 228; PCIN63-71M1a; Motif #7
QVLET

SEQ ID NO: 229; PCIN63-71N1a; Motif #7
QVYQT

SEQ ID NO: 230; PCIN63-71O; Motif #7
QVFEW

SEQ ID NO: 231; PCIN63-71P; Motif #7
QVFEW

SEQ ID NO: 232; PCIN63-77B1b; Motif #7
QVLET

SEQ ID NO: 233; PCIN63-77C; Motif #7
QVLET

SEQ ID NO: 234; PCIN63-77D; Motif #7
QAYES

SEQ ID NO: 235; PCIN63-66B; VH
QVQLVQSGAEVKKPGASMRVSCKASGYTFTACYIHWFRQAPGQGLEWMGWINPINGARNNPRKFQGRVTM
TRDTSIDTAYLELRNLASDDTAMYYCTRDSSRRDTNWWLDPWGQGTLVTVSS

SEQ ID NO: 236; PCIN63-71B; VH
QVQLVQSGAEVKKPGASVRVSCKASGYTFTAYFIHWVRQAPGQGLEWVGWINPLHGAVNYAHKFQGRVSM
TRDTSISTAYMELRSLKSDDTAIYYCTTHSSSRDFQWSLDPWGQGTLVTVSS

SEQ ID NO: 237; PCIN63-71C; VH
QVQLVQSGAEVKKPGASMRVSCKASGYTFTSCYIHWFRQAPGQGLEWMGWLNPINGARNNPHKFQGRITL
TRDTSTDTAYLELRNLRSDDTAVYYCTRDSSRRDTNWWLDPWGQGTLVTVSS

SEQ ID NO: 238; PCIN63-71D2b; VH
QVQLVQSGAEVKKPGASMRVSCKASGYTFTACYIHWFRQAPGQGLEWMGWLNPINGARNNPHKFQGRITL
TRDTSTDTAYLELRNLRSDDTAVYYCTRDSSRRDTNWWLDPWGQGALVTVSS

SEQ ID NO: 239; PCIN63-71F; VH
QVQLVQSGAEVKKPGASVRVSCKASGYSFTDYFVHWVRQAPGQGLEWVGWINPINGAPNYAPNFRGRITL
TRDTSIDTLYMDLRSLRVDDTAVYFCTRDSSRQQRDWWLDPWGQGTLVTVSS

SEQ ID NO: 240; PCIN63-71G; VH

QVQLVQSGAEVKKPGASVRVSCKASGYTFNSCLIHWWRQAPGQGLQWMAWINPLHGAVNYAHQFQGRITV
TRDTSIDTAYMELRGLRSDDTATYYCTRDASRDDRAWRLDPWGQGTLVTVSS

SEQ ID NO: 241; PCIN63-71H; VH
QVQLVQSGVAVKKPGASVWVSCKASGYTFTSCYIHWFRQAPGQGLEWMGWLNPINGARNNPYQFQGRISL
TRDTSSETAYLELRNLRSDDTAVYYCARDSSREETNWWLDPWGQGTLVTVSS

SEQ ID NO: 242; PCIN63-71I1a; VH
QVQLVQSGAEVKKPGASVRVSCKASGYTFNSCLIHWWRQAPGQGLQWMAWINPLHGAVNYAHQFQGRITV
TRDTSIDTAYMELRGLRSDDTATYYCTRDASRDDRAWRLDPWGQGTLVTVSS

SEQ ID NO: 243; PCIN63-71J2a; VH
QVQLVQSGAEVKKPGASMRVSCKASGYTFTACYIHWFRQAPGQGLEWMGWLNPINGARNNPHKFQGRITL
TRDTSTDTAYLELRNLRSDDTAVYYCTRDSSRRDTNWWLDPWGQGTLVTVSS

SEQ ID NO: 244; PCIN63-71K; VH
QVQLVQSGAAVKKPGASVWVSCKASGYTFTSCYIHWFRQAPGQGLEWMGWLNPINGARNNPYQFQGRISL
TRDTSSETAYLELRNLTPDDTAVYYCTRDSSRDETNWWLDPWGQGTLVTVSS

SEQ ID NO: 245; PCIN63-71L; VH
QVQLVQSGAAVKKPGASVWVSCKASGYTFTSCYIHWFRQAPGQGLEWMGWLNPINGARNNPYQFQGRISL
TRDTSSETAYLELRNLTPDDTAVYYCTRDSSRDETNWWLDPWGQGTLVIVSS

SEQ ID NO: 246; PCIN63-71M1a; VH
QVQLVQSGAAVKKPGASVWVSCKASGYTFTSCYIHWFRQAPGQGLEWMGWLNPINGARNQAYQFQGRISL
TRDTPSETAYLELRDLRSDDTAVYYCARDSSRDETNWWLDPWGQGTLVTVSS

SEQ ID NO: 247; PCIN63-71N1a; VH
QVQLVQSGAEVKKPGASVRVSCKASGYTFNTCLIHWWRQAPGQGLQWLAWINPLHGAVNYAHNFQGRITV
TRDTSIDTAYMELRGLRSDDTATYYCTRDSSRGNTEWRLDPWGQGTLVTVSS

SEQ ID NO: 248; PCIN63-71O; VH
QVQLVQSGAEVKKPGASVRVSCKASGYTFNTCLIHWWRQAPGQGLQWVAWINPLHGAVNYAHQLQGRITV
TRDTSIDTAYMELRGLRADDTATYYCTRDSSRDNLEWRLDPWGQGTLVTVSS

SEQ ID NO: 249; PCIN63-71P; VH
QVQLVQSGAEVKKPGASVRVSCKASGYTFNTCLIHWWRQAPGQGLQWVAWINPLHGAVNYAHQLQGRITV
TRDTSIDTAHMELRGLRSDDTATYYCTRDSSRGDTEWRLDPWGQGTLVTVSS

SEQ ID NO: 250; PCIN63-77B1b; VH
QVQLVQSGAEVKKPGASARVSCKASGYTFTAYFIHWVRQAPGQGLEWVGWINPLHGAVNYAHKFQGRVSM
TRDTSISTAYMELRSLKSDDTAIYYCTTHLSSRDFSWSWDPWGQGTLVTVSP

SEQ ID NO: 251; PCIN63-77C; VH
QVQLVQSGAEVKKPGASVRVSCKASGYTFTACYIQWFRQAPGQGLEWMGWINPINGARNNNPQTFQGRVT
LTRDTSIDTAYLELRNLRDDDTAIYYCTRDSSRRDLEWRLDPWGQGTLVTVSS

SEQ ID NO: 252; PCIN63-77D; VH
QVQLVQSGAAVKKPGASVWVSCKASGYTFTSCYIHWFRQAPGQGLEWMGWLNPINGARNHAYQFQGRISL
TRDTSSETAYLELRNLRSDDTAVYYCARDSSRDETNWWLDPWGQGTLVTVSS

SEQ ID NO: 253; PCIN63-66B; VL

AIRMTQSPATLSASVGERVTITCRASQGIGSDLGWYQQKPGKSPKLLIFKASNLKDGVPPRFSGGGFHTE
FTLTISSLQPDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 254; PCIN63-71B; VL
AIRMTQSPATLSASVGDRVTITCRASQGIGNKLGWFQQKPGKAPKPLIFKASTLKDGVPSRFSGSGFGTD
FTLTISSLQPDDFATYYCQVYESFGQGTKVEIK

SEQ ID NO: 255; PCIN63-71C; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKSGQAPKLLIFKASNLKNGVPPRFSGSGFHTD
FTLTISGLQPDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 256; PCIN63-71D2b; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKSGQAPKLLIFKASNLKNGVPPRFSGSGFHTD
FTLTISGLQSDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 257; PCIN63-71F; VL
AIRMTQSPPTVSASAGDRVTITCRAGQHIGNDLAWYQTKVGMAPKLLIYQASNLKSGVPSRFSGSGSGTE
FTLSITSLQPDDFATYYCQVYESFGQGTKVEIK

SEQ ID NO: 258; PCIN63-71G; VL
AIRMTQSPATLSASVGDRVTLTCRAGQGIGSDLGWYQQKPGKAPKLLIHKASNLINGVPSRFSGSGFHTE
FTLTISSLQPDDFATYYCQVVEWFGQGTKVEIK

SEQ ID NO: 259; PCIN63-71H; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKPGQAPKLLIFKASNLKNGVPTRFTGSGFHTD
FTLTINGLQSDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 260; PCIN63-71I1a; VL
AIRMTQSPATLSASVGDRVTLTCRAGQGIGSDLGWYQQKPGKAPKLLIHKASNLINGVPSRFSGSGFHTE
FTLTINSLQPDDFATYYCQVFEWFGPGTKVEIK

SEQ ID NO: 261; PCIN63-71J2a; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKSGQAPKLLIFKASNLKNGVPPRFSGSGFHTD
FTLTISGLQPDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 262; PCIN63-71K; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKPGQAPKLLIFKASRLKNGVPTRFTGSGFHTE
FTLTISGLQSDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 263; PCIN63-71L; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKPGQAPKLLIFKASRLKNGVPTRFTGSGFHTE
FTLTISGLQSDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 264; PCIN63-71M1a; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKSGQAPKLLIFKASNLKNGVPPRFSGSGFHTD
FTLTISGLQPDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 265; PCIN63-71N1a; VL
AIRMTQSPATLSASVGDKVTITCRASQGIGNNLGWYQQKPGQAPKLLIFKASNSKDGVPPRFSGSGSHTE
FTLTINSLQPDDFATYYCQVYQTFGQGTKVEIK

SEQ ID NO: 266; PCIN63-71O; VL

AIRMTQSPATLSASVGDRVTLTCRAGQGIGSDLGWYQQKPGKAPKLLIHKASNLLNGVPSRFSGSGFHTE
FTLTISSLQPDDFATYYCQVFEWFGQGTKVEIK

SEQ ID NO: 267; PCIN63-71P; VL
AIRMTQSPATLSASVGDRVTLTCRAGQGIGSDLGWYQQKPGKAPKLLIHKASNLANGVPSRFSGRGFHTE
FTLTISSLQPDDFATYYCQVFEWFGQGTKVEIK

SEQ ID NO: 268; PCIN63-77B1b; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKPGQAPKLLIFKASNLKNGVPTRFTGSGFHTD
FTLTISGLQSDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 269; PCIN63-77C; VL
AIRMTQSPATLSASVGDRVTITCRAGQGIGSDLAWYQQKPGQAPKLLIFKASNLKKGVPTRFTGSGFHTD
FTLTISGLQSDDFATYYCQVLETFGQGTKVEIK

SEQ ID NO: 270; PCIN63-77D; VL
AIRMTQSPATLSAFVGDRVTITCRASQGIGDDLGWYQQKPGKVPKPLIFKASNLKDGVPSRFSGSGFGTD
FTLTINNLQPDDFATYYCQAYESFGQGTKVEIK

SEQ ID NO: 271; PCIN63-66B; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAATGAGGGTCTCCTGCAAGG
CCTCTGGATACACCTTCACCGCCTGCTATATACACTGGTTTCGACAGGCCCCTGGACAAGGCCTTGAGTG
GATGGGATGGATCAACCCTATCAATGGTGCCAGAAATAATCCACGCAAGTTTCAGGGCAGGGTCACCATG
ACCAGGGACACGTCCATTGATACAGCGTACTTGGAACTGCGCAACCTGGCATCTGACGACACGGCCATGT
ATTACTGTACGAGAGATTCATCGAGGCGTGATACGAATTGGTGGTTGGACCCCTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 272; PCIN63-71B; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CTTCTGGATACACCTTCACCGCCTATTTTATACACTGGGTGCGACAGGCCCCTGGACAGGGGCTTGAGTG
GGTGGGTTGGATCAACCCTCTCCATGGCGCCGTAAACTATGCACACAAATTTCAAGGCAGGGTCTCCATG
ACCAGGGACACCTCCATCAGCACAGCCTACATGGAACTTCGCAGCCTGAAATCTGACGACACGGCCATTT
ATTACTGTACCACACATTCATCGAGCCGTGATTTTCAGTGGTCGTTGGACCCCTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 273; PCIN63-71C; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAATGAGGGTCTCCTGCAAGG
CCTCTGGATACACCTTCACCTCTTGTTATATACACTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGTGCCAGAAATAATCCACACAAGTTTCAGGGCAGGATCACCCTG
ACCAGGGACACGTCCACTGATACAGCCTACTTGGAACTGCGCAACCTGAGATCTGACGACACGGCCGTAT
ATTATTGTACGAGAGATTCATCGAGGCGTGATACGAATTGGTGGTTGGACCCTTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 274; PCIN63-71D2b; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAATGAGGGTCTCCTGCAAGG
CCTCTGGATACACTTTCACCGCTTGTTATATACACTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGTGCCAGAAATAATCCACACAAGTTTCAGGGCAGGATCACCCTG
ACCAGGGACACGTCCACTGATACAGCCTACTTGGAACTGCGCAACCTGAGATCTGACGACACGGCCGTGT
ATTATTGTACGAGAGATTCATCGAGGCGTGATACGAATTGGTGGTTGGACCCTTGGGGCCAGGGAGCCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 275; PCIN63-71F; VH

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAAGTGAAGAAGCCTGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CCTCTGGATACAGCTTCACCGACTACTTTGTGCACTGGGTGCGACAGGCCCCTGGACAGGGCCTTGAGTG
GGTGGGGTGGATAAACCCTATTAATGGAGCCCCTAATTATGCACCGAACTTTCGGGGCAGGATCACCTTG
ACTAGGGACACATCCATCGACACACTCTATATGGACTTGAGAAGCCTGAGAGTTGACGACACGGCCGTTT
ACTTCTGTACGAGAGATTCATCGAGGCAACAACGGGACTGGTGGTTAGACCCCTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 276; PCIN63-71G; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CCTCCGGATACACCTTCAACTCCTGCTTAATTCATTGGTGGCGACAGGCCCCTGGACAAGGCCTTCAGTG
GATGGCTTGGATCAACCCTCTCCATGGTGCCGTAAATTATGCACACCAGTTTCAGGGGAGGATCACCGTG
ACCAGGGACACGTCCATCGACACTGCCTACATGGAACTGCGCGGCCTGAGATCTGACGACACGGCCACAT
ATTACTGTACGAGAGATGCATCCAGAGATGATCGCGCGTGGCGCTTGGACCCCTGGGGCCAGGGAACACT
GGTCACCGTCTCCTCA

SEQ ID NO: 277; PCIN63-71H; VH
CAGGTGCAGCTGGTGCAGTCTGGGGTAGCGGTGAAGAAGCCTGGGGCCTCAGTGTGGGTCTCCTGCAAGG
CCTCTGGATACACCTTCACCAGTTGCTATATACATTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGTGCCAGAAATAATCCATACCAGTTTCAGGGCAGGATCAGCCTG
ACCAGGGACACGTCCAGTGAAACAGCCTACTTGGAACTGCGTAACCTCAGATCTGACGACACGGCCGTCT
ATTATTGCGCGAGAGATTCTTCGAGGGAAGAGACGAATTGGTGGCTGGACCCTTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 278; PCIN63-71I1a; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CCTCCGGATACACCTTCAATTCCTGCTTAATTCATTGGTGGCGACAGGCCCCTGGACAAGGCCTTCAGTG
GATGGCTTGGATCAACCCTCTCCATGGTGCCGTAAATTATGCACACCAGTTCCAGGGGAGGATCACCGTG
ACCAGGGACACGTCCATCGACACTGCCTACATGGAACTGCGCGGCCTGAGATCTGACGACACGGCCACAT
ATTACTGTACGAGAGATGCATCCAGAGATGATCGCGCGTGGCGCTTGGACCCCTGGGGCCAGGGAACACT
GGTCACCGTCTCCTCA

SEQ ID NO: 279; PCIN63-71J2a; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAATGAGGGTCTCTTGCAAGG
CCTCTGGATACACTTTCACCGCTTGTTATATACACTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGTGCCAGAAATAATCCACACAAGTTTCAGGGCAGGATCACCCTG
ACCAGGGACACGTCCACTGATACAGCCTACTTGGAACTGCGCAACCTGAGATCTGACGACACGGCCGTGT
ATTATTGTACGAGAGATTCATCGAGGCGTGATACGAATTGGTGGTTGGACCCTTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 280; PCIN63-71K; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGCGGTGAAGAAGCCTGGGGCCTCAGTGTGGGTCTCCTGCAAGG
CCTCTGGATACACCTTCACCAGTTGTTATATACATTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGTGCCAGAAATAATCCATACCAGTTTCAGGGGAGGATCAGCCTG
ACCAGGGACACGTCCAGTGAAACAGCCTACTTGGAACTGCGTAACCTCACACCAGACGACACGGCCGTCT
ATTATTGCACGAGAGATTCATCGAGGGATGAGACGAATTGGTGGCTGGACCCTTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 281; PCIN63-71L; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGCGGTGAAGAAGCCTGGGGCCTCAGTGTGGGTCTCCTGCAAGG
CCTCTGGATACACCTTCACCAGTTGTTATATACATTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGTGCCAGAAATAATCCATACCAGTTTCAGGGGAGGATCAGCCTG
ACCAGGGACACGTCCAGTGAAACAGCCTACTTGGAACTGCGTAACCTCACACCAGACGACACGGCCGTCT

ATTATTGCACGAGAGATTCATCGAGGGATGAGACGAATTGGTGGCTGGACCCTTGGGGCCAGGGAACCCT
GGTCATCGTCTCTTCA

SEQ ID NO: 282; PCIN63-71M1a; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGCGGTGAAGAAGCCTGGGGCCTCAGTGTGGGTCTCCTGCAAGG
CCTCTGGATACACCTTTACCAGTTGTTATATACATTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGCGCCAGAAATCAGGCGTACCAGTTTCAGGGCAGGATTAGCCTG
ACCAGGGACACGCCCAGTGAAACAGCCTACTTGGAACTGCGTGACCTCAGATCTGACGACACGGCCGTCT
ATTATTGCGCGAGAGATTCATCGAGGGATGAGACGAATTGGTGGCTGGACCCTTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 283; PCIN63-71N1a; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CTTCCGGATACACTTTCAACACCTGCTTAATTCATTGGTGGCGACAGGCCCCTGGACAAGGCCTTCAGTG
GCTGGCTTGGATCAACCCTCTCCATGGTGCCGTTAACTATGCACACAACTTTCAGGGGAGGATCACCGTG
ACCAGGGACACGTCCATCGACACTGCCTACATGGAACTTCGCGGCCTGAGATCTGACGACACGGCCACAT
ACTACTGCACCAGAGATTCATCGAGAGGTAATACGGAGTGGCGCTTGGACCCCTGGGGCCAGGGAACACT
GGTCACCGTCTCCTCA

SEQ ID NO: 284; PCIN63-71O; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAAAAGCCTGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CTTCCGGATACACGTTCAACACCTGCTTGATTCATTGGTGGCGACAGGCCCCTGGACAGGGCCTTCAGTG
GGTGGCTTGGATCAACCCTCTCCATGGTGCCGTTAATTATGCACACCAATTACAGGGGAGGATCACCGTG
ACCAGGGACACGTCTATCGACACTGCCTACATGGAACTGCGCGGCCTCAGAGCTGACGACACGGCCACCT
ACTACTGTACGAGAGATTCATCGAGAGATAATCTGGAGTGGCGCTTGGACCCCTGGGGCCAGGGAACACT
GGTCACCGTCTCCTCA

SEQ ID NO: 285; PCIN63-71P; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAAAAGCCTGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CTTCCGGATACACCTTCAACACCTGCTTAATTCATTGGTGGCGACAGGCCCCTGGACAGGGCCTTCAGTG
GGTGGCTTGGATCAACCCTCTCCATGGTGCCGTTAACTATGCACACCAGTTACAGGGGAGGATCACGGTG
ACCAGGGACACGTCTATCGACACTGCCCACATGGAACTGCGCGGCCTCAGATCTGACGACACGGCCACAT
ACTATTGTACCAGAGATTCATCGAGAGGTGATACGGAGTGGCGCTTGGACCCCTGGGGCCAGGGAACACT
GGTCACCGTCTCCTCA

SEQ ID NO: 286; PCIN63-77B1b; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGCGAGGGTCTCCTGCAAGG
CTTCTGGATACACCTTCACCGCCTATTTTATACACTGGGTGCGACAAGCCCCTGGACAGGGACTTGAGTG
GGTGGGTTGGATCAACCCTCTCCATGGCGCCGTAAATTATGCACACAAATTTCAGGGCAGGGTCTCCATG
ACCAGAGACACCTCCATCAGCACAGCCTACATGGAACTTCGCAGCCTGAAATCTGACGACACGGCCATTT
ATTACTGTACCACACATTTGTCGAGTCGTGATTTTTCGTGGTCGTGGGACCCCTGGGGCCAGGGAACCCT
GGTCACCGTCTCCCCA

SEQ ID NO: 287; PCIN63-77C; VH
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAACCCGGGGCCTCAGTGAGGGTCTCCTGCAAGG
CCTCTGGATACACCTTCACCGCCTGTTATATACAGTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGATCAACCCTATCAATGGTGCCAGAAATAATAATCCACAGACGTTTCAGGGCAGGGTCACC
CTGACCAGGGACACGTCCATTGATACCGCCTACTTGGAACTGCGCAACCTGAGAGATGACGACACGGCCA
TATATTATTGTACGAGAGATTCATCGAGGCGTGATCTGGAGTGGCGGTTGGACCCCTGGGGCCAGGGAAC
CCTGGTCACCGTCTCCTCA

SEQ ID NO: 288; PCIN63-77D; VH

CAGGTGCAGCTGGTGCAGTCTGGGGCTGCGGTGAAGAAGCCTGGGGCCTCAGTGTGGGTCTCCTGCAAGG
CCTCTGGATACACCTTCACCAGTTGTTATATACATTGGTTTCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGATGGCTCAACCCTATCAATGGCGCCAGAAATCATGCATACCAGTTTCAGGGCAGGATTAGCCTG
ACCAGGGACACGTCCAGTGAAACAGCCTACTTGGAACTGCGTAACCTCAGATCTGACGACACGGCCGTCT
ATTATTGCGCGAGAGATTCATCGAGGGATGAGACGAATTGGTGGCTGGACCCTTGGGGCCAGGGAACCCT
GGTCACCGTCTCCTCA

SEQ ID NO: 289; PCIN63-66B; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGAAAGAGTCACCATCACTTGCC
GGGCAAGTCAGGGCATTGGAAGTGATTTAGGTTGGTATCAGCAGAAACCAGGGAAATCCCCTAAACTTCT
TATCTTTAAGGCGTCTAATTTAAAAGATGGCGTCCCGCCGAGGTTCAGCGGCGGTGGATTTCACACAGAA
TTTACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 290; PCIN63-71B; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
GGGCTAGTCAGGGCATTGGAAATAAATTAGGGTGGTTTCAGCAGAAACCAGGGAAAGCCCCTAAGCCCCT
GATCTTTAAGGCGTCTACTTTGAAAGATGGGGTCCCATCAAGGTTCAGCGGCAGTGGATTTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGACTTTGCAACTTACTATTGTCAAGTCTATGAAAGCT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 291; PCIN63-71C; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAATCAGGGCAAGCCCCTAAACTTCT
TATCTTTAAGGCGTCTAATTTAAAAAATGGAGTCCCGCCAAGATTCAGCGGCAGTGGATTTCACACAGAC
TTCACTCTCACCATCAGCGGCCTGCAGCCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 292; PCIN63-71D2b; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAATCAGGGCAAGCCCCTAAACTTCT
TATCTTTAAGGCGTCTAATTTAAAAAATGGAGTCCCGCCAAGATTCAGCGGCAGTGGATTTCACACAGAC
TTCACTCTCACCATCAGCGGCCTGCAGTCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 293; PCIN63-71F; VL
GCCATCCGGATGACCCAGTCTCCTCCCACCGTGTCTGCATCTGCGGGAGACAGAGTCACCATCACTTGCC
GGGCCGGTCAGCACATTGGTAACGACTTGGCCTGGTATCAGACGAAAGTGGGGATGGCCCCTAAACTCCT
CATCTATCAGGCGTCTAATTTAAAAAGTGGGGTCCCATCAAGGTTCAGCGGCAGTGGGTCTGGGACAGAG
TTCACTCTTTCCATCACCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAAGTTTATGAGTCGT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 294; PCIN63-71G; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCTTGACTTGCC
GGGCAGGACAGGGCATTGGAAGTGATTTAGGCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAACTCCT
CATACATAAGGCGTCCAATTTAATAAATGGAGTGCCATCAAGGTTCAGCGGCAGTGGATTTCACACAGAA
TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGTCAAGTTGTTGAATGGT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 295; PCIN63-71H; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAACCAGGGCAAGCCCCTAAACTTCT

