

TRISPECIFIC AND/OR TRIVALENT BINDING PROTEINS FOR PREVENTION OR TREATMENT OF HIV INFECTION

CROSS REFERENCES TO RELATED APPLICATIONS

[0001] This application claims the priority benefit of U.S. Provisional Application Serial No. 62/246,113, filed October 25, 2015, EP Application No. EP16305211.1, filed February 24, 2016, U.S. Provisional Application Serial No. 62/322,029, filed April 13, 2016, and U.S. Provisional Application Serial No. 62/331,169, filed May 03, 2016, which are incorporated herein by reference in their entirety.

[0002] This invention was created in the performance of a Cooperative Research and Development Agreement (NIAID #2014-0038) with the National Institutes of Health, an agency of the Department of Health and Human Services. The Government of the United States has certain rights in this invention.

SUBMISSION OF SEQUENCE LISTING ON ASCII TEXT FILE

[0003] The content of the following submission on ASCII text file is incorporated herein by reference in its entirety: a computer readable form (CRF) of the Sequence Listing (file name: 183952027041SEQLIST.txt, date recorded: October 19, 2016, size: 1,064 KB).

FIELD OF THE INVENTION

[0004] The disclosure relates to trispecific and/or trivalent binding proteins comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins, wherein a first pair of polypeptides forming the binding protein possess dual variable domains having a cross-over orientation and wherein a second pair of polypeptides forming the binding protein possess a single variable domain. The disclosure also relates to methods for making trispecific and/or trivalent binding proteins and uses of such binding proteins for treating and/or preventing HIV/AIDS.

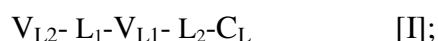
BACKGROUND

[0005] One of the challenges in treating HIV/AIDS with neutralizing antibodies is potential breakthrough infection due to the high mutation rate of HIV-1 viruses. Additionally, virological events in the early weeks following HIV-1 transmission set the

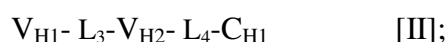
stage for lifelong chronic infection that remains incurable with currently available combination antiretroviral therapy (cART). This is due, at least in part, to the early establishment of viral reservoirs, including latently infected cells, which persist despite cART, leading to recrudescence infection when treatment is interrupted. Newly discovered anti-HIV-1 neutralizing antibodies with improved breadth and potency may provide more options for HIV/AIDS treatment and prevention; however, breakthrough infection remains a major issue in the field.

BRIEF SUMMARY

[0006] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



a second polypeptide chain comprises a structure represented by the formula:



a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

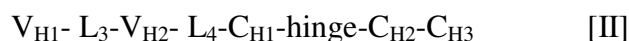
[0007] In some embodiments, the second polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the third polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at

positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

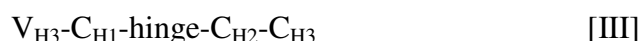
[0008] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0009] In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1

according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0010] In some embodiments, the one or more HIV target protein is selected from the group consisting of glycoprotein 120, glycoprotein 41 and glycoprotein 160. In some embodiments, the binding protein is trispecific and capable of specifically binding three different epitopes on a single HIV target protein. In some embodiments, the binding protein is trispecific and capable of specifically binding