AATCTTTAAGGCGTCTAATTTAAAAAATGGAGTCCCGACAAGATTCACCGGCAGTGGATTTCACACAGAC
TTCACTCTCACCATCAACGGCCTGCAGTCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAGACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 296; PCIN63-71I1a; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCTTGACTTGCC
GGGCAGGGCAGGGCATTGGAAGTGATTTAGGCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAACTCCT
CATACACAAGGCGTCTAATTTAATAAATGGGGTGCCATCAAGGTTCAGCGGCAGTGGATTTCACACAGAA
TTCACACTCACCATCAACAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGTCAAGTTTTTGAGTGGT
TCGGCCCAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 297; PCIN63-71J2a; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAATCAGGGCAAGCCCCTAAACTTCT
AATCTTTAAGGCGTCTAATTTAAAAAATGGAGTCCCGCCAAGATTTAGCGGCAGTGGATTTCACACAGAC
TTCACTCTCACCATCAGCGGCCTGCAGCCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 298; PCIN63-71K; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAACCTGGGCAAGCCCCTAAACTTCT
AATCTTTAAGGCGTCTCGTTTAAAAAATGGAGTCCCGACAAGATTCACCGGCAGTGGATTTCACACAGAG
TTCACTCTCACCATCAGCGGCCTGCAGTCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 299; PCIN63-71L; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAACCTGGGCAAGCCCCTAAACTTCT
AATCTTTAAGGCGTCTCGTTTAAAAAATGGAGTCCCGACAAGATTCACCGGCAGTGGATTTCACACAGAG
TTCACTCTCACCATCAGCGGCCTGCAGTCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 300; PCIN63-71M1a; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAATCAGGGCAAGCCCCTAAACTTCT
TATCTTTAAGGCGTCTAATTTAAAAAATGGAGTCCCGCCAAGATTCAGCGGCAGTGGATTTCACACAGAC
TTCACTCTCACCATCAGCGGCCTGCAGCCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 301; PCIN63-71N1a; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTAGGAGACAAAGTCACCATCACTTGCC
GGGCAAGTCAGGGCATTGGAAATAATTTAGGCTGGTATCAGCAGAAACCAGGGCAGGCCCCTAAACTCCT
CATCTTTAAGGCGTCTAATTCAAAAGATGGAGTCCCACCAAGATTCAGCGGTAGTGGATCTCATACAGAG
TTCACTCTCACCATCAACAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAGGTTTATCAAACCT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 302; PCIN63-71O; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCTTGACTTGCC
GGGCAGGGCAGGGCATTGGAAGTGATTTAGGGTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAACTCCT
CATACATAAGGCGTCTAATTTACTAAATGGGGTGCCATCAAGGTTCAGCGGCAGTGGATTTCACACGGAA
TTCACTCTCACCATCAGCAGCCTGCAACCTGATGATTTTGCAACTTATTACTGTCAAGTTTTTGAATGGT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 303; PCIN63-71P; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCTTGACTTGCC
GGGCAGGGCAGGGCATTGGAAGTGATTTAGGGTGGTATCAGCAGAAGCCAGGAAAAGCCCCTAAACTCCT
CATACATAAGGCGTCTAATTTAGCAAATGGGGTGCCATCAAGGTTCAGCGGCCGTGGATTTCACACAGAG
TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGTCAAGTTTTTGAATGGT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 304; PCIN63-77B1b; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAACCAGGGCAAGCCCCTAAACTTCT
AATCTTTAAGGCGTCTAATTTAAAAAATGGAGTCCCGACAAGATTCACCGGCAGTGGATTTCACACAGAC
TTCACTCTCACCATCAGCGGCCTGCAGTCTGATGATTTTGCGACTTATTACTGCCAAGTTTTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 305; PCIN63-77C; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATCTGTGGGAGATAGAGTCACCATCACTTGCC
GGGCAGGTCAGGGCATTGGAAGTGATTTAGCCTGGTATCAGCAGAAACCAGGGCAAGCCCCTAAACTTCT
AATCTTTAAGGCGTCCAATTTAAAAAAAGGAGTCCCGACAAGATTCACCGGCAGTGGATTTCACACAGAC
TTCACTCTCACCATCAGCGGCCTGCAGTCTGATGATTTTGCGACTTATTACTGCCAAGTTCTGGAAACAT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 306; PCIN63-77D; VL
GCCATCCGGATGACCCAGTCTCCTGCCACCCTGTCTGCATTTGTAGGAGACAGAGTCACCATCACTTGCC
GGGCTAGTCAGGGCATTGGAGATGATTTAGGCTGGTATCAGCAAAAACCAGGGAAAGTCCCTAAGCCCCT
GATCTTTAAGGCGTCTAATTTAAAAGATGGGGTCCCATCGAGGTTCAGCGGCAGCGGATTTGGGACAGAT
TTCACTCTCACCATCAACAACCTGCAGCCTGATGACTTTGCAACTTACTATTGCCAAGCCTATGAAAGCT
TCGGCCAAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 307; PCIN63-UCA-HC; VH
QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGRVTM
TRDTSISTAYMELSRLRSDDTAVYYCARDSSRQQLEWWFDPWGQGTLVTVSS

SEQ ID NO: 308; PCIN63-UCA-KC1; VL
DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPSRFSGSGSGTE
FTLTISSLQPDDFATYYCQQSEAFGQGTKVEIK

SEQ ID NO: 309; PCIN63-UCA-KC2; VL
DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPSRFSGSGSGTE
FTLTISSLQPDDFATYYCQLYETFGQGTKVEIK

SEQ ID NO: 310; Motif #1
AXFIXXV

SEQ ID NO: 311; Motif #1
AXYIXXF

SEQ ID NO: 312; Motif #1
DXFVXXV

SEQ ID NO: 313; Motif #1
SXLIXXW

SEQ ID NO: 314; Motif #1
SXYIXXF

SEQ ID NO: 315; Motif #1
TXLIXXW

SEQ ID NO: 316; Motif #2
NXINXAP

SEQ ID NO: 317; Motif #2
NXINXAR

SEQ ID NO: 318; Motif #2
NXLHXAV

SEQ ID NO: 319; Motif #4
GXGXGXDXA

SEQ ID NO: 320; Motif #4
GXGXGXDXG

SEQ ID NO: 321; Motif #4
GXHXGXDXA

SEQ ID NO: 322; Motif #4
SXGXGXDXG

SEQ ID NO: 323; Motif #4
SXGXGXKXG

SEQ ID NO: 324; Motif #4
SXGXGXNXG

SEQ ID NO: 325; Motif #5
FXXXNXKD

SEQ ID NO: 326; Motif #5
FXXXNXKK

SEQ ID NO: 327; Motif #5
FXXXNXKN

SEQ ID NO: 328; Motif #5
FXXXRXKN

SEQ ID NO: 329; Motif #5
FXXXSXKD

SEQ ID NO: 330; Motif #5
FXXXTXKD

SEQ ID NO: 331; Motif #5
HXXXNXAN

SEQ ID NO: 332; Motif #5
HXXXNXIN

SEQ ID NO: 333; Motif #5
HXXXNXLN

SEQ ID NO: 334; Motif #5
YXXXNXKS

SEQ ID NO: 335; Motif #6
FGXD

SEQ ID NO: 336; Motif #6
FHXD

SEQ ID NO: 337; Motif #6
FHXE

SEQ ID NO: 338; Motif #6
SGXE

SEQ ID NO: 339; Motif #6
SHXE

CLAIMS

What is claimed is:

1. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

2. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

3. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

4. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37-54.

5. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37, 39, 40, 42-48, or 50-53.

6. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 44 or 47.

7. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

8. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

9. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

10. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

11. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

12. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

13. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

14. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K,

PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

15. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

16. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 1-18;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 19-36; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37-54.

17. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 1, 3, 4, 6-12, or 14-17;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 19, 21, 22, 24-30, or 32-35; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37, 39, 40, 42-48, or 50-53.

18. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 8 or 11;

(b) the VH CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 26 or 29; and

(c) the VH CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 44 or 47.

19. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

20. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

21. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

22. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

23. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1, 3, 4, 6-12, or 14-17 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19, 21, 22, 24-30, or 32-35 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

24. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 8 or 11 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 26 or 29 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

25. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

26. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

27. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the VH CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VH CDR2 comprises the VH CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VH CDR3 comprises the VH CDR3 of PCIN63-71I1a, or PCIN63-71L.

28. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54.

29. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1, 3, 4, 6-12, or 14-17;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19, 21, 22, 24-30, or 32-35; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37, 39, 40, 42-48, or 50-53.

30. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 8 or 11;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 26 or 29; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 44 or 47.

31. The isolated monoclonal antibody of any one of claims 1 to 30 comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62.

32. The isolated monoclonal antibody of any one of claims 1 to 30 comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62.

33. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

34. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

35. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

36. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

37. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

38. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-71I1a, or PCIN63-71L comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

39. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

40. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

41. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the VL CDR1 of PCIN63-71I1a, or PCIN63-71L;

(b) the VL CDR2 comprises the VL CDR2 of PCIN63-71I1a, or PCIN63-71L; and

(c) the VL CDR3 comprises the VL CDR3 of PCIN63-71I1a, or PCIN63-71L.

42. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 55-72;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 73-90; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 91-108.

43. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 55, 57, 58, 60-66, or 68-71;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 73, 75, 76, 78-84, or 86-89; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 91, 93, 94, 96-102, or 104-107.

44. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 62 or 65;

(b) the VL CDR2 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 80 or 83; and

(c) the VL CDR3 comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 98 or 101.

45. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

46. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55, 57, 58, 60-66, or 68-71 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73, 75, 76, 78-84, or 86-89 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91, 93, 94, 96-102, or 104-107 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

47. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 62 or 65 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 80 or 83 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 98 or 101 comprising 0, 1, 2, 3, 4, or 5 substitutions, insertions, or deletions.

48. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108.

49. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55, 57, 58, 60-66, or 68-71;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73, 75, 76, 78-84, or 86-89; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91, 93, 94, 96-102, or 104-107.

50. The isolated monoclonal antibody of any one of claims 1 to 32, wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 62 or 65;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 80 or 83; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 98 or 101.

51. The isolated monoclonal antibody of any one of claims 33 to 50 comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

52. The isolated monoclonal antibody of any one of claims 33 to 50 comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VL comprises

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

53. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively.

54. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively.

55. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-

71I1a, or PCIN63-71L VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively.

56. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of

(a) SEQ ID NO: 1, 19, 37, 55, 73, and 91, respectively;

(b) SEQ ID NO: 2, 20, 38, 56, 74, and 92, respectively;

(c) SEQ ID NO: 3, 21, 39, 57, 75, and 93, respectively;

(d) SEQ ID NO: 4, 22, 40, 58, 76, and 94, respectively;

(e) SEQ ID NO: 5, 23, 41, 59, 77, and 95, respectively;

(f) SEQ ID NO: 6, 24, 42, 60, 78, and 96, respectively;

(g) SEQ ID NO: 7, 25, 43, 61, 79, and 97, respectively;

(h) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively;

(i) SEQ ID NO: 9, 27, 45, 63, 81, and 99, respectively;

(j) SEQ ID NO: 10, 28, 46, 64, 82, and 100, respectively;

(k) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively;

(l) SEQ ID NO: 12, 30, 48, 66, 84, and 102, respectively;

(m) SEQ ID NO: 13, 31, 49, 67, 85, and 103, respectively;

(n) SEQ ID NO: 14, 32, 50, 68, 86, and 104, respectively;

(o) SEQ ID NO: 15, 33, 51, 69, 87, and 105, respectively;

(p) SEQ ID NO: 16, 34, 52, 70, 88, and 106, respectively;

(q) SEQ ID NO: 17, 35, 53, 71, 89, and 107, respectively; or

(r) SEQ ID NO: 18, 36, 54, 72, 90, and 108, respectively.

57. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of

(a) SEQ ID NO: 1, 19, 37, 55, 73, and 91, respectively;

(b) SEQ ID NO: 3, 21, 39, 57, 75, and 93, respectively;

(c) SEQ ID NO: 4, 22, 40, 58, 76, and 94, respectively;

(d) SEQ ID NO: 6, 24, 42, 60, 78, and 96, respectively;

(e) SEQ ID NO: 7, 25, 43, 61, 79, and 97, respectively;

(f) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively;

(g) SEQ ID NO: 9, 27, 45, 63, 81, and 99, respectively;

(h) SEQ ID NO: 10, 28, 46, 64, 82, and 100, respectively;

(i) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively;

(j) SEQ ID NO: 12, 30, 48, 66, 84, and 102, respectively;

(k) SEQ ID NO: 14, 32, 50, 68, 86, and 104, respectively;

(l) SEQ ID NO: 15, 33, 51, 69, 87, and 105, respectively;

(m) SEQ ID NO: 16, 34, 52, 70, 88, and 106, respectively; or

(n) SEQ ID NO: 17, 35, 53, 71, 89, and 107, respectively.

58. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region comprising a VH CDR1, VH CDR2, and VH CDR3 and a light chain variable region comprising a VL CDR1, VL CDR2, and VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of

(a) SEQ ID NO: 8, 26, 44, 62, 80, and 98, respectively; or

(b) SEQ ID NO: 11, 29, 47, 65, 83, and 101, respectively.

59. The isolated monoclonal antibody of any one of claims 53 to 58, wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises one or more of

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

60. The isolated monoclonal antibody of any one of claims 53 to 58, wherein the VH comprises the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56, and the VL comprises the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34, and the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70.

61. The isolated monoclonal antibody of any one of claims 53 to 58, wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

62. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

63. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

64. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VH of PCIN63-71I1a, or PCIN63-71L.

65. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235-252.

66. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235, 237, 238, 240-246, or 248-251.

67. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 242 or245.

68. The isolated monoclonal antibody of any one of claims 62 to 67, wherein the VH CDR1, VH CDR2, and VH CDR3, comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH CDR1, VH CDR2, and VH CDR3, respectively.

69. The isolated monoclonal antibody of any one of claims 62 to 67, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36; and

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54.

70. The isolated monoclonal antibody of any one of claims 62 to 69, wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62.

71. The isolated monoclonal antibody of any one of claims 60 to 68, wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62.

72. The isolated monoclonal antibody of any one of claims 62 to 71, wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

73. The isolated monoclonal antibody of any one of claims 62 to 71, wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

74. The isolated monoclonal antibody of any one of claims 62 to 71, wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the VL of PCIN63-71I1a, or PCIN63-71L.

75. The isolated monoclonal antibody of any one of claims 62 to 71, wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253-270.

76. The isolated monoclonal antibody of any one of claims 62 to 71, wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253, 255, 256, 258-264, or 266-269.

77. The isolated monoclonal antibody of any one of claims 62 to 71, wherein the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 260 or 263.

78. The isolated monoclonal antibody of any one of claims 72 to 77, wherein the VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VL CDR1, VL CDR2, and VL CDR3, respectively.

79. The isolated monoclonal antibody of any one of claims 72 to 77, wherein

(a) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72;

(b) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90; and

(c) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108..

80. The isolated monoclonal antibody of any one of claims 72 to 79, wherein the VL comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

81. The isolated monoclonal antibody of any one of claims 72 to 79, wherein the VL comprises

(a) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(b) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(c) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(d) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

82. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH and VL, respectively.

83. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C VH and VL, respectively.

84. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to the PCIN63-71I1a, or PCIN63-71L VH and VL, respectively.

85. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 235-252 and the VL comprises an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 253-270.

86. An isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise an amino acid sequence that is at least about 90%, 95%, 97%, 98%, 99% or 100% identical to

(a) SEQ ID NO: 235 and 253, respectively;

(b) SEQ ID NO: 236 and 254, respectively;

(c) SEQ ID NO: 237 and 255, respectively;

(d) SEQ ID NO: 238 and 256, respectively;

(e) SEQ ID NO: 239 and 257, respectively;

(f) SEQ ID NO: 240 and 258, respectively;

(g) SEQ ID NO: 241 and 259, respectively;

(h) SEQ ID NO: 242 and 260, respectively;

(i) SEQ ID NO: 243 and 261, respectively;

(j) SEQ ID NO: 244 and 262, respectively;

(k) SEQ ID NO: 245 and 263, respectively;

(l) SEQ ID NO: 246 and 264, respectively;

(m) SEQ ID NO: 247 and 265, respectively;

(n) SEQ ID NO: 248 and 266, respectively;

(o) SEQ ID NO: 249 and 267, respectively;

(p) SEQ ID NO: 250 and 268, respectively;

(q) SEQ ID NO: 251 and 269, respectively; or

(r) SEQ ID NO: 252 and 270, respectively.

87. The isolated monoclonal antibody of any one of claims 82 to 86, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, respectively.

88. The isolated monoclonal antibody of any one of claims 82 to 86, wherein

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 1-18;

(b) the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 19-36;

(c) the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 37-54,

(d) the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 55-72;

(e) the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 73-90; and

(f) the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 91-108..

89. The isolated monoclonal antibody of any one of claims 82 to 88, wherein the VH comprises one or more of

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises one or more of

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

90. The isolated monoclonal antibody of any one of claims 82 to 88, wherein the VH comprises the amino acid sequence of SEQ ID NO: 127-144 or 316-318 at Kabat positions H52-H56, and the VL

comprises the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34, and the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70.

91. The isolated monoclonal antibody of any one of claims 82 to 88, wherein the VH comprises

(a) the amino acid sequence of SEQ ID NO: 109-126 or 310-315 at Kabat positions H31-H37;

(b) the amino acid sequence of SEQ ID NO: 127-144 or 316-318 or 316-318 at Kabat positions H52-H56; and

(c) the amino acid sequence of SEQ ID NO: 145-162 at Kabat positions H61-H62; and

wherein the VL comprises

(d) the amino acid sequence of SEQ ID NO: 163-180 or 319-324 at Kabat positions H26-H34;

(e) the amino acid sequence of SEQ ID NO: 181-198 or 325-334 at Kabat positions H49-H56;

(f) the amino acid sequence of SEQ ID NO: 199-216 or 335-339 at Kabat positions H67-H70; and

(g) the amino acid sequence of SEQ ID NO: 217-234 at Kabat positions H89-H97.

92. The isolated antibody of any one of claims 1 to 91, wherein the antibody is not PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D.

93. The isolated antibody of any one of claims 1 to 91, wherein the antibody is not PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C.

94. The isolated antibody of any one of claims 1 to 91, wherein the antibody is not PCIN63-71I1a, or PCIN63-71L.

95. The monoclonal antibody of any one of claims 1 to 94, further comprising a heavy and/or light chain constant region.

96. The monoclonal antibody of any one of claims 1 to 94, further comprising a human heavy and/or light chain constant region.

97. The antibody of claim 95 or claim 96, wherein the heavy chain constant region is selected from the group consisting of a human immunoglobulin IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, and IgA_2 constant region.

98. The antibody of any one of claims 95 to 97, wherein the heavy chain constant region comprises a native amino acid sequence.

99. The antibody of any one of claims 95 to 97, wherein the heavy chain constant region comprises a variant amino acid sequence.

100. The isolated monoclonal antibody of any one of claims 1 to 99, wherein the antibody is a recombinant antibody, a chimeric antibody, a human antibody, an antibody fragment, a bispecific antibody, or a trispecific antibody.

101. The isolated monoclonal antibody of claim 100, wherein the antibody fragment comprises a single-chain Fv (scFv), F(ab) fragment, F(ab')2 fragment, or an isolated VH domain.

102. The monoclonal antibody of any one of claims 1 to 101, wherein the antibody is capable of neutralizing at least two cross-clade isolates of HIV.

103. The monoclonal antibody of any one of claims 1 to 101, wherein the antibody is capable of neutralizing at least one clade A HIV isolate, at least one clade B HIV isolate, and at least one clade C HIV isolate.

104. The antibody of claim 102, wherein the antibody is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 8.

105. The antibody of claim 102, wherein the antibody is capable of neutralizing at least about 40%, 50%, 60%, 70%, 80%, 90%, or 100% of cross-clade HIV isolates in the indicator virus panel of Figure 9.

106. The antibody of claim 104 or claim 105, wherein the antibody is capable of neutralizing the cross-clade HIV isolates with a median IC_{50} equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml.

107. The antibody of claim 104 or claim 105, wherein the antibody is capable of neutralizing the cross-clade HIV isolates with a mean IC_{50} equal to or less than about 1 μg/ml, about 0.8 μg/ml, 0.5 μg/ml, or 0.3 μg/ml.

108. A pharmaceutical composition comprising the monoclonal antibody of any one of claims 1 to 101 and a pharmaceutically acceptable excipient.

109. The pharmaceutical composition of claim 108, which is lyophilized.

110. An isolated polynucleotide encoding the heavy chain variable region or heavy chain of the antibody of any one of claims 1 to 101.

111. An isolated polynucleotide encoding the light chain variable region or light chain of the antibody of any one of claims 1 to 101.

112. An isolated polynucleotide encoding the heavy chain variable region or heavy chain of the antibody of any one of claims 1 to 101 and the light chain variable region or light chain of the antibody of any one of claims 1 to 101.

113. The isolated polynucleotide of claim 110 or claim 112, wherein the polynucleotide encodes a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 235-252.

114. The isolated polynucleotide of claim 111 or claim 112, wherein the polynucleotide encodes a light chain variable region comprising the amino acid sequence of SEQ ID NO: 253-270.

115. The isolated polynucleotide of any one of claims 110 to 114, which is a DNA.

116. The isolated polynucleotide of any one of claims 110 to 114, which is an mRNA.

117. The isolated polynucleotide of claim 116, wherein the mRNA comprises a modified nucleotide.

118. An isolated vector comprising the polynucleotide of any one of claims 110 to 114.

119. The isolated vector of claim 117, wherein the vector is a viral vector.

120. A recombinant virus comprising the polynucleotide of any one of claims 110 to 114.

121. The recombinant virus of claim 119, which is a recombinant adeno-associated virus (AAV).

122. A host cell comprising the polynucleotide of any one of claims 110 to 115, the vector of claim 118 or claim 119, or a first vector comprising the nucleic acid of claim 110 and a second vector comprising the nucleic acid of claim 111.

123. The host cell of claim 122, which is selected from the group consisting of E. coli, Pseudomonas, Bacillus, Streptomyces, yeast, CHO, YB/20, NS0, PER-C6, HEK-293T, NIH-3T3, HeLa, BHK, Hep G2, SP2/0, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, BMT10 cell, plant cell, insect cell, and human cell in tissue culture.

124. A method of producing an antibody that binds to HIV comprising culturing the host cell of claim 123 so that the polynucleotide is expressed and the antibody is produced.

125. An isolated antibody that specifically binds to HIV Env and is encoded by the isolated polynucleotide of any one of claims 110 to 117.

126. A method of neutralizing an HIV virus comprising contacting the virus with a sufficient amount of the antibody of any one of claims 1 to 101, or the pharmaceutical composition of claim 108.

127. A method of reducing the likelihood of HIV infection in a subject exposed to HIV comprising administering to the subject a therapeutically sufficient amount of the antibody of any one of claims 1 to 101, or of the pharmaceutical composition of claim 108.

128. A method of reducing the risk of a subject becoming infected with HIV comprising administering to the subject in need thereof an effective amount of the antibody of any one of claims 1 to 101, or the pharmaceutical composition of claim 108.

129. A method for passively immunizing a subject comprising administering to the subject in need thereof an effective amount of the antibody of any one of claims 1 to 101, or the pharmaceutical composition of claim 108.

130. A method of preventing HIV infection comprising administering to a subject in need thereof a therapeutically sufficient amount of the antibody of any one of claims 1 to 101, the pharmaceutical composition of claim 108, the isolated polynucleotide of any one of claims 110 to 117, or the recombinant virus of any claim 120 or claim 121.

131. A method of treating HIV/AIDS comprising administering to a subject in need thereof a therapeutically sufficient amount of the antibody of any one of claims 1 to 101, the pharmaceutical composition of claim 108, the isolated polynucleotide of any one of claims 110 to 117, or the recombinant virus of any claim 120 or claim 121

132. The method of any one of claims 127 to 131, wherein the administering to the subject is by at least one mode selected from oral, parenteral, subcutaneous, intramuscular, intravenous, vaginal, rectal, buccal, sublingual, and transdermal.

133. The method of any one of claims 127 to 132, further comprising administering at least one additional therapeutic agent.

134. The method of claim 133, wherein the additional therapeutic agent is an antiretroviral agent or a second antibody.

135. The method of claim 134, wherein the additional therapeutic agent comprises a broadly neutralizing antibody.

136. The method of claim 134, wherein the additional therapeutic agent comprises two broadly neutralizing antibodies.

137. The method of claim 134, wherein the additional therapeutic agent comprises three broadly neutralizing antibodies.

138. A method for detecting HIV in a sample comprising contacting the sample with the antibody of any one of claims 1 to 101.

139. A method of purifying HIV from a sample comprising contacting the sample with the antibody of any one of claims 1 to 101.

140. A kit comprising the antibody of any one of claims 1 to 101, or the pharmaceutical composition of claim 108 and a) a detection reagent, b) an HIV antigen, c) a notice that reflects approval for use or sale for human administration, or d) any combination thereof.

141. The antibody of any one of claims 1 to 101, wherein the antibody specifically binds the Env of at least one HIV isolate in the indicator virus panel of Figure 8.

142. The antibody of any one of claims 1 to 101, wherein the antibody specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 8.

143. The antibody of any one of claims 1 to 101, wherein the antibody specifically binds the Env of at least one HIV isolate in the indicator virus panel of Figure 9.

144. The antibody of any one of claims 1 to 101, wherein the antibody specifically binds the Env of at least two, at least three, at least four, or at least five HIV isolates in the indicator virus panel of Figure 9.

145. A method of producing an engineered variant of a PCIN63 antibody comprising

(a) substituting one or more amino acid residues of the VH; and/or substituting one or more amino acid residues of the VL to create an engineered variant antibody, and

(b) and producing the engineered variant antibody,

wherein the PCIN63 antibody is

i. PCIN63-66B, PCIN63-71B, PCIN63-71C, PCIN63-71D2b, PCIN63-71F, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71N1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, PCIN63-77C, or PCIN63-77D;

ii. PCIN63-66B, PCIN63-71C, PCIN63-71D2b, PCIN63-71G, PCIN63-71H, PCIN63-71I1a, PCIN63-71J2a, PCIN63-71K, PCIN63-71L, PCIN63-71M1a, PCIN63-71O, PCIN63-71P, PCIN63-77B1b, or PCIN63-77C; or PCIN63-71I1a, or PCIN63-71L.

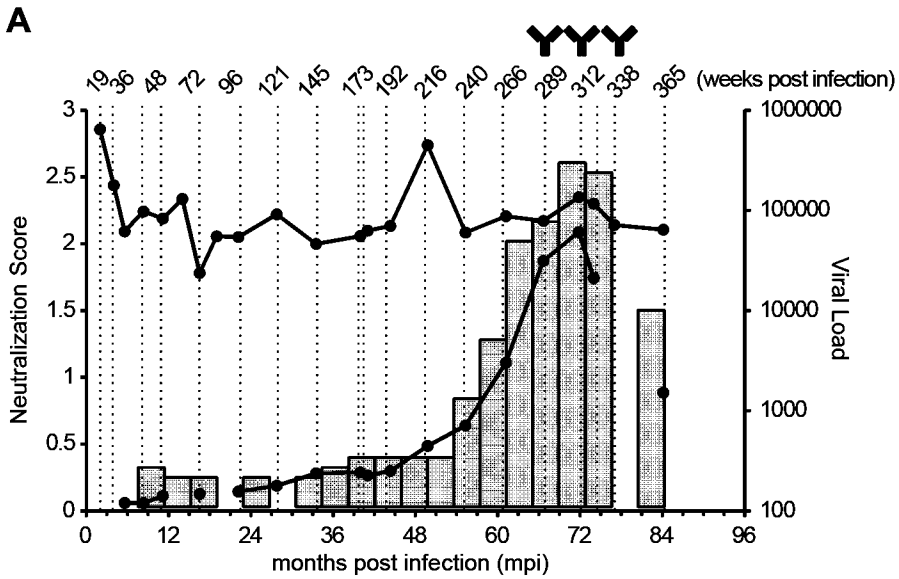

A
YYY
19 36 48 72 96 121 145 173 192 216 240 266 289 312 338 365 (weeks post infection)
Neutralization Score
Viral Load
3
2.5
2
1.5
1
0.5
0
1000000
100000
10000
1000
100
0 12 24 36 48 60 72 84 96
months post infection (mpi)

Figure 1

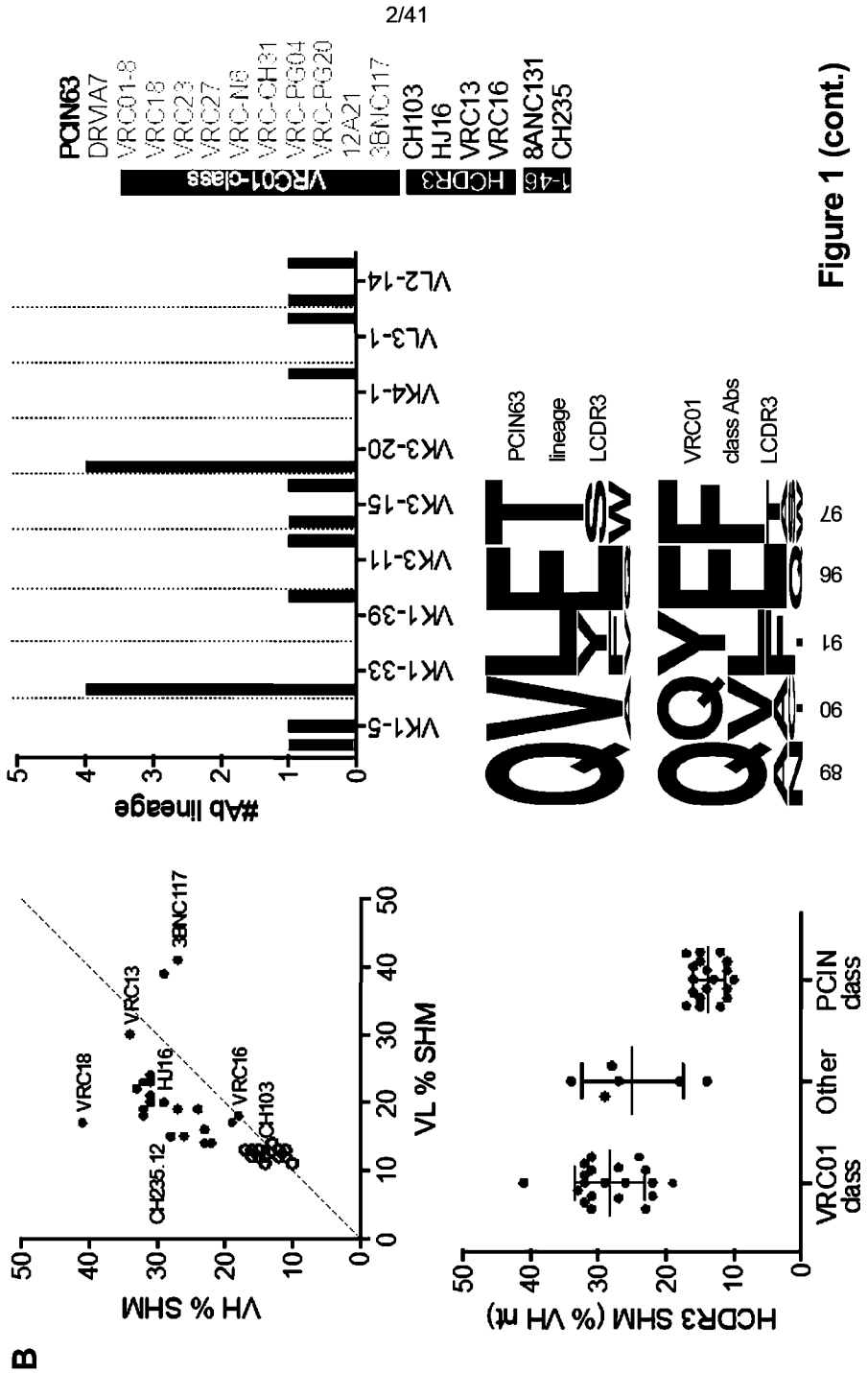


Figure 1 (cont.)

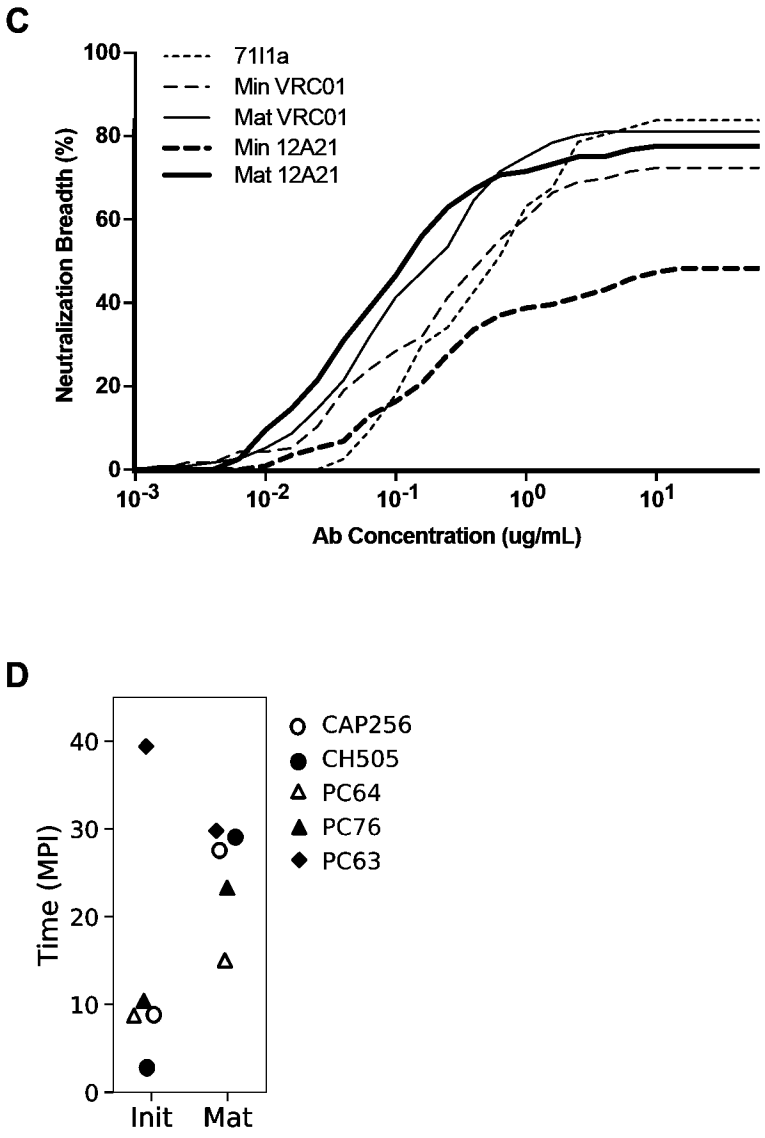


Figure 1 (cont.)

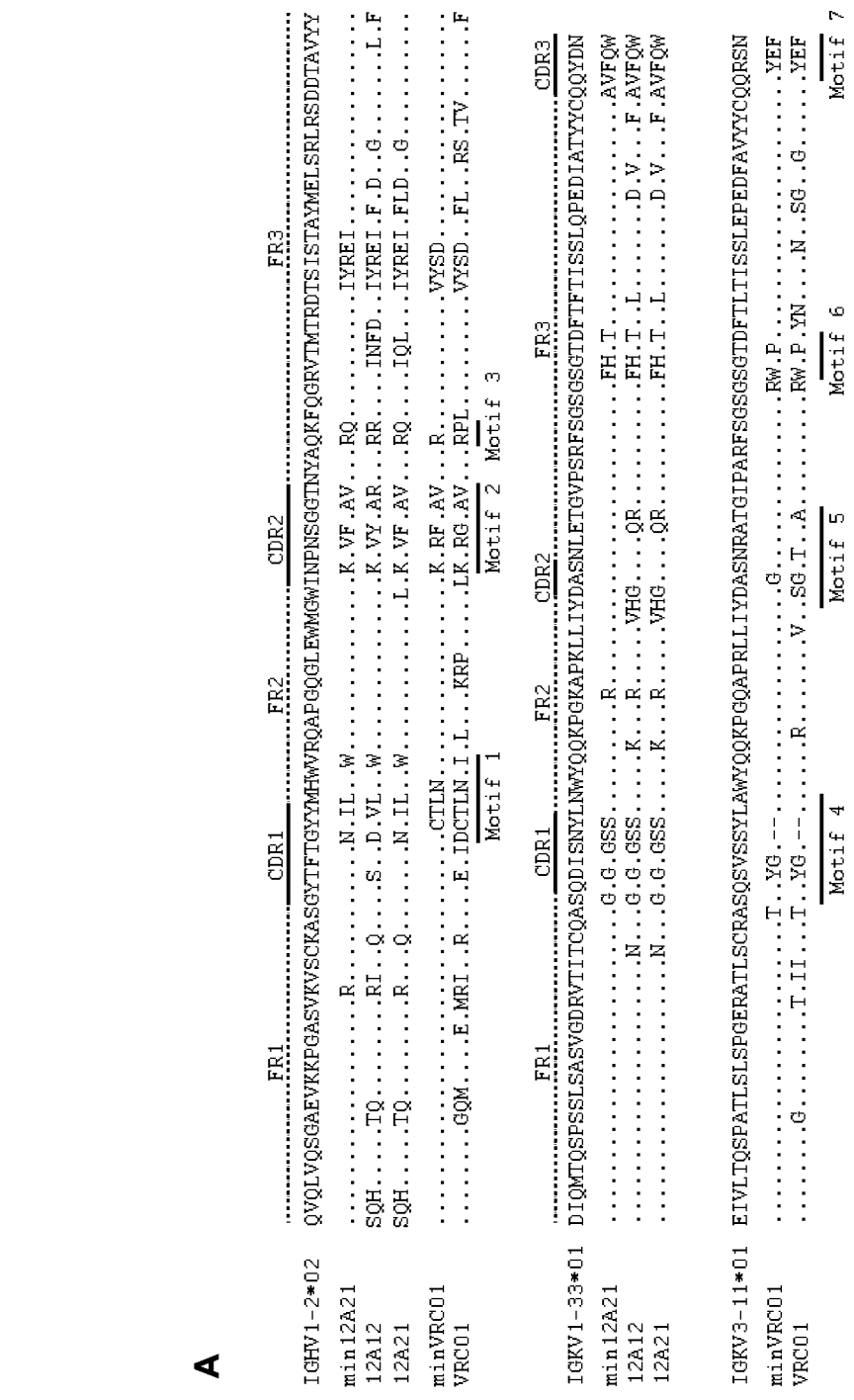

A
FR1
CDR1
FR2
CDR2
FR3
IGHV1-2*02 QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYY
min12A21 .....R.....N.IL..W.....K.VF.AV...RQ.....IYREI.....
12A12 SQH.....TQ.....RI..Q.....S..D.VL..W.....K.VY.AR...RR....INFD..IYREI.F.D..G.....L.F
12A21 SQH.....TQ.....R...Q.....N.IL..W.....L.K.VF.AV...RQ....IQL...IYREI.FLD..G.....
minVRC01 .....CTLN.....K.RF.AV...R.....VYSD.....
VRC01 .....GQM....E.MRI..R....E.IDCTLN.I.L...KRP.....LK.RG.AV...RPL.....VYSD..FL..RS.TV.....F
Motif 1
Motif 2
Motif 3
FR1
CDR1
FR2
CDR2
FR3
CDR3
IGKV1-33*01 DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQYDN
min12A21 .....G.G.GSS.....R.....FH.T.....AVFQW
12A12 .....N...G.G.GSS.....K....R.....VHG.....QR.....FH.T..L.....D.V...F.AVFQW
12A21 .....N...G.G.GSS.....K...R.....VHG.....QR.....FH.T..L.....D.V...F.AVFQW
IGKV3-11*01 EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSN
minVRC01 .....T..YG.--.....G.....RW.P.....YEF
VRC01 .....G.....T.II...T..YG.--.....R.....V..SG.T..A.....RW.P.YN...N..SG..G.....YEF
Motif 4
Motif 5
Motif 6
Motif 7

Figure 2

B

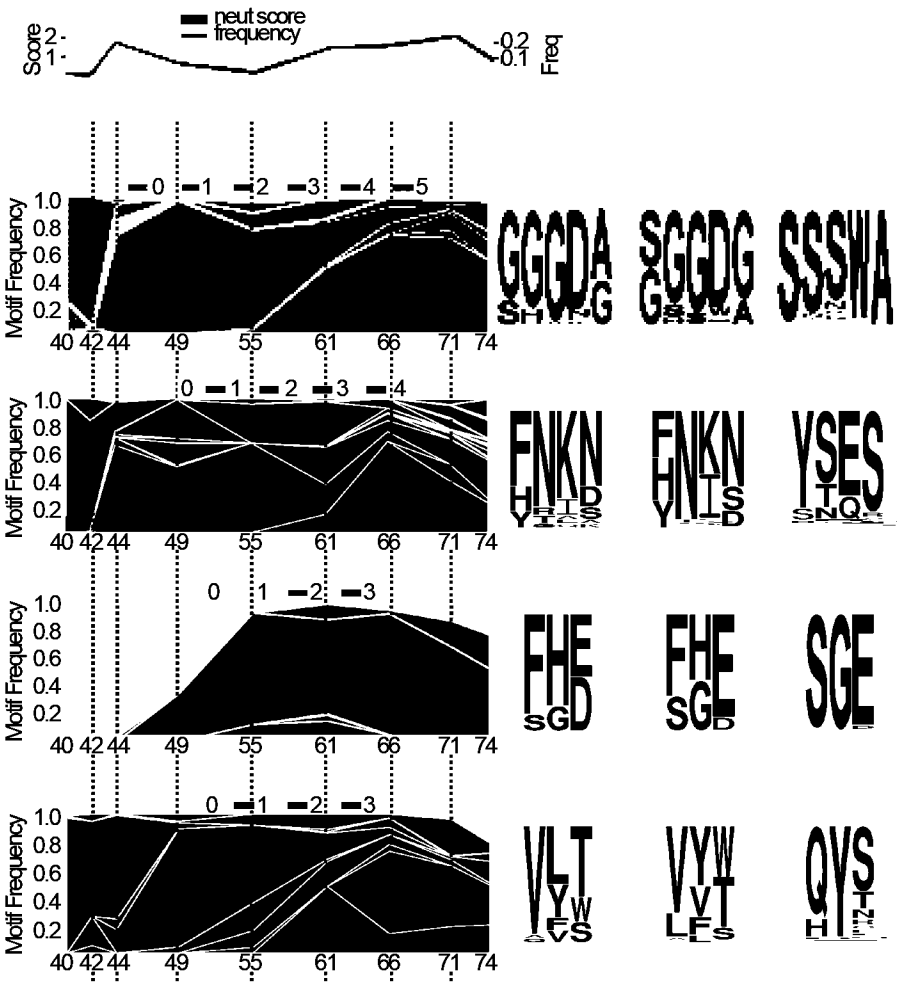


Figure 2 (cont.)

B (cont.)

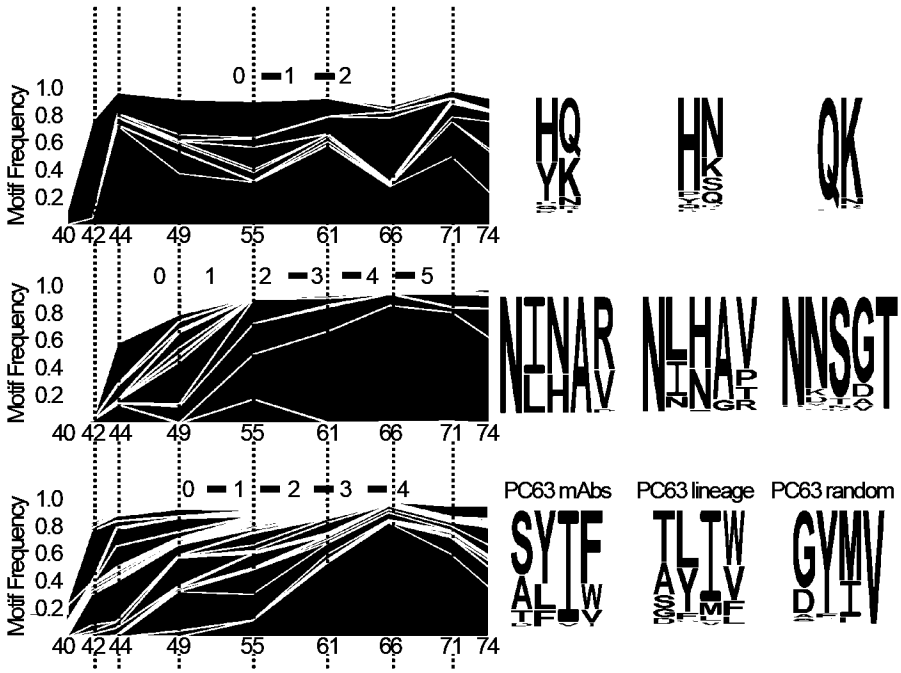


Figure 2 (cont.)

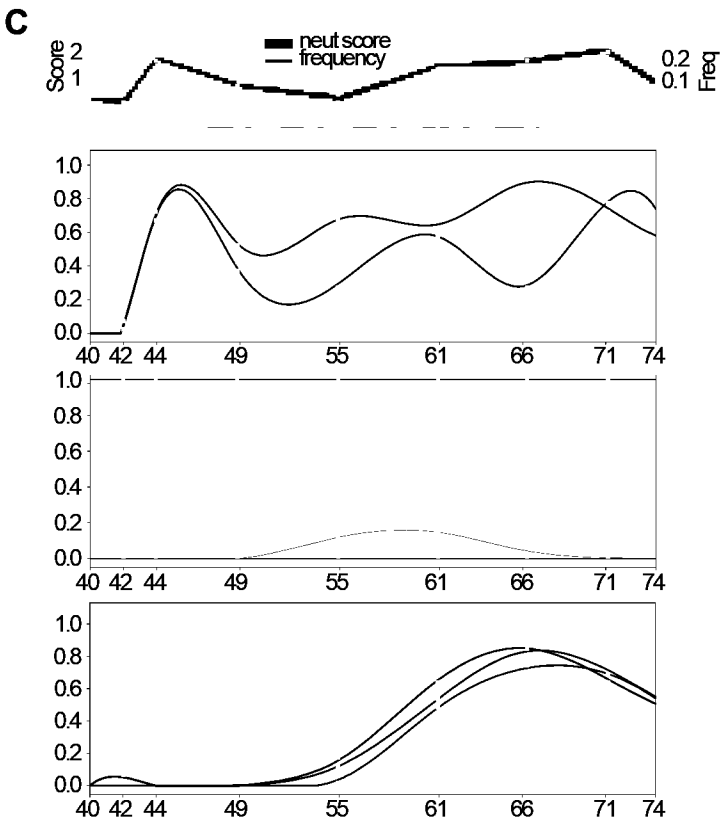


Figure 2 (cont.)

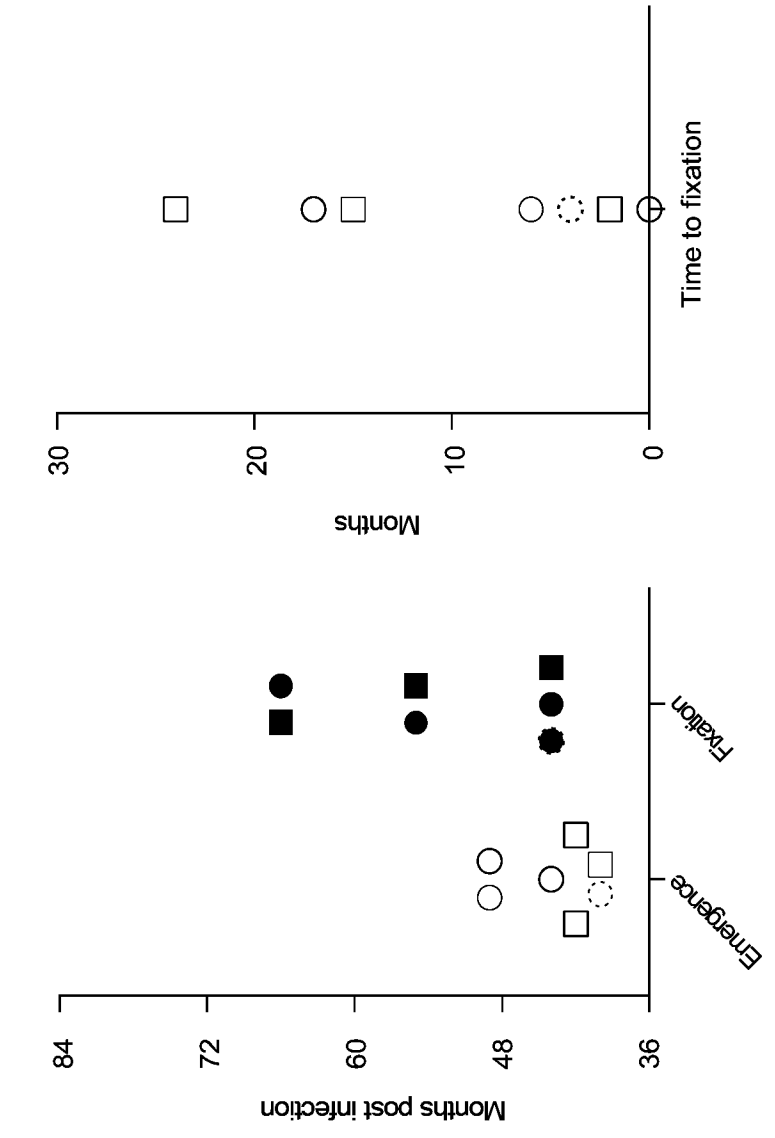


Figure 2 (cont.)

D?

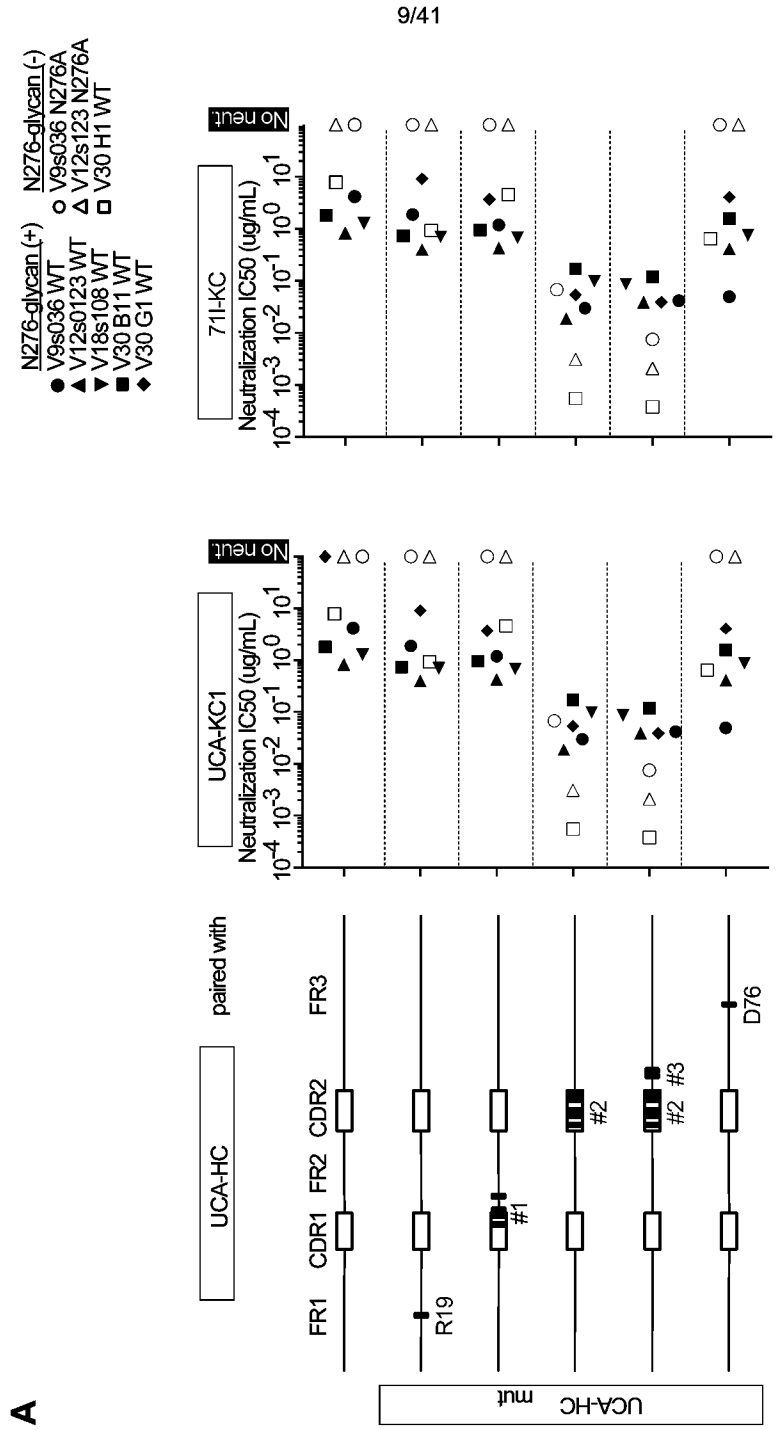

A
UCA-HC mut
FR1
CDR1
FR2
CDR2
FR3
R19
#1
#2
#2 #3
D76
paired with
UCA-KC1
Neutralization IC50 (ug/mL)
No neut
71I-KC
Neutralization IC50 (ug/mL)
No neut
N276-glycan (+)
V9s036 WT
V12s0123 WT
V18s108 WT
V30 B11 WT
V30 G1 WT
N276-glycan (-)
V9s036 N276A
V12s123 N276A
V30 H1 WT

Figure 3

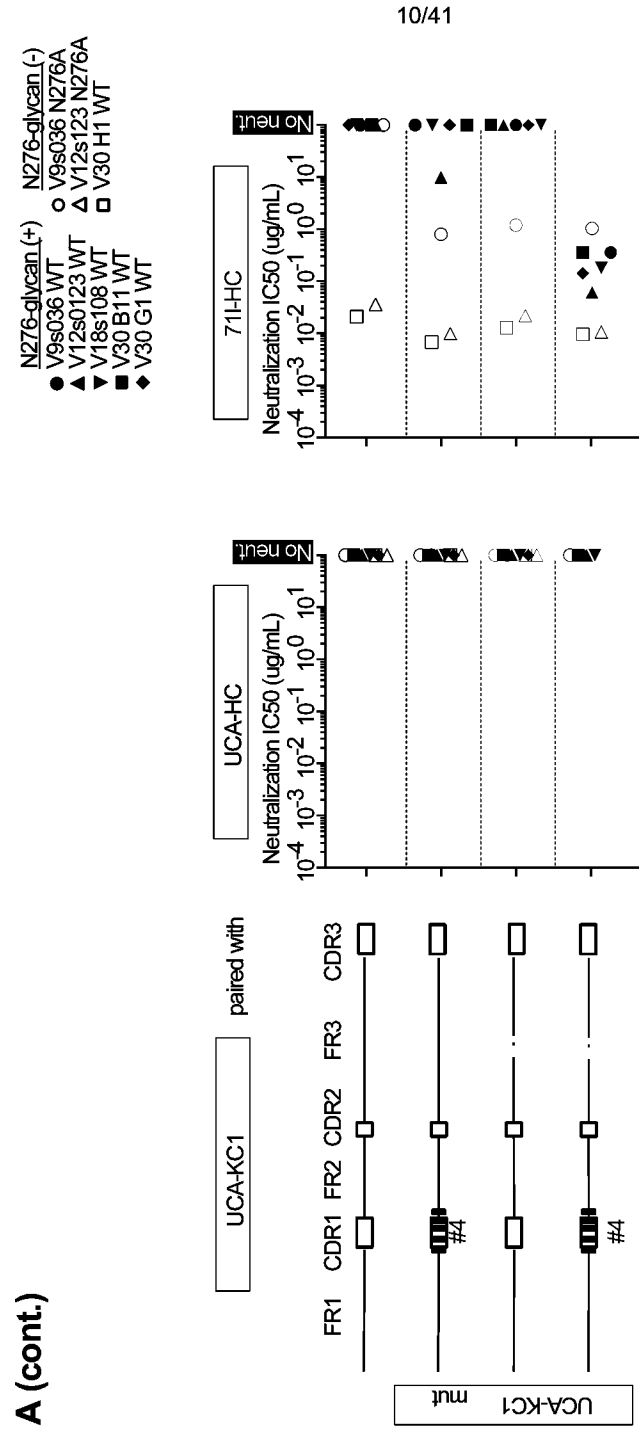


Figure 3 (cont.)

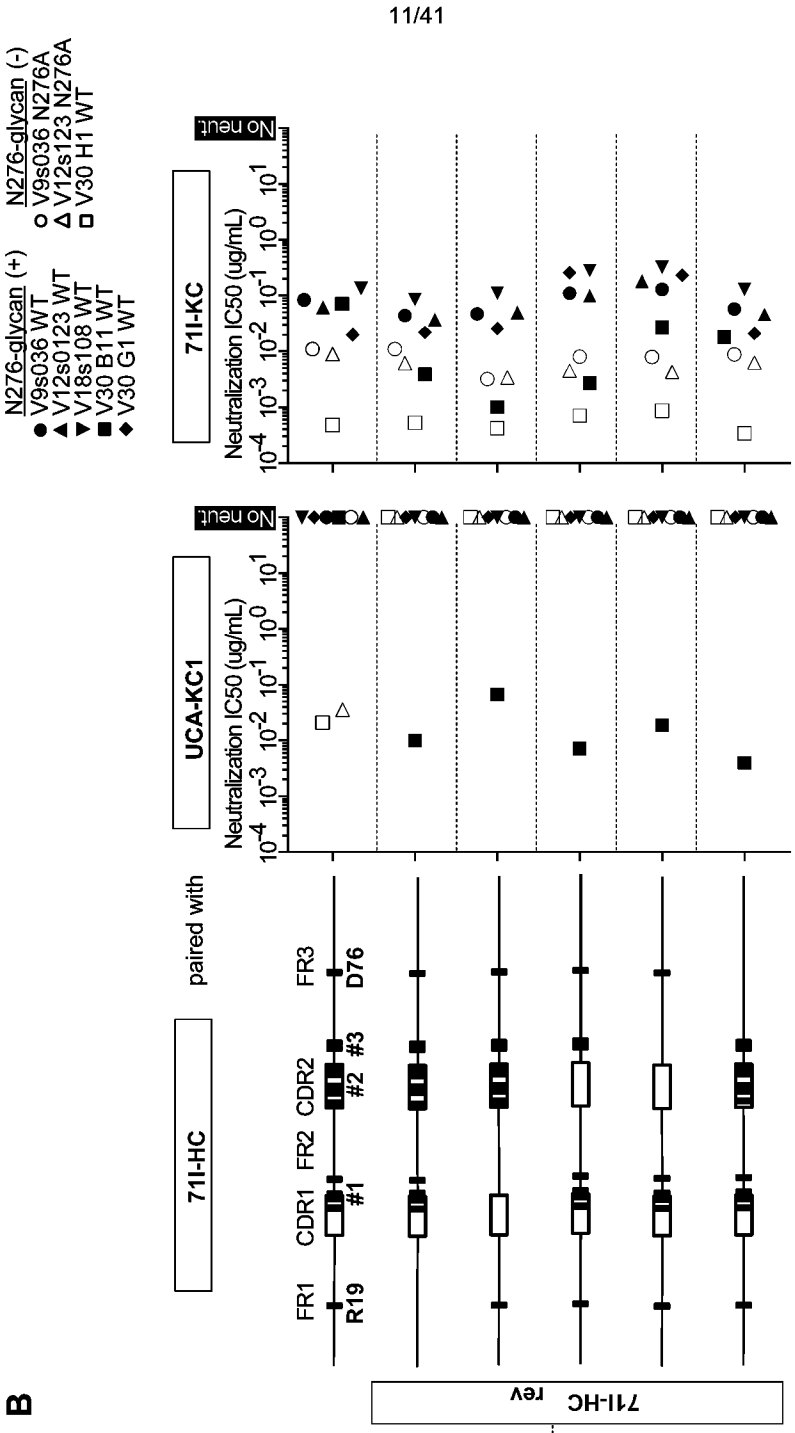


Figure 3 (Cont.)

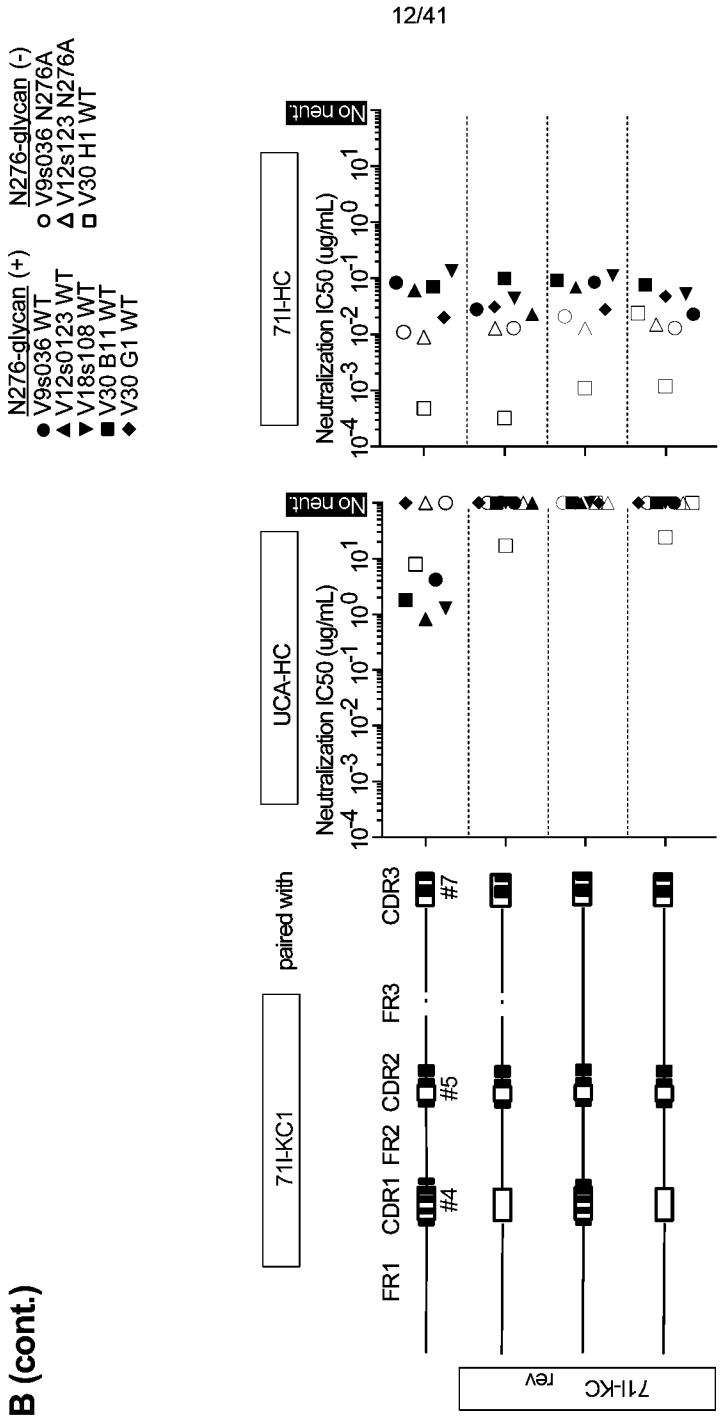


Figure 3 (Cont.)

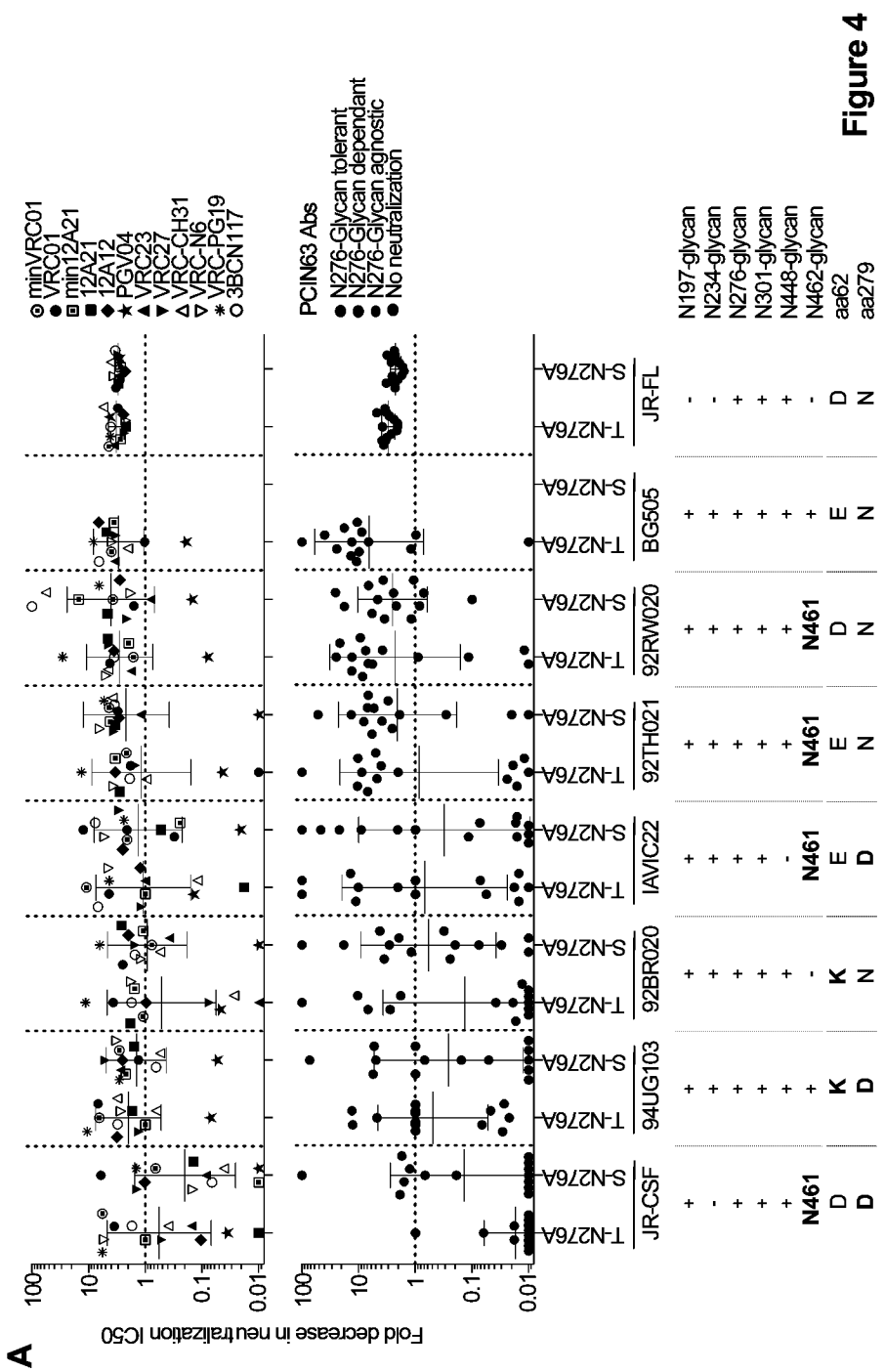

A
Fold decrease in neutralization IC50
100
10
1
0.1
0.01
minVRC01
VRC01
min12A21
12A21
12A12
PGV04
VRC23
VRC27
VRC-CH31
VRC-N6
VRC-PG19
3BCN117
PCIN63 Abs
N276-Glycan tolerant
N276-Glycan dependant
N276-Glycan agnostic
No neutralization
T-N276A
S-N276A
JR-CSF
94UG103
92BR020
IAVIC22
92TH021
92RW020
BG505
JR-FL
N197-glycan
N234-glycan
N276-glycan
N301-glycan
N448-glycan
N462-glycan
aa62
aa279
N461
K
E
D
N
+
-

Figure 4

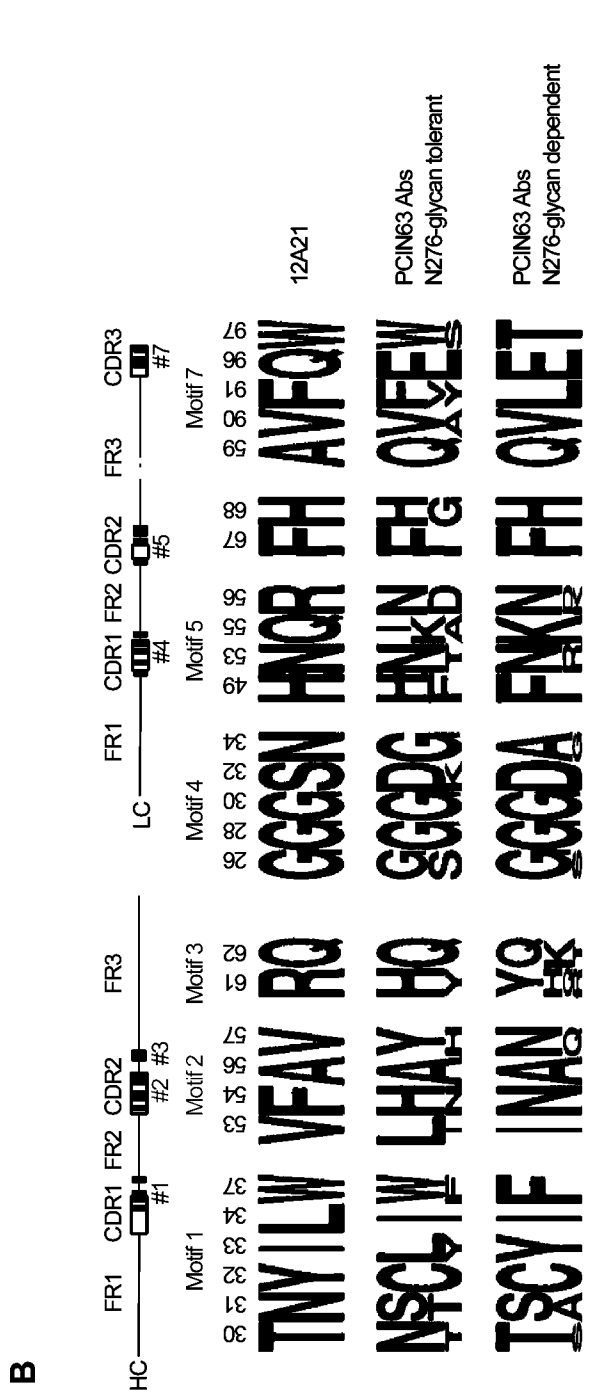
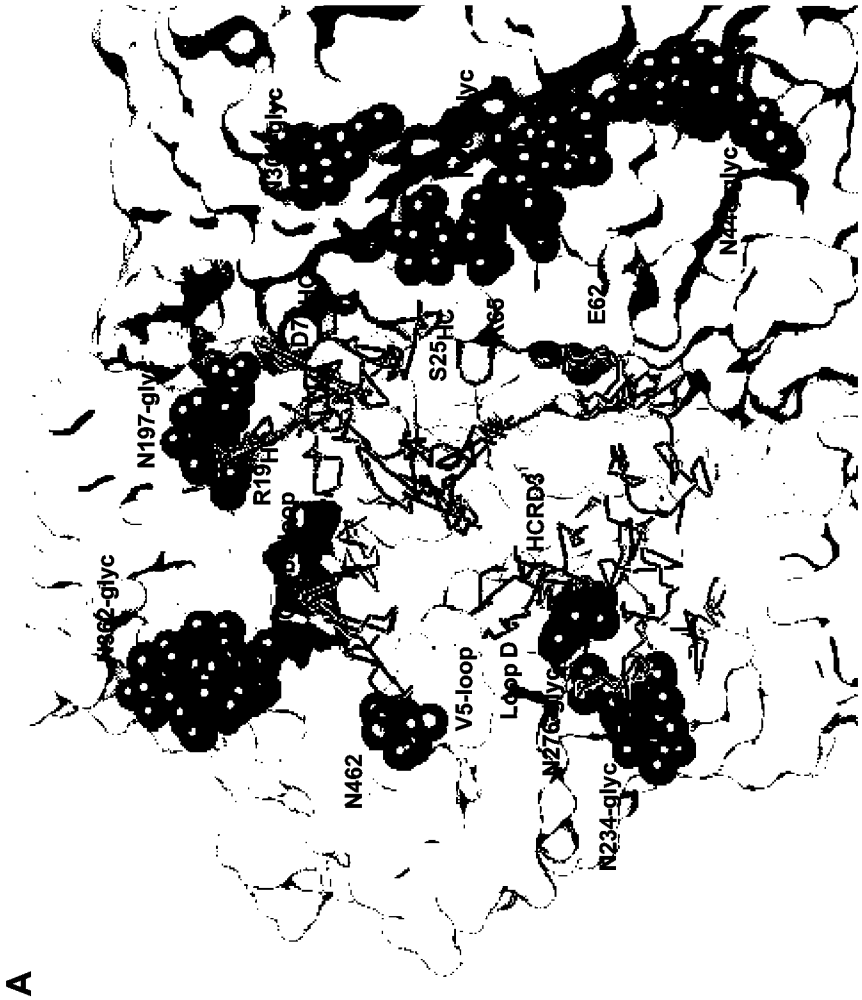


Figure 4 (cont.)

Figure 5


A
N197-glyc
R19HC
S25HC
E62
N448-glyc
HCRB3
Loop D
V5-loop
N462
N234-glyc

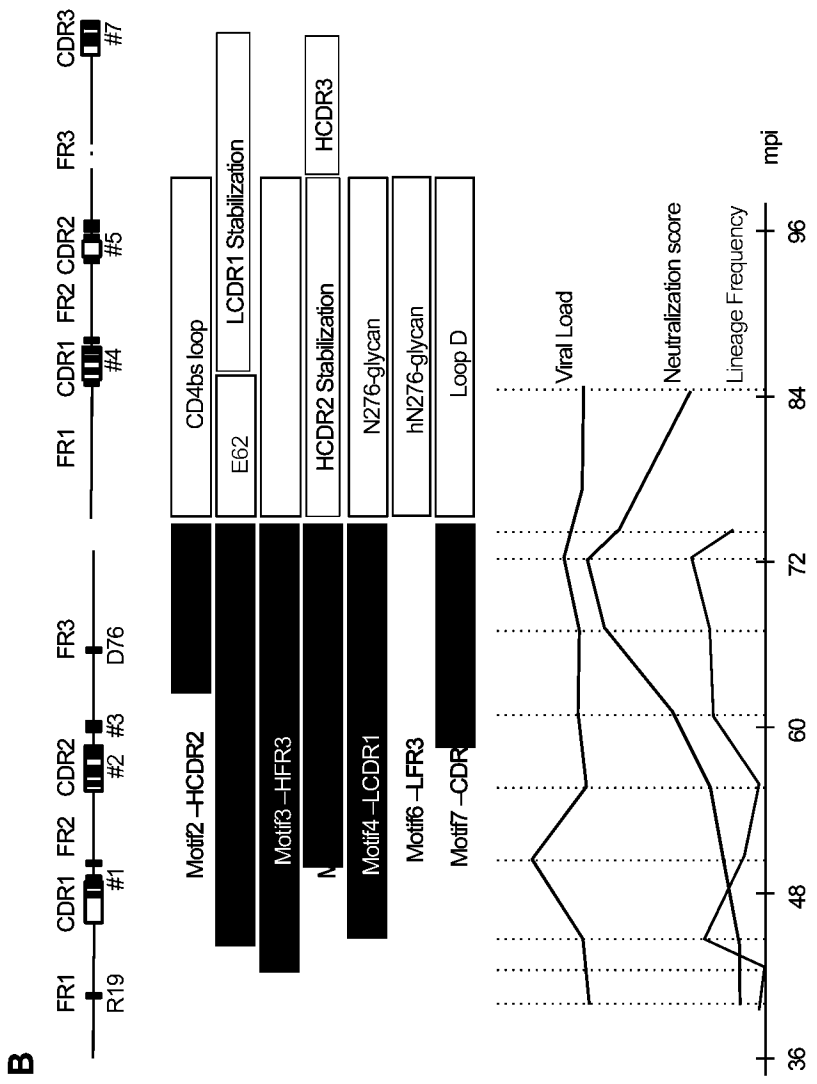


Figure 5 (cont.)

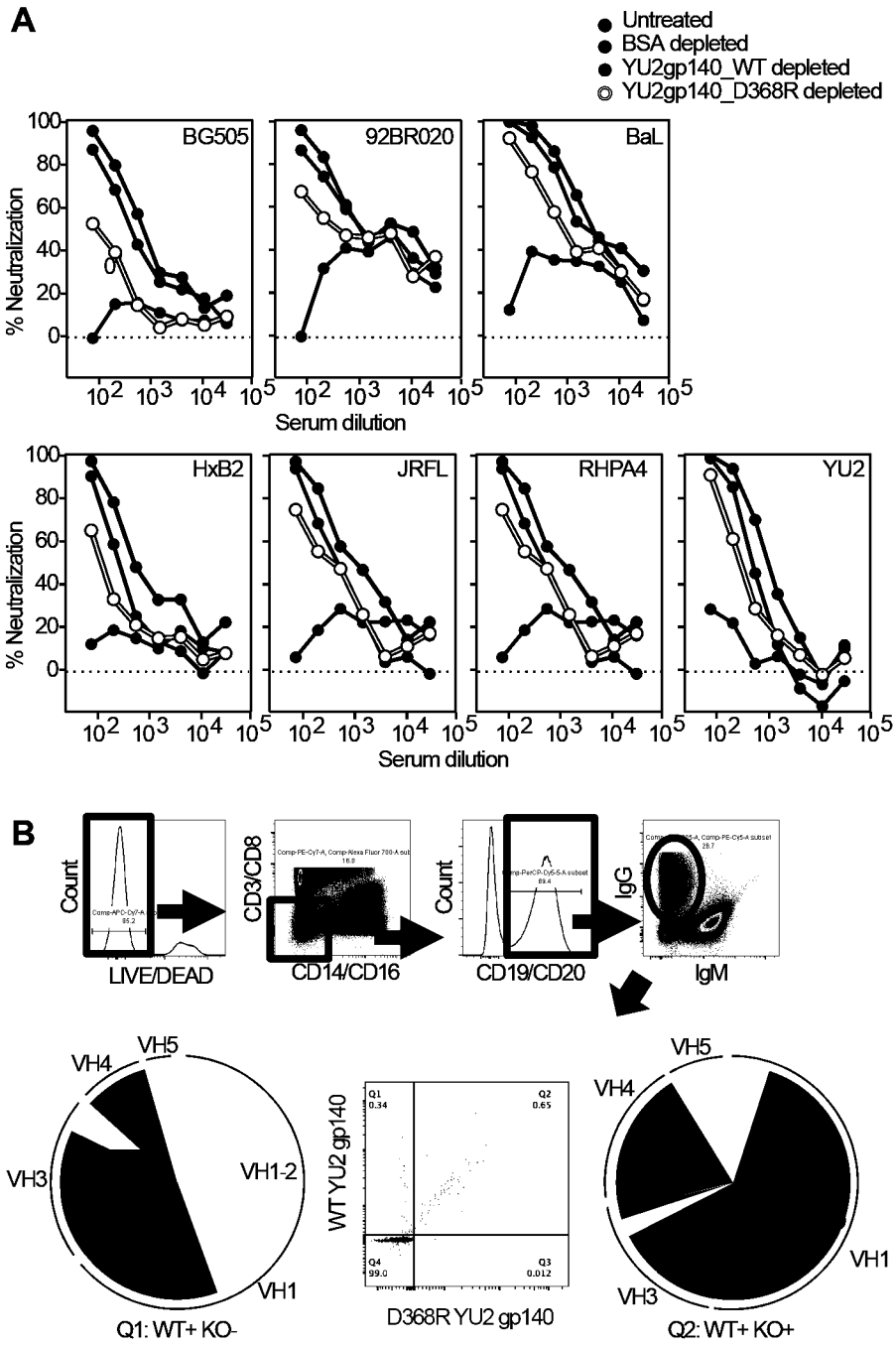

A
Untreated
BSA depleted
YU2gp140_WT depleted
YU2gp140_D368R depleted
BG505
92BR020
BaL
HxB2
JRFL
RHPA4
YU2
% Neutralization
Serum dilution
B
Count
LIVE/DEAD
CD3/CD8
CD14/CD16
CD19/CD20
IgG
IgM
VH5
VH4
VH3
VH1-2
VH1
Q1: WT+ KO-
WT YU2 gp140
D368R YU2 gp140
Q2: WT+ KO+

Figure 6

C

				Heavy Chain						Light Chain Chain					
				Putative Germline Genes: IGHV1-2*02 / IGHJ5*02						IGKV1-5*03 / IGKJ1*01					
VC	mAb name	mpi	mAb name	CDRH3 sequence (15aa)	V_H+J_H % SHM (nt)	V_H+J_H % SHM (aa)	UCA-H % SHM (nt)	UCA-H % SHM (aa)	CDRL3 sequence (5aa)	V_K+J_K % SHM (nt)	V_K+J_K % SHM (aa)	UCA-K % SHM (nt)	UCA-K % SHM (aa)	
72	P2D11#1a	66	66Aa						QVVQW	12.04	15.63	14.56	17.76	
72	P2C3	66	66B	TRDSSRRDTNWWLDP	9.59	18.42	11.38	20.33	QVLET	12.71	17.71	14.24	18.69	
78	P1B5#1a	71	71Aa						QVYES	10.70	19.79	12.30	20.56	
78	P1C11	71	71B	TTHSSSRDFQWSLDP	9.88	16.67	11.92	20.33	QVYES	11.04	16.67	12.94	17.76	
78	P2B10#2b	71	71D2b	TRDSSRRDTNWWLDP	10.47	21.05	12.20	22.76	QVLET	12.71	19.79	14.24	20.56	
78	P3F5	71	71C	TRDSSRRDTNWWLDP	10.76	20.18	12.47	21.95	QVLET	12.37	18.75	13.92	19.63	
78	P3C6#1a	71	71E1	TRDSSRRDTNWWLDP	10.76	20.18	12.47	21.95						
78	P3D6	71	71F	TRDSSRQQRDWWLDP	12.50	21.05	13.01	21.14	QVYES	11.04	18.75	12.62	19.63	
78	P2C6	71	71G	TRDASRDDRAWRLDP	13.08	21.05	15.72	23.58	QVVEW	12.37	15.63	14.56	16.82	
78	P1D5	71	71H	ARDSSREETNWWLDP	13.08	21.93	14.36	23.58	QVLET	13.04	20.83	14.24	21.50	
78	P1D7#1a	71	71I1a	TRDASRDDRAWRLDP	13.66	21.05	16.26	23.58	QVFEW	13.04	17.71	14.56	18.69	
78	P1G8#2a	71	71J2a	TRDASRDDRAWRLDP	10.76	20.18	12.47	21.95	QVLET	12.71	18.75	14.24	19.63	
78	P1B9	71	71K	TRDSSRDETNWWLDP	14.24	23.68	15.45	25.20	QVLET	13.04	18.75	14.56	19.63	
78	P3B9	71	71L	TRDSSRDETNWWLDP	14.24	24.56	15.45	26.02	QVLET	13.04	18.75	14.56	19.63	
78	P2F8#1a	71	71M1a	ARDSSRDETNWWLDP	14.53	21.05	15.72	22.76	QVLET	12.37	18.75	13.92	19.63	
78	P2E4#1a	71	71N1a	TRDSSRGNTEWRLDP	14.53	21.05	15.72	22.76	QVYQT	12.71	18.75	14.89	20.56	
78	P1C4	71	71O	TRDSSRDNLEWRLDP	15.99	23.68	17.07	23.58	QVFEW	12.71	15.63	14.56	16.82	
78	P3F6	71	71P	TRDSSRGDTEWRLDP	15.99	23.68	17.89	24.39	QVFEW	13.04	16.67	14.89	17.76	
84	P3C7	77	77A	TTHSSRRDFQWSLDP	10.47	17.54	12.20	20.33						
84	P2B6#1b	77	77B1b	TRDSSRDETNWWLDP	11.34	23.68	13.82	25.20	QVLET	12.71	19.79	14.24	20.56	
84	P1C8	77	77C	TRDSSRRDLEWRLDP	11.92	21.05	12.74	21.14	QVLET	13.71	19.79	15.53	20.56	
84	P3B6	77	77D	ARDSSRDETNWWLDP	13.08	20.18	14.36	21.95	QAYES	12.37	19.79	14.24	20.56	
84	P3C9#1a	77	77E1	TRDSSRDETNWWLDP	13.95	23.68	15.18	25.20						
84	P2B9#1a	77	77F1	TRDSSRDETNWWLDP	14.53	23.68	15.72	25.20						

Figure 6 (cont.)

D



E

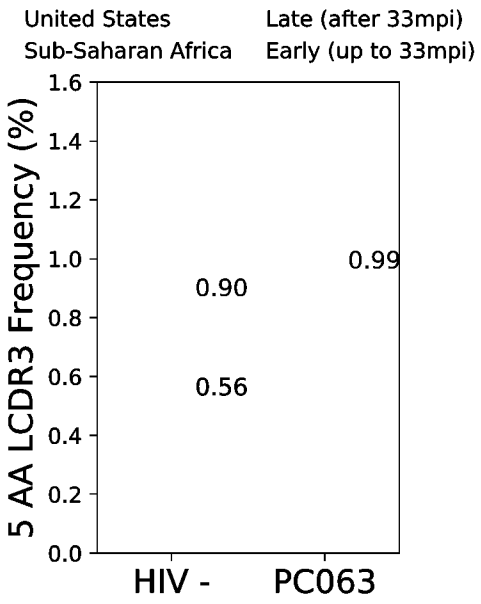
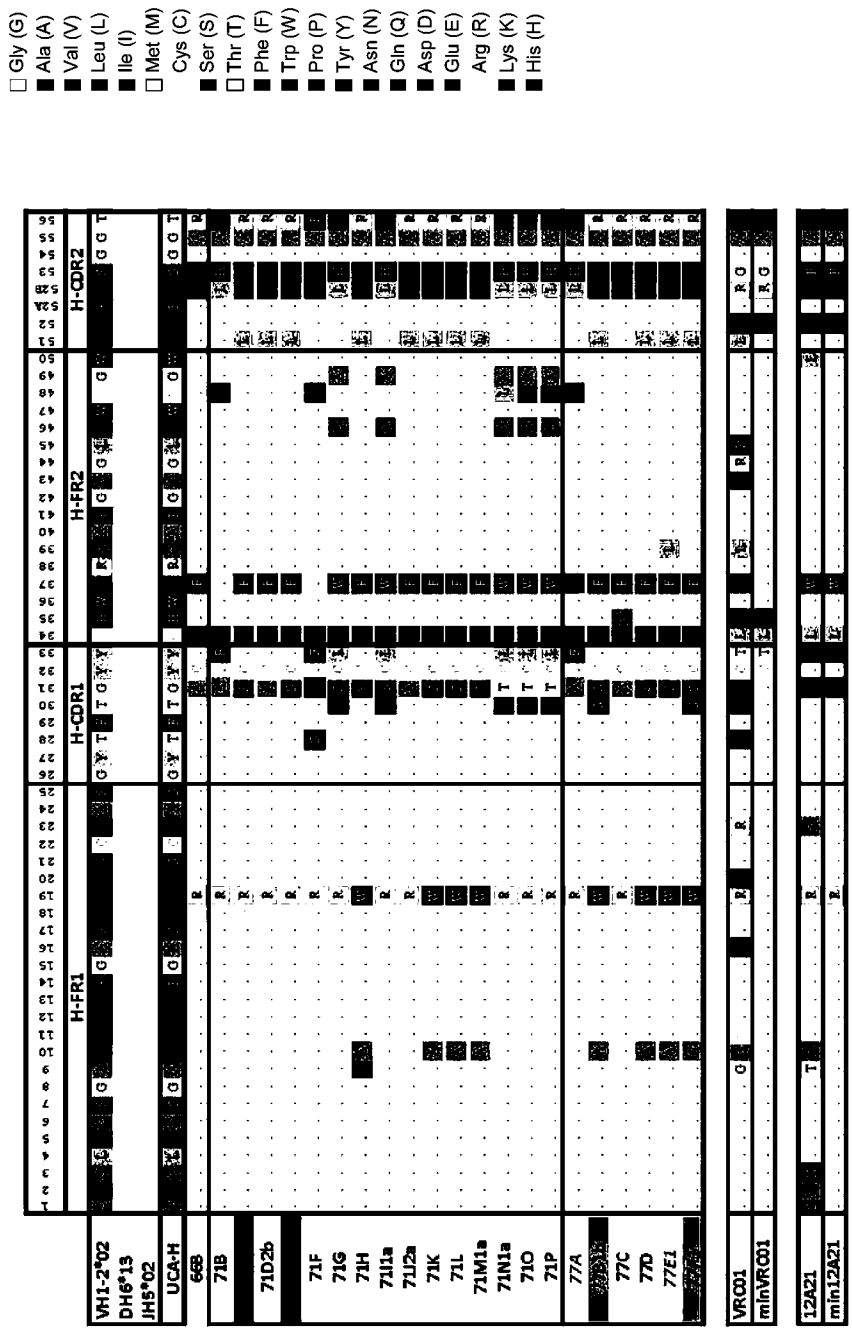


Figure 6 (cont.)

Figure 7


Gly (G)
Ala (A)
Val (V)
Leu (L)
Ile (I)
Met (M)
Cys (C)
Ser (S)
Thr (T)
Phe (F)
Trp (W)
Pro (P)
Tyr (Y)
Asn (N)
Gln (Q)
Asp (D)
Glu (E)
Arg (R)
Lys (K)
His (H)
H-FR1
H-CDR1
H-FR2
H-CDR2
VH1-2*02
DH6*13
JH5*02
UCA-H
66B
71B
71D2b
71F
71G
71H
71I1a
71J2a
71K
71L
71M1a
71N1a
71O
71P
77A
77C
77D
77E1
VRC01
minVRC01
12A21
min12A21

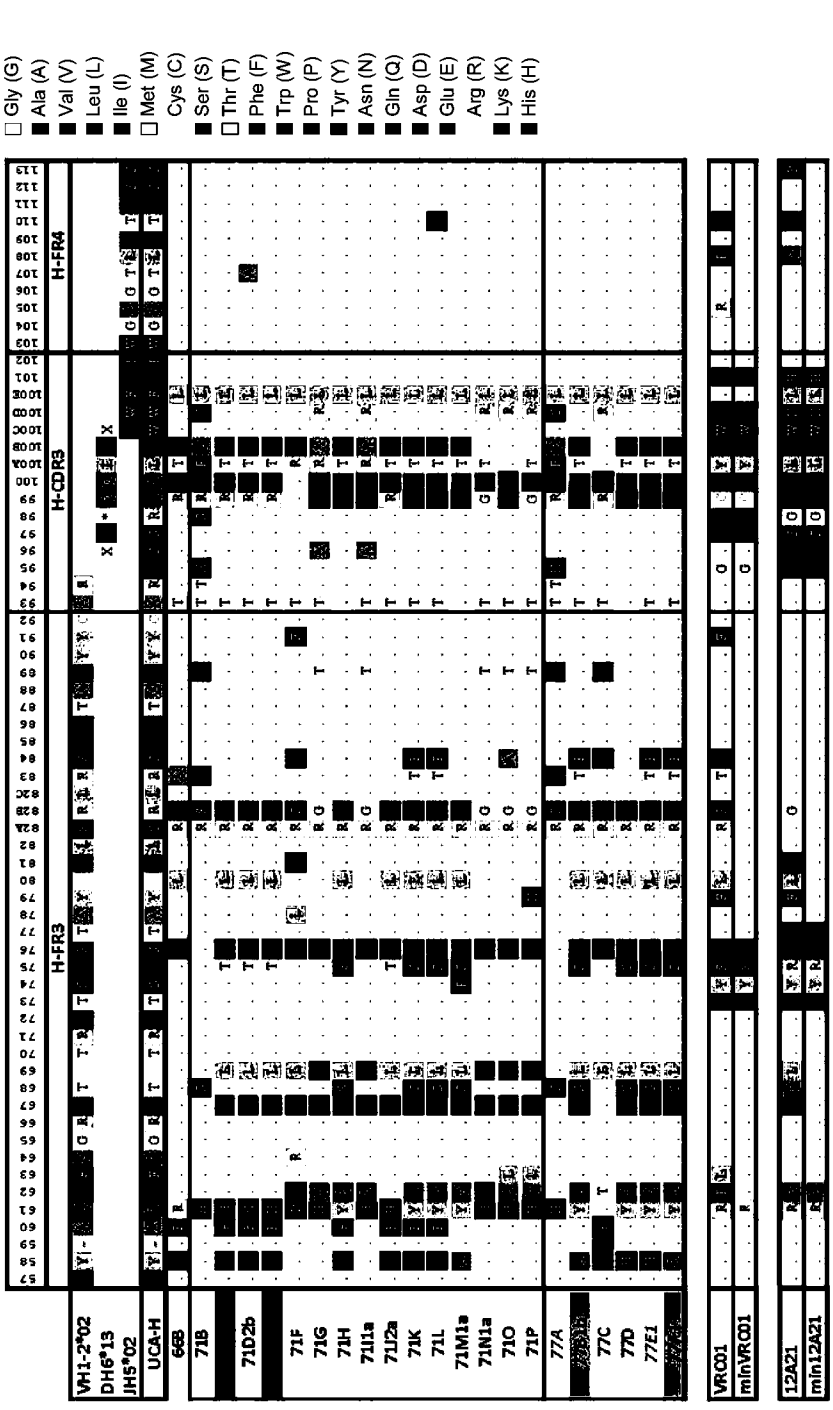


Figure 7 (cont.)

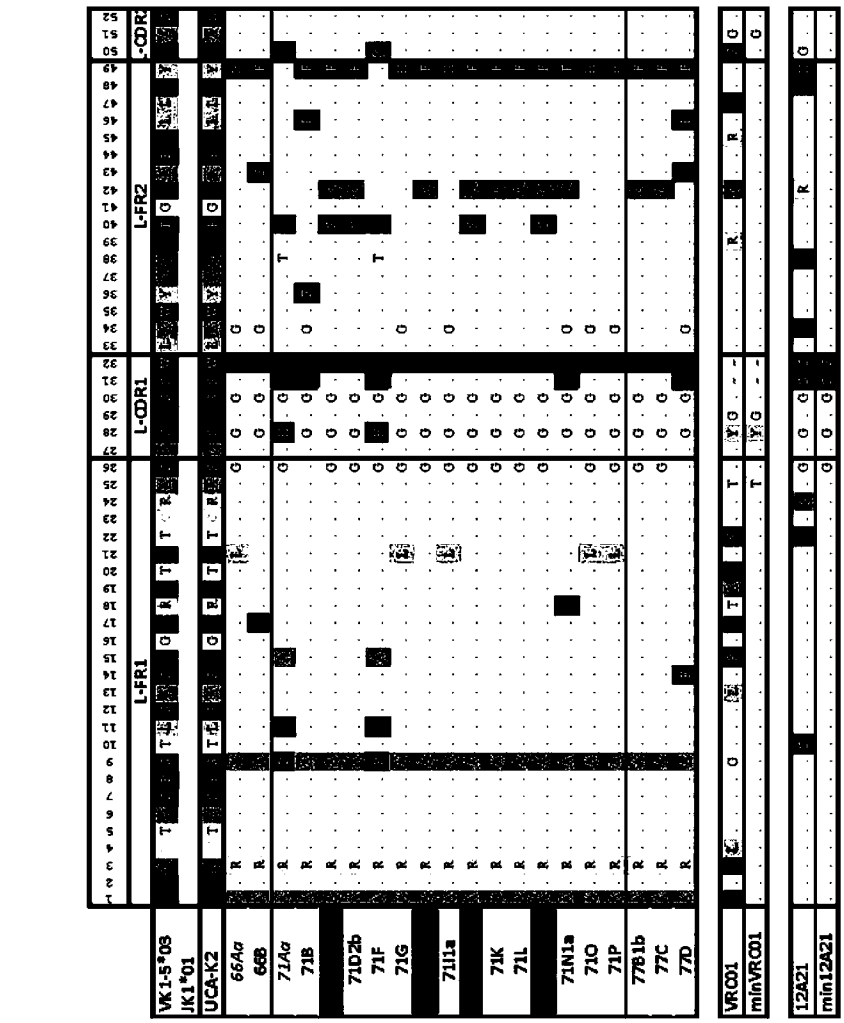


Figure 7 (cont.)

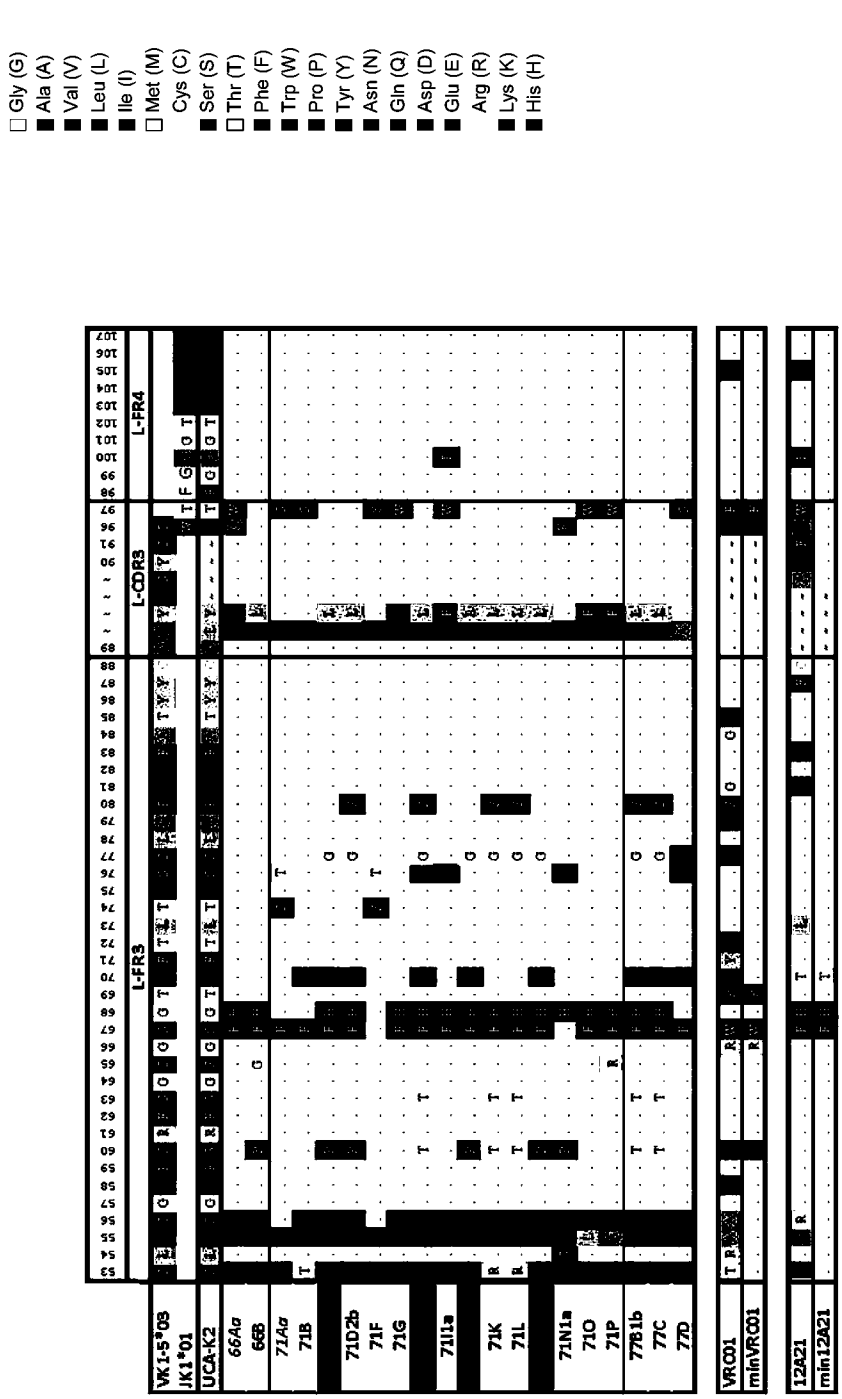


Figure 7 (cont.)

A

| | | |

Breadth (viruses neutralized)	Potency mAb (GeoMean IC_{50})	Potency Plasma (GeoMean ID_{50})
0-10%	10-50 µg/mL	/
10-25%	1-10 µg/mL	50-100
25-50%	0.1-1 µg/mL	100-300
50-75%	0.01-0.1 µg/mL	300-900
75-100%	<0.01 µg/mL	>900

Figure 8 (cont.)

B

Ab name	Breadth (% viruses)				GeoMean	SHM	SHM
	IC_{50} <0.1 µg/mL	IC_{50} <1 µg/mL	IC_{50} <10 µg/mL	IC_{50} <50 µg/mL	IC_{50} (µg/mL)	(V_H+J_H)	(V_K+J_K)
68B	3%	45%	70%	75%	0.8	9.6	12.7
71B	3%	3%	3%	3%	0.04	9.9	11.0
71C	15%	63%	85%	88%	0.50	10.8	12.4
71D2b	10%	55%	75%	83%	0.73	10.5	12.7
71F	0%	5%	8%	8%	0.72	12.5	11.0
71G	13%	58%	90%	93%	0.57	13.1	12.4
71H	23%	55%	75%	83%	0.48	13.1	13.0
71I1a	30%	75%	95%	98%	0.28	13.7	13.0
71J2a	15%	55%	85%	88%	0.56	10.8	12.7
71K	23%	63%	80%	90%	0.42	14.2	13.0
71L	30%	63%	80%	85%	0.27	14.2	13.0
71M1a	20%	58%	80%	85%	0.55	14.5	12.4
71N1a	0%	0%	0%	0%	/	14.5	12.7
71O	10%	65%	95%	95%	0.630	16.0	12.7
71P	8%	55%	78%	95%	1.1	16.0	13.0
77B1b	5%	18%	40%	58%	4.2	11.3	12.7
77C	5%	33%	53%	58%	0.92	11.9	13.7
77D	0%	5%	15%	30%	7.3	13.1	12.4
PC63M33	25%	65%	83%	88%	125		
min VRC01	25%	68%	78%	83%	0.37	6.5	7.2
VRC01	30%	88%	93%	93%	0.21	29.3	21.3
min 12A21	8%	33%	48%	50%	0.64	8.3	3.4
12A21	25%	65%	83%	88%	0.47	21.9	12.4

A

	Time point	PC63V72	PC63V78	PC63V78	PC63V78	PC63V81	PC63V36	VRC01	VRC01	12A21	12A21
	Ab name	P2C3	P2C6	P1D7#1a	P3B9	P3B6	Serum	Min	Mat	Min	Mat
		Neutralization IC_{50} (mg/mL)									
Subtype	HIV.1 Isolate	PCIN 66B	PCIN 71G	PCIN 71I	PCIN 71L	PCIN 77D	PC63 M33 serum	Min VRC01	Mat VRC01	Min 12A21	Mat 12A21
-	aMLV	>100	>100	>100	>100	>100	<20	>100	>100	>100	>100
A	0260.v5.c1	1.5	1.7	1.7	0.58	0.95	NT	0.85	0.33	0.51	0.19
	0330.v4.c3	0.45	0.29	0.19	0.077	74	735	NT	NT	NT	NT
	191084 B7.19	0.86	0.21	0.17	0.19	>100	634	0.057	0.043	7.3	0.042
	19195S A11	>100	1.2	0.036	6.3	>100	2018	>100	>100	>100	>100
	9004SS A3 4	>100	>100	>100	>100	>100	NT	>100	>100	>100	>100
	MS208.A1	0.73	0.28	0.24	0.19	>100	530	>100	0.024	>100	6.0
	Q168ENVa2	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
	Q23ENV17	0.36	0.18	0.15	0.080	0.17	736	0.074	0.042	0.12	0.026
	Q259ENVd2.17	>100	0.77	0.073	>100	>100	93	0.20	0.029	>100	0.10
	Q461ENVe2	6.8	7.7	7.1	2.2	>100	57	1.2	0.27	0.29	0.087
	Q769ENVd22	0.22	0.094	0.070	0.079	>100	1355	0.036	0.019	0.035	0.0089
	Q842ENVd12	>100	>100	>100	>100	>100	NT	>100	>100	>100	>100
AC	3301.v1.c24	0.68	0.49	0.39	0.33	>100	558	0.11	0.14	>100	0.049
	6041.v3.c23	0.063	0.066	0.057	0.022	0.097	<20	1.8	0.013	0.014	0.0069
	6540.v4.c1	>100	>100	>100	>100	>100	24	>100	>100	>100	>100
	6545.v4.c1	>100	>100	>100	>100	>100	2	>100	>100	>100	>100
ACD	0815.v3.c3	0.12	0.057	0.062	0.032	>100	1019	0.056	0.0100	0.033	0.012
	3103.v3.c10	>100	4.0	6.4	>100	>100	<20	4.1	1.3	>100	0.47
AE	620345.c01	>100	>100	>100	>100	>100	170	>100	>100	>100	>100
	BJOX009000.02.4	>100	4.2	2.9	11	>100	<20	2.9	0.64	>100	>100
	BJOX010000.06.2	>100	16	8.5	9.9	>100	57	6.5	3.9	>100	8.0
	BJOX015000.11.5	>100	1.4	0.99	0.44	>100	36	2.0	0.19	0.60	0.13
	BJOX025000.01.1	>100	0.58	0.49	26	0.16	311	7.3	2.7	0.27	0.13
	BJOX028000.10.3	0.079	0.11	0.076	0.052	>100	1813	11	0.086	0.029	0.0091
	C1080.c03	46	3.7	2.1	1.2	>100	466	>100	0.55	0.33	0.11
	C3347.c11	5.9	0.042	0.034	0.016	0.016	3162	0.039	0.050	0.0090	0.011
	C4118.c09	>100	>100	>100	>100	>100	477	>100	>100	>100	>100
	CNE5	4.0	0.29	0.18	0.35	>100	21	0.20	0.060	0.19	0.045
	CNE8	>100	0.44	0.36	0.36	>100	76	0.42	0.74	>100	0.28
	R1166.c01	4.0	0.46	0.33	0.23	2.3	337	0.62	0.39	0.17	0.097
	R2184.c04	4.0	0.17	0.13	0.24	>100	594	0.030	0.024	0.84	0.027
	R3265.c06	0.72	0.57	0.78	0.21	>100	138	0.73	0.17	0.057	0.044
AG	928.28	0.42	0.69	0.39	0.13	>100	1116	1.1	0.22	0.42	0.20
	T211.9	2.1	1.3	0.88	0.48	>100	NT	>100	0.90	>100	>100
	T235.47	>100	0.042	0.043	0.059	>100	432	>100	0.028	0.40	0.012
	T250.4	>100	>100	>100	>100	>100	25	>100	>100	>100	>100
	T251.18	9.7	7.3	8.8	1.9	>100	114	1.7	1.3	1.9	0.43
	T255.34	0.37	0.20	0.23	0.070	1.0	264	0.71	0.39	0.072	0.028
	T257.31	0.57	0.96	1.2	0.22	>100	203	0.71	0.31	0.078	0.028
	T263.8	0.35	0.14	0.17	0.070	1.6	NT	0.094	0.12	0.11	0.044
	T278.5	>100	>100	>100	>100	>100	<20	>100	>100	>100	>100
B	1006.11.C3.1601	0.25	0.18	0.13	0.049	>100	1173	2.5	0.095	0.15	0.036
	1012.11.TC21.3257	0.28	0.87	0.49	0.65	>100	146	0.035	0.070	>100	0.035
	1054.07.TC4.1499	2.2	3.3	3.1	1.9	>100	33	0.20	0.83	>100	0.50
	1056.10.TA11.1826	2.0	1.1	0.68	0.20	>100	106	0.33	0.55	>100	0.18
	62357.14.D3.4589	0.29	0.19	0.10	0.083	0.029	4317	0.43	0.39	0.44	0.11
	6240.08.TA5.4622	6.5	4.1	2.5	0.85	>100	71	1.6	0.60	1.2	0.39
	6244.13.B5.4567	0.57	0.95	0.65	0.26	1.2	340	0.16	0.12	0.21	0.072
	AC10.0.29	>100	1.9	1.0	>100	>100	79	1.6	1.1	8.3	0.63
	CAAN5342.A2	0.72	2.6	2.2	0.76	>100	38	0.45	0.55	>100	0.49
	SC05.8C11.2344	22	2.3	1.8	6.7	>100	95	0.26	0.49	>100	1.8
	TRO.11	0.47	0.17	0.14	0.065	>100	649	0.79	0.25	0.20	0.077
	WEAU.d15.410.787	1.81	0.27	0.20	0.098	>100	214	0.027	0.046	9.98	0.012
BC	CNE17	>100	3.7	2.6	5.93	>100	<20	0.18	0.38	>100	2.7
	CNE19	0.092	0.12	0.098	0.036	0.41	708	0.027	0.074	0.13	0.019
	CNE20	0.051	0.12	0.12	0.048	>100	1510	>100	1.3	>100	0.0078
	CNE21	0.25	0.55	0.50	0.19	>100	1668	0.58	0.078	2.0	0.016
	CNE30	6.1	3.2	2.6	0.99	3.6	441	0.60	0.28	0.45	0.14
	CNE52	0.87	0.60	0.41	0.11	1.2	630	0.10	0.084	0.092	0.025
	CNE53	0.10	0.11	0.069	0.057	0.061	11658	0.035	0.046	0.065	0.027
	CNE58	0.71	0.10	0.12	0.076	1.3	2315	0.49	0.087	>100	0.078

Figure 9

A (cont.)

	Time point	PC63V72	PC63V78	PC63V78	PC63V78	PC63V81	PC63V36	VRC01	VRC01	12A21	12A21
	Ab name	P2C3	P2C6	P1D7#1a	P3B9	P3B6	Serum	Min	Mat	Min	Mat
		Neutralization IC_{50} (mg/mL)									
Subtype	HIV.1 Isolate	PCIN 66B	PCIN 71G	PCIN 71I	PCIN 71L	PCIN 77D	PC63 M33 serum	Min VRC01	Mat VRC01	Min 12A21	Mat 12A21
	1394C9G1(Rev.)	0.12	0.43	0.23	0.18	>100	465	1.2	0.15	0.058	0.058
	7030102001E5(Rev.)	12	1.4	0.91	0.39	>100	701	0.23	0.37	>100	0.22
	BF1266.431a	0.68	0.56	0.056	0.13	>100	355	**0.0079**	**0.0077**	>100	>100
	Ce0393 C3	0.15	0.38	0.26	0.15	>100	299	>100	0.12	0.015	0.013
	Ce0682 E4	>100	>100	>100	>100	>100	NT	>100	>100	>100	>100
	Ce1086 B2	>100	>100	>100	>100	>100	NT	>100	>100	>100	>100
	Ce1172 H1	>100	>100	>100	3.2	>100	<20	>100	>100	>100	>100
	Ce1176 A3	4.0	1.4	1.2	0.72	68	129	1.5	0.77	0.45	0.22
	Ce2010 F5	1.1	0.54	0.52	0.11	6.8	208	0.31	0.19	0.42	0.22
	Ce2060 G9	1.6	1.0	1.3	0.89	18	203	0.34	0.14	0.25	0.11
	Ce703010054 2A2	>100	2.0	2.8	2.4	>100	<20	0.99	0.43	>100	0.16
	Ce704809221 1B3	3.5	0.52	0.79	0.33	>100	58	0.32	0.24	0.29	0.20
	Du156.12	>100	0.088	0.11	0.18	>100	311	0.029	0.036	>100	0.22
	Du172.17	0.73	0.22	0.12	0.097	0.40	401	>100	>100	0.017	0.068
C	Du422.1	>100	>100	>100	>100	>100	31	>100	>100	>100	2.0
	HIV-0013095.2.11	1.7	0.52	0.56	0.46	>100	92	0.035	0.038	>100	0.048
	HIV-001428.2.42	0.45	0.062	0.058	0.077	>100	1077	**0.0067**	0.011	2.2	**0.0087**
	HIV-16055.2.3	0.65	0.24	0.20	0.26	>100	431	0.027	0.024	0.052	**0.0087**
	HIV-16845.2.22	>100	>100	>100	>100	>100	NT	>100	>100	>100	>100
	ZM109F.PB4	1.1	0.44	0.55	0.23	>100	<20	0.29	0.035	>100	0.21
	ZM135M.PL10a	2.2	2.0	2.3	0.62	>100	74	>100	0.57	>100	>100
	ZM197M.PB7	>100	0.53	0.66	0.55	>100	281	0.27	0.28	>100	>100
	ZM214M.PL15	1.3	1.7	2.2	0.43	1.7	199	0.48	0.36	0.31	0.085
	ZM233M.PB6	>100	4.0	2.3	>100	>100	57	>100	>100	>100	>100
	ZM246F.D5	>100	0.77	0.87	0.22	>100	<20	>100	2.2	>100	0.088
	ZM247F.F7	>100	>100	>100	>100	>100	<20	>100	0.16	>100	0.097
	ZM249M.B10	0.64	0.12	0.13	0.051	>100	301	0.044	0.056	>100	0.031
	ZM249M.PL1	0.78	0.16	0.11	0.062	>100	313	0.044	0.073	>100	0.060
	ZM53M.PB12	7.2	2.7	2.9	1.7	32	119	0.69	0.42	0.53	0.22
	3817.v2.c59	>100	2.6	3.4	3.1	>100	232	>100	>100	3.8	0.82
	6480.v4.c25	0.83	0.083	0.12	0.091	>100	416	0.031	0.029	0.090	0.016
CD	6811.v7.c18	1.5	0.86	1.1	0.72	>100	141	0.045	0.068	0.20	0.028
	6952.v1.c20	>100	0.17	0.16	0.55	>100	230	0.063	0.020	>100	>100
	89.F1 2 25	>100	>100	>100	>100	>100	NT	>100	>100	>100	>100
	191821 E6 1	>100	>100	>100	>100	>100	NT	>100	>100	>100	>100
D	231965.c01	>100	2.3	2.8	>100	>100	59	0.25	0.32	>100	>100
	3016.v5.c45	>100	0.24	0.36	4.4	>100	NT	1.7	0.068	0.23	0.048
	A07412M1.vrc12	0.23	0.29	0.18	0.18	>100	1037	0.11	0.088	0.027	0.016
	P0402 c2 11	0.99	0.54	0.54	0.46	>100	431	0.050	0.038	0.052	0.056
	P1981 C5 3	>100	4.27	4.14	15	>100	62	0.055	0.079	14	0.19
	X1193 c1	0.78	0.28	0.17	0.28	>100	344	**0.0026**	**0.0013**	6.46	0.066
G	X1254 c3	>100	1.39	1.10	>100	>100	68	0.019	0.024	>100	0.15
	X1632 S2 B10	0.70	1.25	1.14	1.03	>100	193	**0.0028**	**0.0047**	>100	0.055
	X2088 c9	>100	>100	>100	>100	>100	<20	>100	>100	>100	>100
	X2131 C1 B5	3.61	0.80	0.81	2.71	>100	411	**0.0075**	0.014	>100	0.26

Figure 9 (cont.)

B

	GeoMean (IC50 mg/mL)									
Env Subtype	PCIN 66B	PCIN 71G	PCIN 71I	PCIN 71L	PCIN 77D	PC63 M33 serum	Min VRC01	Mat VRC01	Min 12A21	Mat 12A21
A	0.80	0.54	0.24	0.33	2.3	476	0.18	0.058	0.34	0.100
AC	0.21	0.18	0.15	0.086	0.097	30	0.45	0.042	0.014	0.018
ACD	0.12	0.48	0.63	0.032	/	1019	0.48	0.12	0.033	0.076
AE	2.7	0.64	0.48	0.59	0.18	234	0.83	0.28	0.14	0.087
AG	0.92	0.50	0.48	0.18	1.3	205	0.61	0.27	0.24	0.057
B	1.1	0.88	0.61	0.34	0.19	192	0.34	0.29	0.84	0.15
BC	0.33	0.40	0.33	0.18	0.68	1448	0.16	0.15	0.23	0.051
C	1.2	0.57	0.49	0.31	7.6	208	0.15	0.13	0.17	0.092
CD	1.1	0.42	0.53	0.58	/	237	0.044	0.034	0.41	0.072
D	0.23	0.54	0.56	0.90	/	246	0.36	0.12	0.079	0.028
G	1.2	0.98	0.85	1.4	/	191	0.012	0.014	1.7	0.11
Overall	0.93	0.58	0.46	0.34	1.1	255	0.21	0.13	0.25	0.084

	Breadth (% viruses)									
Env Subtype	PCIN 66B	PCIN 71G	PCIN 71I	PCIN 71L	PCIN 77D	PC63 M33 serum	Min VRC01	Mat VRC01	Min 12A21	Mat 12A21
A	64%	82%	82%	73%	27%	100%	60%	70%	50%	70%
AC	50%	50%	50%	50%	25%	25%	50%	50%	25%	50%
ACD	50%	100%	100%	50%	0%	50%	100%	100%	50%	100%
AE	50%	86%	86%	86%	21%	79%	79%	86%	64%	79%
AG	67%	78%	78%	78%	22%	71%	56%	78%	67%	67%
B	92%	100%	100%	92%	17%	83%	100%	100%	58%	100%
BC	88%	100%	100%	100%	63%	88%	88%	100%	63%	100%
C	62%	79%	79%	79%	21%	77%	62%	76%	38%	72%
CD	40%	80%	80%	80%	0%	100%	60%	60%	60%	60%
D	25%	75%	75%	50%	0%	100%	75%	75%	50%	50%
G	57%	86%	86%	71%	0%	86%	86%	86%	43%	86%
Overall	63%	84%	84%	79%	21%	80%	72%	81%	51%	77%

Breadth (viruses neutralized)	Potency mAb (GeoMean IC_{50})	Potency Plasma (GeoMean ID_{50})
0-10%	10-50 μg/mL	/
10-25%	1-10 μg/mL	50-100
25-50%	0.1-1 μg/mL	100-300
50-75%	0.01-0.1 μg/mL	300-900
75-100%	<0.01 μg/mL	>900

Figure 9 (cont.)

C

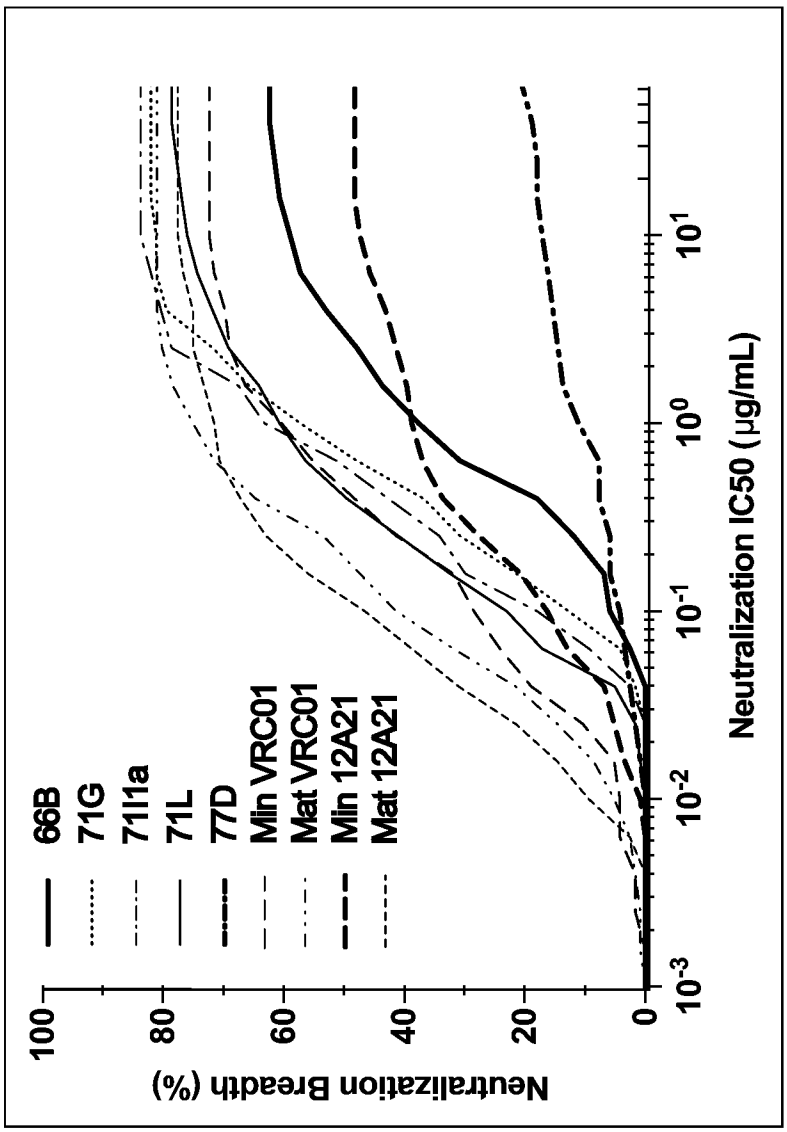


Figure 9 (cont.)

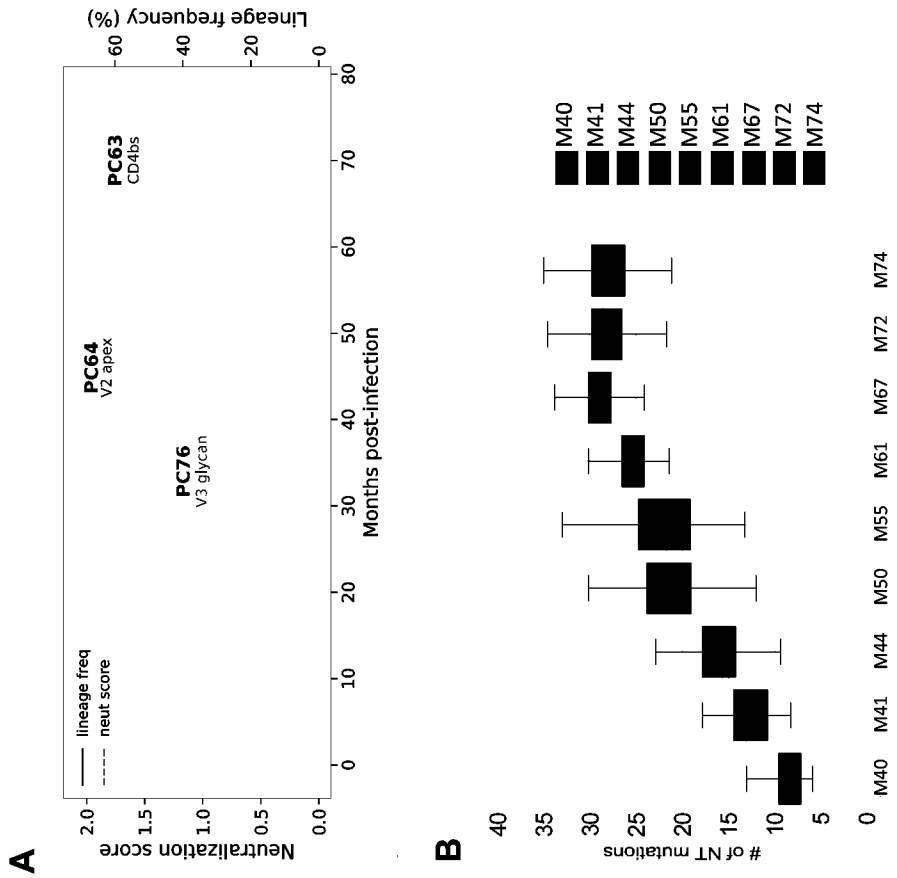

A
Neutralization score
2.0
1.5
1.0
0.5
0.0
lineage freq
neut score
PC64
V2 apex
PC63
CD4bs
PC76
V3 glycan
0
10
20
30
40
50
60
70
80
Months post-infection
Lineage frequency (%)
60
40
20
0
B
# of NT mutations
40
35
30
25
20
15
10
5
0
M40
M41
M44
M50
M55
M61
M67
M72
M74

Figure 10

C

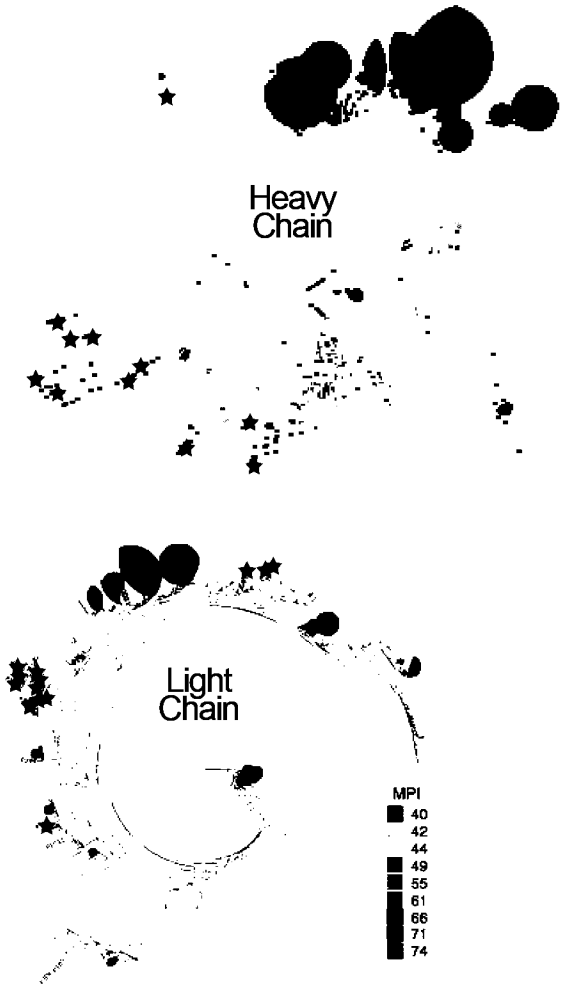


Figure 10 (cont.)

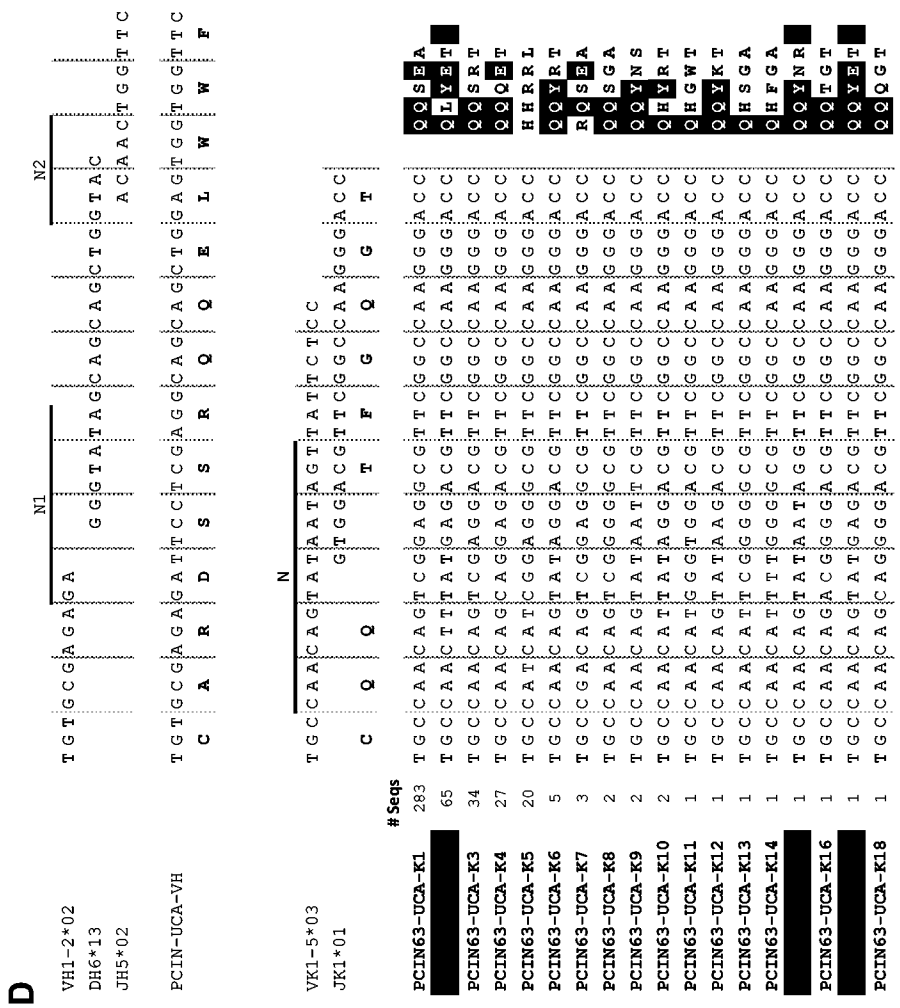


Figure 10 (cont.)

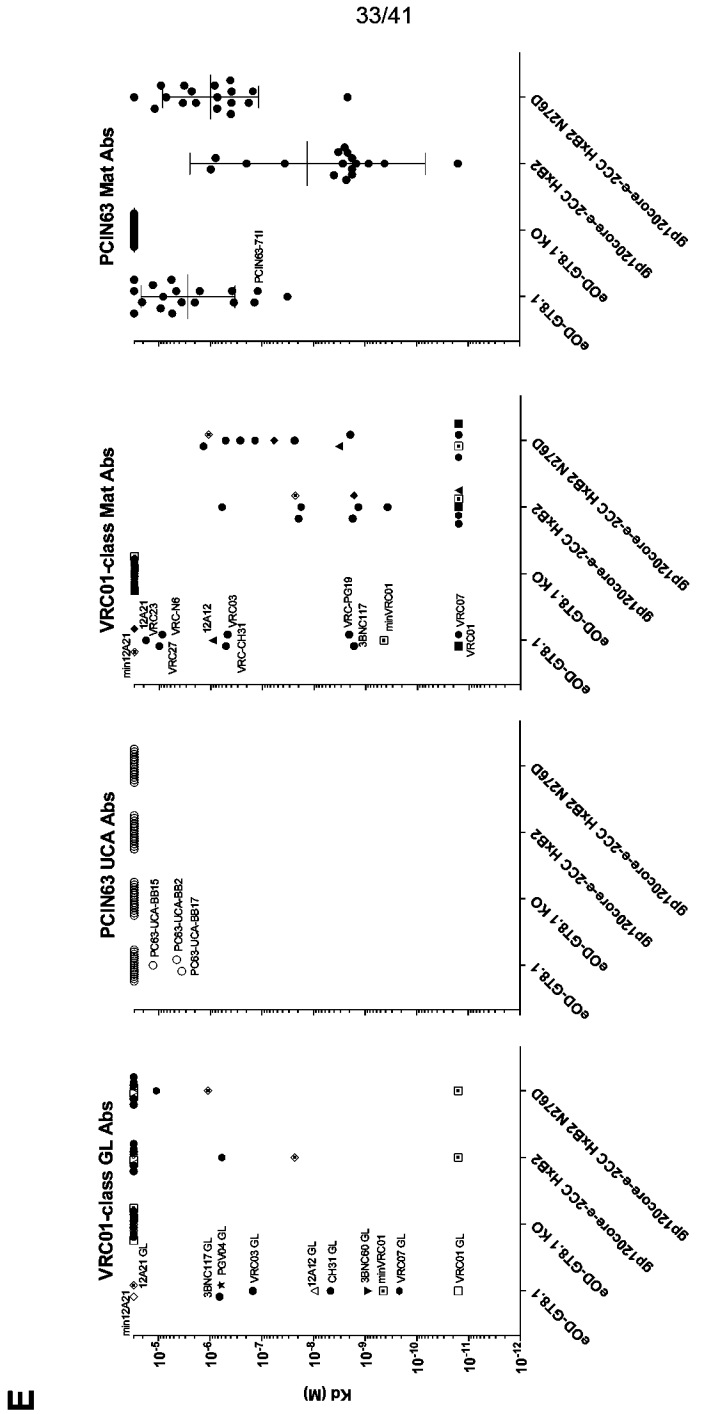
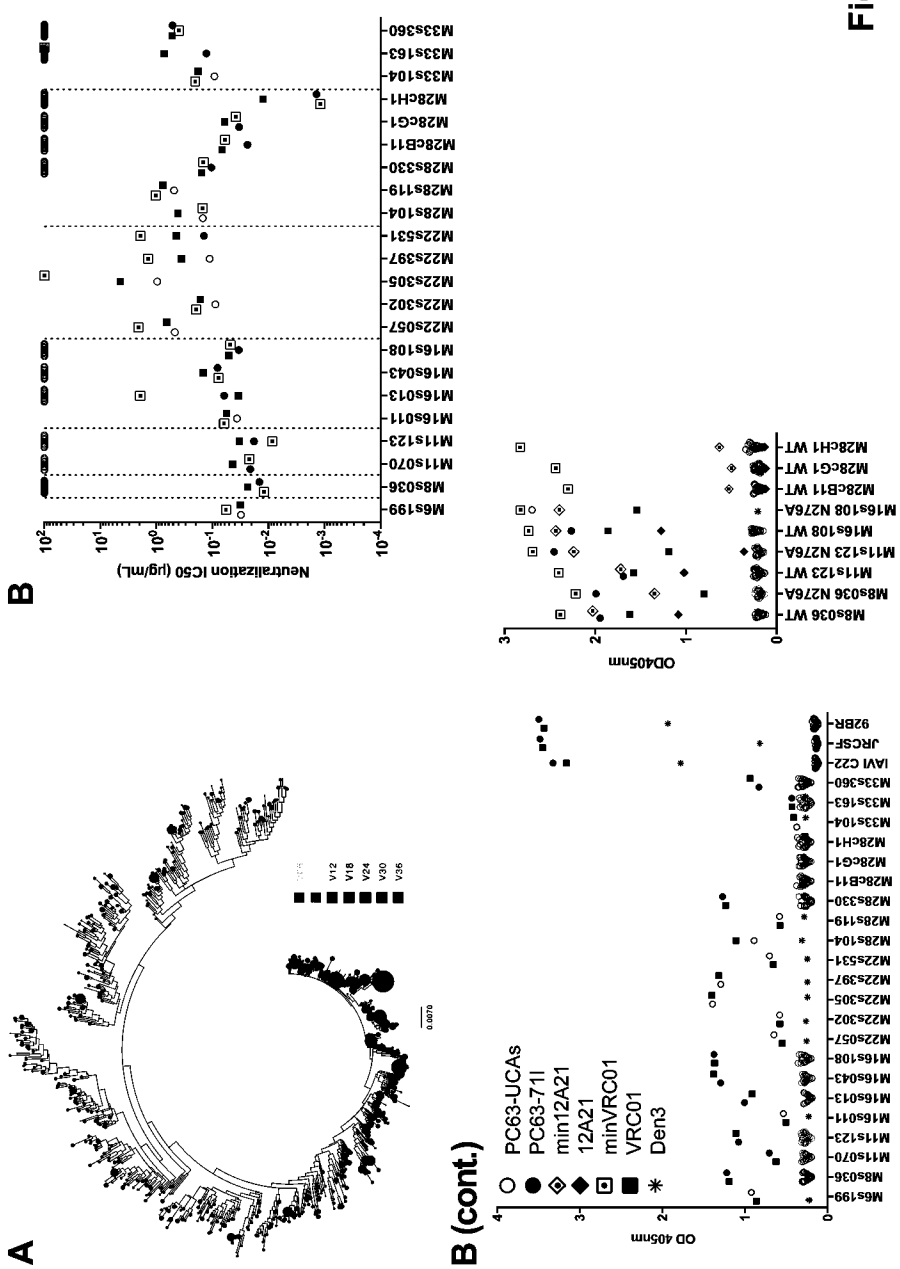


Figure 10 (cont.)

Figure 11


A
V12
V18
V24
V30
V36
0.0070
B
Neutralization IC50 (μg/mL)
M6s199
M8s036
M11s070
M11s123
M16s011
M16s013
M16s043
M16s108
M22s057
M22s302
M22s305
M22s397
M22s531
M28s104
M28s119
M28s330
M28cB11
M28cG1
M28cH1
M33s104
M33s163
M33s360
B (cont.)
PC63-UCAs
PC63-71I
min12A21
12A21
minVRC01
VRC01
Den3
OD 405nm
M6s199
M8s036
M11s070
M11s123
M16s011
M16s013
M16s043
M16s108
M22s057
M22s302
M22s305
M22s397
M22s531
M28s104
M28s119
M28s330
M28cB11
M28cG1
M28cH1
M33s104
M33s163
M33s360
IAVI C22
JRCSF
92BR
M8s036 WT
M8s036 N276A
M11s123 WT
M11s123 N276A
M16s108 WT
M16s108 N276A
M28cB11 WT
M28cG1 WT
M28cH1 WT
OD405nm

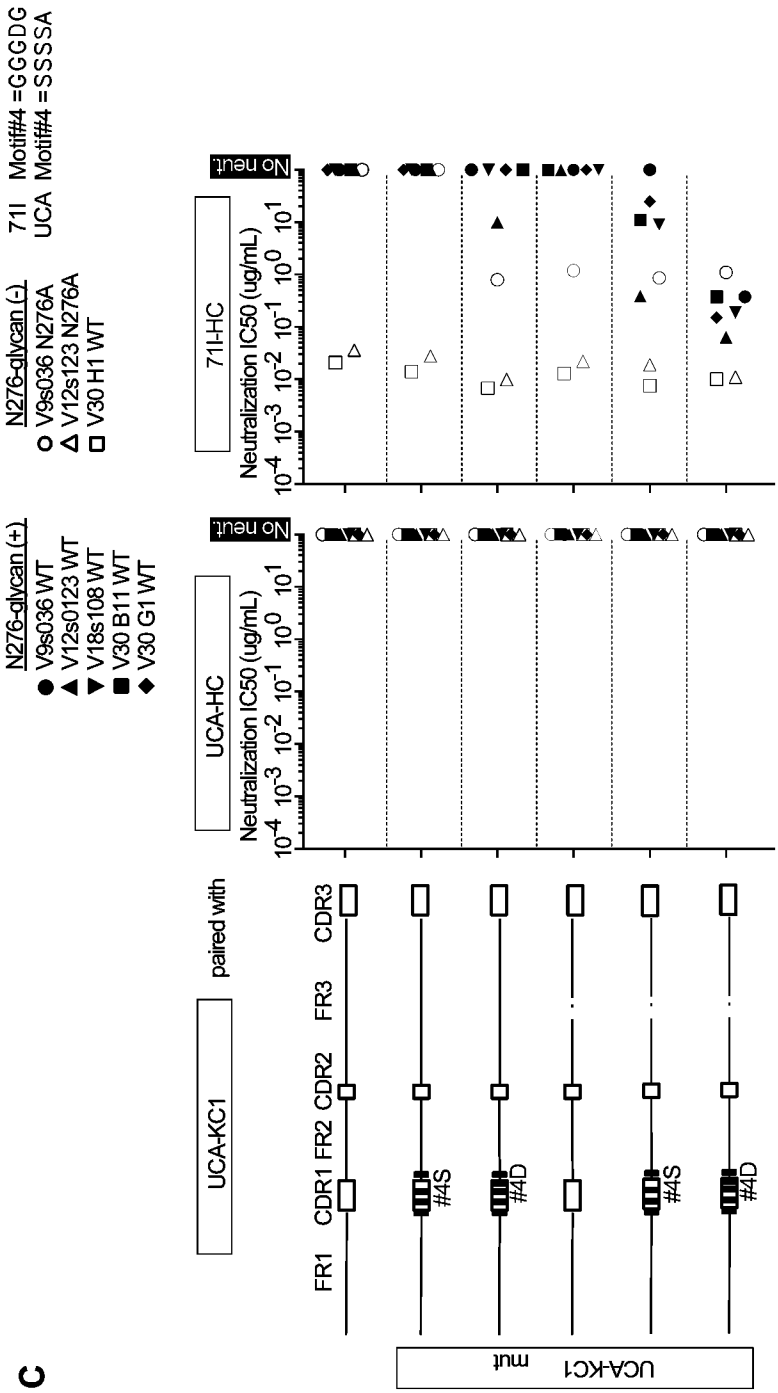


Figure 11 (cont.)

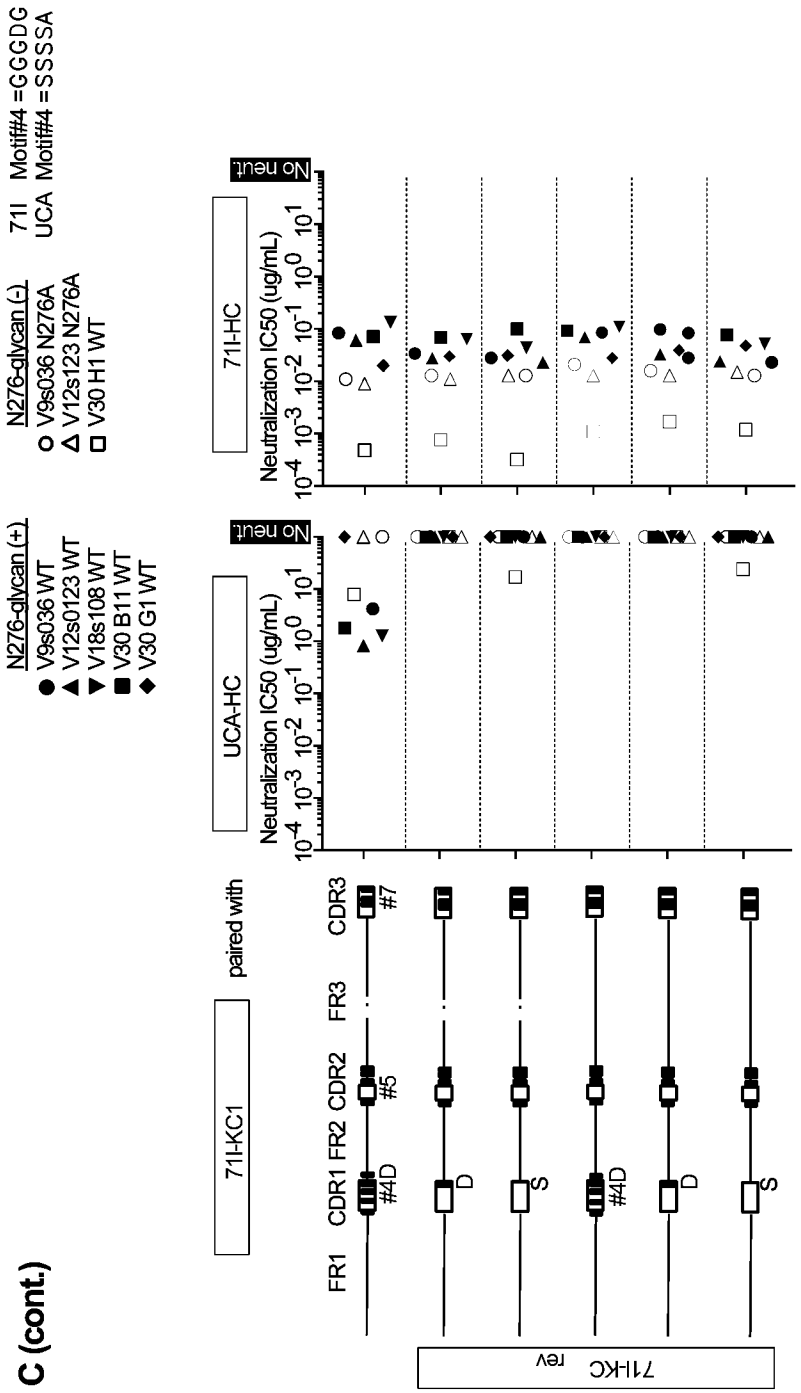
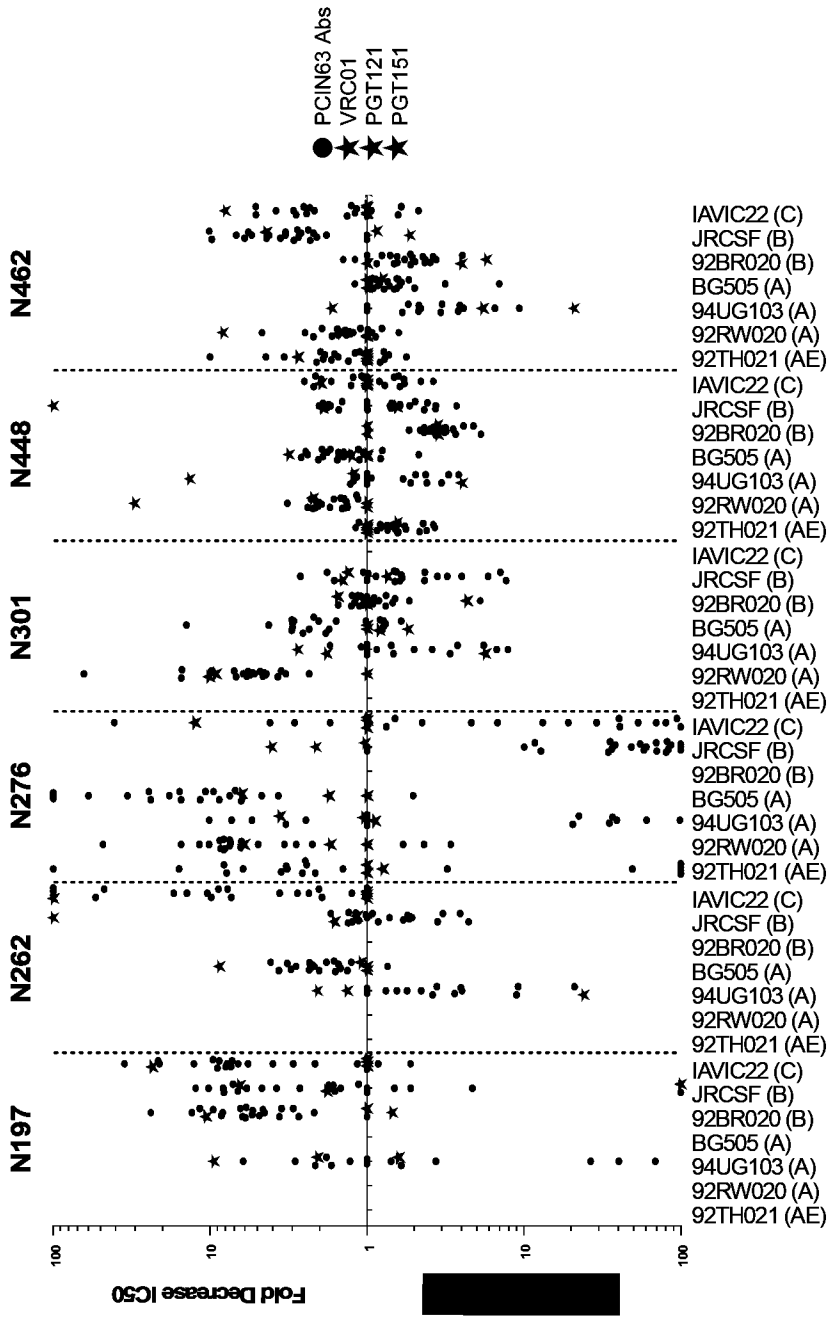


Figure 11 (cont.)

Figure 12


PCIN63 Abs
VRC01
PGT121
PGT151
N462
N448
N301
N276
N262
N197
IAVIC22 (C)
JRCSF (B)
92BR020 (B)
BG505 (A)
94UG103 (A)
92RW020 (A)
92TH021 (AE)
100
10
1
10
100
Fold Decrease IC50

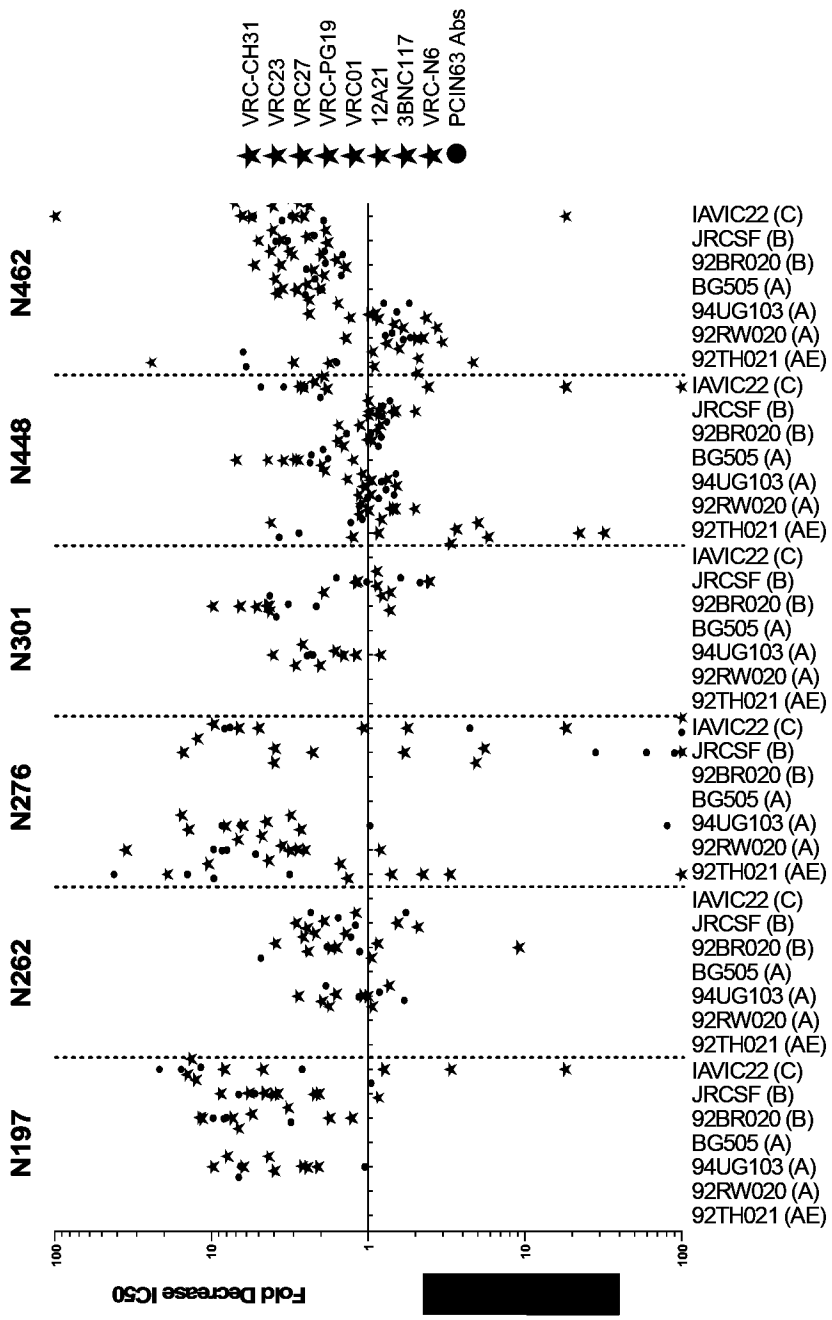
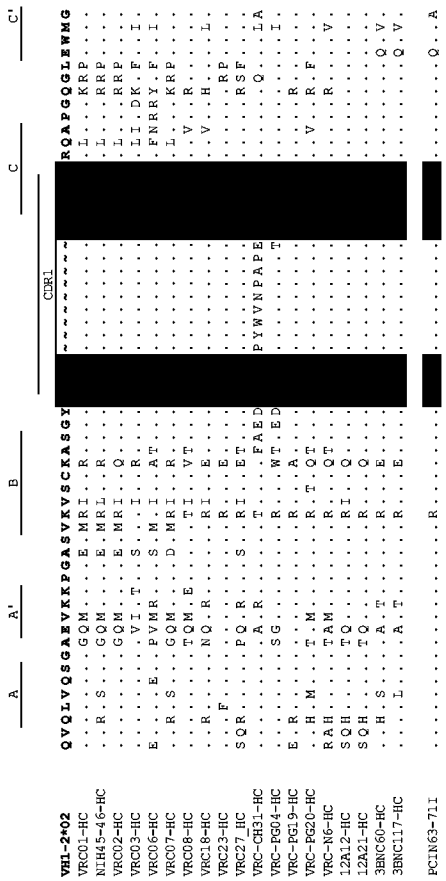


Figure 12 (cont.)

Figure 13


A
A'
B
CDR1
C
C'
VH1-2*02 QVQLVQSGAEVKKPGASVKVSCKASGY ~~~~~~~~~~ RQAPGQGLEWMG
VRC01-HC .....GQM....E.MRI..R..... .....I...KRP....
NIH45-46-HC ..R.S...GQM....E.MRL..R..... .....L....RRP....
VRC02-HC .....GQM....E.MRI..Q..... .....L....RRP....
VRC03-HC .....VI.T..S...I..R..... .....LI.DK.F.I.
VRC06-HC .....E..PVMR....S.M.I..AT..... .....FNRRY.F.I.
VRC07-HC ..R.S...GQM....D.MRI..R..... .....L....KRP....
VRC08-HC .....TQM.E.....TI..VT..... .....V..R.....L.
VRC18-HC ..R.....NQ.R.....RI..E..... .....V..H.....L.
VRC23-HC ...F.....R....E..... .....RP....
VRC27_HC SQR.....PQ.R....S..RI..ET..... .....RSF....
VRC-CH31-HC .....A.R.....T....FAED PYWVNPAPE .....Q....LA
VRC-PG04-HC .....SG.....R...WT.ED T .....I.
VRC-PG19-HC E.R.....A..... .....R.....
VRC-PG20-HC ..H.M...T.M.....R.T.QT..... .....V..R.F....
VRC-N6-HC RAH.....TAM.....R...QT..... .....R....V.
12A12-HC SQH.....TQ.....RI..Q..... .....
12A21-HC SQH.....TQ.....R...Q..... .....
3BNC60-HC ..H.S....A.T.....R...E..... .....Q.V.
3BNC117-HC ....L....A.T.....R...E..... .....Q.V.
PC1N63-711 .....R..... ....Q...A

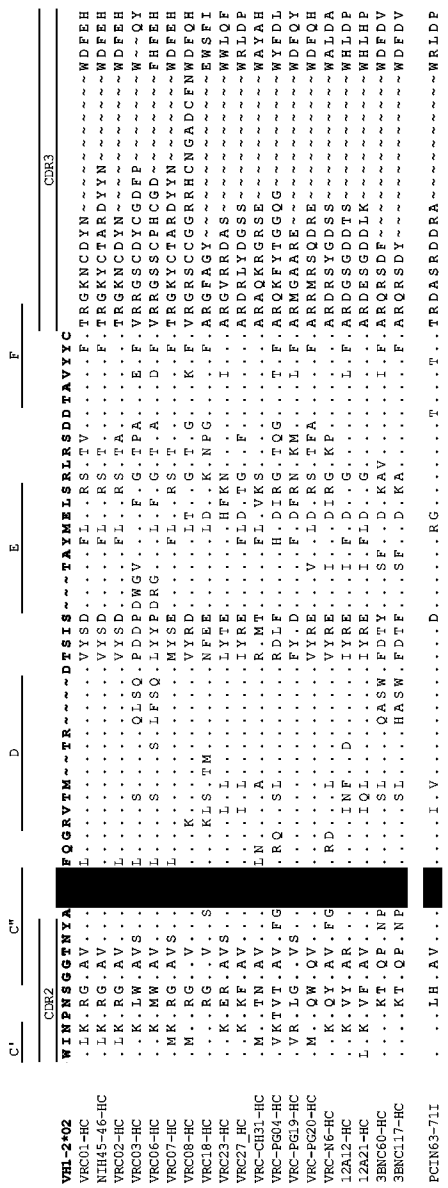


Figure 13 (cont.)

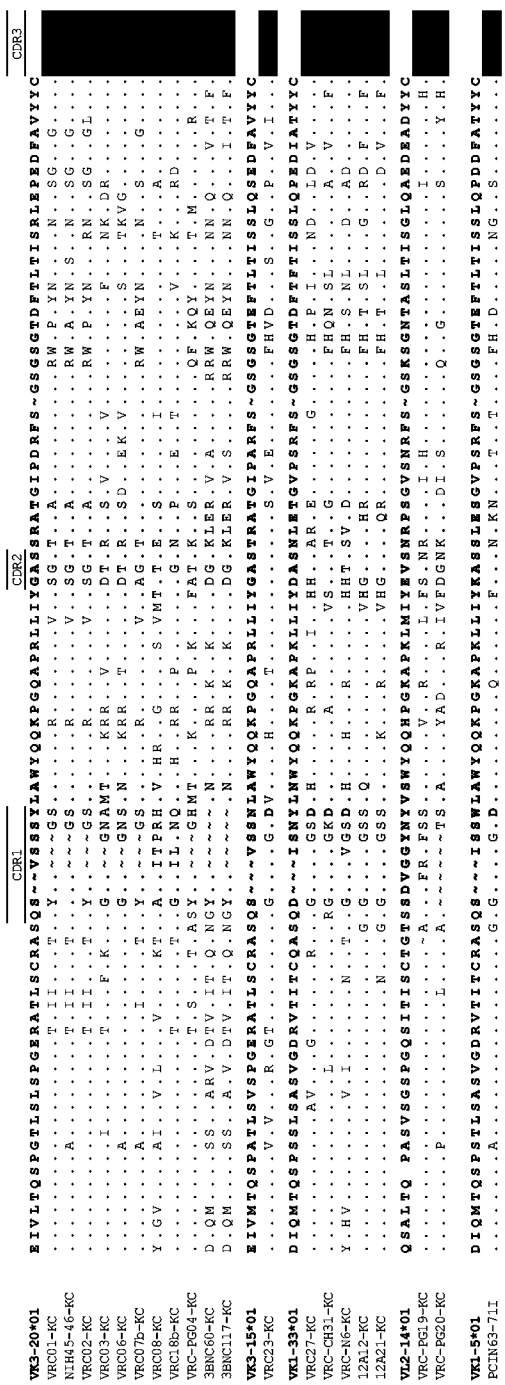


Figure 13 (cont.)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US19/57180

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 39/395; C07K 16/10, 14/16 (2020.01)

CPC - A61K 39/395; C07K 16/1063, 16/1045, 14/162

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2018/0298083 A1 (THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES) 18 October 2018; paragraphs [0099], [0185]	1-2, 4-5, 7-8, 10-11, 13-14, 16-17, 19-20, 22-23, 25-26, 28-29, 53-54, 56-57, 62-63, 65-66, 68/62-63, 68/65-66, 69/62-63, 69/65-66, 82-83, 85-86, 87/82-83, 87/85-86, 88/82-83, 88/85-86,145
A	US 2018/0194809 A1 (INTERNATIONAL AIDS VACCINE INITIATIVE et al.) 12 July 2018; paragraph [0113]	1-2, 4-5, 7-8, 10-11, 13-14, 16-17, 19-20, 22-23, 25-26, 28-29, 53-54, 56-57, 62-63, 65-66, 68/62-63, 68/65-66, 69/62-63, 69/65-66, 82-83, 85-86, 87/82-83, 87/85-86, 88/82-83, 88/85-86,145
A	(NUSBAUM, C et al.) Conserved Hypothetical Protein [Phytophthora Infestans T30-4]. National Center for Biotechnology Information. Genbank Entry. 22 July 2010 [retrieved from the internet on 04 February 2020]; Retrieved from the Internet: <URL: https://www.ncbi.nlm.nih.gov/protein/XP_002896469>; pages 1-2	1-2, 4-5, 7-8, 10-11, 13-14, 16-17, 19-20, 22-23, 25-26, 28-29, 53-54, 56-57

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 February 2020 (10.02.2020)	27 FEB 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US19/57180

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	(HAVENAR-DAUGHTON, C et al.) The Human Naive B Cell Repertoire Contains Distinct Subclasses for a Germline-Targeting HIV-1 Vaccine Immunogen. Scientific Translational Medicine. 04 July 2018; Vol. 10, No. 448; pages 1-20; Genbank supplemental pages 1-3; DOI: 10.1126/scitranslmed.aat0381	62-63, 65-66, 68/62-63, 68/65-66, 69/62-63, 69/65-66, 82-83, 85-86, 87/82-83, 87/85-86, 88/82-83, 88/85-86
A	(LANDAIS, E et al.) Development of Broadly Neutralizing Antibodies in HIV-1 Infected Elite Neutralizers. Retrovirology. 05 September 2018; Vol. 15, No. 1; pages 1-14; page 4, column 2, paragraph 3; DOI: 10.1186/s12977-018-0443-0	145

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US19/57180

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 33-52, 70-81, 89-144
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

-***- Please See within the Next Supplemental Page-***-

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Group 1+ Claims 1-2, 4-5, 7-8, 10-11, 13-14, 16-17, 19-20, 22-23, 25-26, 28-29, 53-54, 56-57, 62-63, 65-66, 68-69, 82-83, 85-88, 145

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US19/57180

-***-Continued from Box III Observations where unity of invention is lacking -***-

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups I+, Claims 1-32, 53-69, 82-88, 145, antibody PCIN63-66B, encompassing SEQ ID NO: 235 (VH), SEQ ID NO: 1 (VHCDR1), SEQ ID NO: 19 (VHCDR2), SEQ ID NO: 37 (VHCDR3), SEQ ID NO: 253 (VL), SEQ ID NO: 55 (VLCDR1), SEQ ID NO: 73 (VLCDR2), and SEQ ID NO: 91 (VLCDR3) are directed toward an isolated monoclonal antibody and method of producing the antibody.

The antibody and method of producing the antibody will be searched to the extent they encompass antibody PCIN63-66B, encompassing SEQ ID NO: 235 (VH), SEQ ID NO: 1 (VHCDR1), SEQ ID NO: 19 (VHCDR2), SEQ ID NO: 37 (VHCDR3), SEQ ID NO: 253 (VL), SEQ ID NO: 55 (VLCDR1), SEQ ID NO: 73 (VLCDR2), and SEQ ID NO: 91 (VLCDR3). Applicant is invited to elect additional antibody(ies), with specified set(s) of VH and VL and CDR(s) thereof, with specified SEQ ID NO: for each, or with specified substitution(s) at specified site(s) of a SEQ ID NO:, such that the sequence of each elected species is fully specified (i.e. no optional or variable residues or substituents), and where available as an option within at least one searchable claim, to be searched. Additional antibody sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part), 2 (in-part), 4 (in-part), 5 (in-part), 7 (in-part), 8 (in-part), 10 (in-part), 11 (in-part), 13 (in-part), 14 (in-part), 16 (in-part), 17 (in-part), 19 (in-part), 20 (in-part), 22 (in-part), 23 (in-part), 25 (in-part), 26 (in-part), 28 (in-part), 29 (in-part), 53 (in-part), 54 (in-part), 56 (in-part), 57 (in-part), 62 (in-part), 63 (in-part), 65 (in-part), 66 (in-part), 68 (in-part), 69 (in-part), 82 (in-part), 83 (in-part), 85-88 (each in-part), and 145 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass antibody PCIN63-66B, encompassing SEQ ID NO: 235 (VH), SEQ ID NO: 1 (VHCDR1), SEQ ID NO: 19 (VHCDR2), SEQ ID NO: 37 (VHCDR3), SEQ ID NO: 253 (VL), SEQ ID NO: 55 (VLCDR1), SEQ ID NO: 73 (VLCDR2), and SEQ ID NO: 91 (VLCDR3). Applicants must specify the searchable claims that encompass any additionally elected sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be antibody PCIN63-71B, encompassing SEQ ID NO: 236 (VH), SEQ ID NO: 2 (VHCDR1), SEQ ID NO: 20 (VHCDR2), SEQ ID NO: 38 (VHCDR3), SEQ ID NO: 254 (VL), SEQ ID NO: 56 (VLCDR1), SEQ ID NO: 74 (VLCDR2), and SEQ ID NO: 92 (VLCDR3).

No technical features are shared between the antibody sequences of Groups I+ and, accordingly, these groups lack unity a priori.

Groups I+ share the technical features including: an isolated monoclonal antibody that specifically binds to HIV Env and comprises a heavy chain variable region (VH) and light chain variable region (VL), wherein the VH and VL comprise a VH CDR1, VH CDR2, and VH CDR3, and a VL CDR1, VL CDR2, and VL CDR3, respectively; and a method of producing an engineered variant of a PCIN63 antibody comprising (a) substituting one or more amino acid residues of the VH; and/or substituting one or more amino acid residues of the VL to create an engineered variant antibody, and (b) and producing the engineered variant antibody.

However, these shared technical features are previously disclosed by US 2018/0298083 A1 to The United States of America, as represented by the Secretary, Department of Health and Human Services (hereinafter 'HHS'), in view of the article 'Development of broadly neutralizing antibodies in HIV-1 infected elite neutralizers' by Landias et al. (hereinafter 'Landias').

HHS discloses an isolated monoclonal antibody that specifically binds to HIV Env (an isolated monoclonal antibody that specifically binds to the CD4 binding site on gp120 of HIV (Env); abstract, paragraphs [0005], [0006]) and comprises a heavy chain variable region (VH) and light chain variable region (VL) (and comprises a heavy chain variable region (VH) and light chain variable region (VL); paragraph [0006]), wherein the VH and VL comprise a VH CDR1, VH CDR2, and VH CDR3, and a VL CDR1, VL CDR2, and VL CDR3, respectively (wherein the VH and VL comprise a VH CDR1, VH CDR2, and VH CDR3, and a VL CDR1, VL CDR2, and VL CDR3, respectively; paragraph [0006]); and a method of producing an engineered variant of an antibody (a method of producing an engineered variant of an antibody; paragraphs [0244], [0249]) comprising (a) substituting one or more amino acid residues of the VH; and/or substituting one or more amino acid residues of the VL to create an engineered variant antibody (comprising (a) substituting one or more amino acid residues of the VH; and/or substituting one or more amino acid residues of the VL to create an engineered variant antibody; paragraphs [0244], [0249]), and (b) and producing the engineered variant antibody (and producing the engineered variant antibody; paragraphs [0244], [0249], [0302]).

HHS does not disclose a PCIN63 antibody.

Landias discloses an antibody to HIV-1 Env, comprising a PCIN63 antibody (an antibody to HIV-1 Env, comprising a PCIN63 antibody; abstract, page 1, second column, first paragraph; Table 1, page 4, second column, third paragraph).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the disclosure of HHS to have used the light and/or heavy chains of any antibodies known or suspected to bind HIV Env, such as PCIN63, as disclosed by Landias, to produce an engineered antibody with substitutions in the light and/or heavy chains, in order to provide antibodies with improved binding characteristics, or effector functions, for use in therapy or prevention of HIV.

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by a combination of the HHS and Landias references, unity of invention is lacking.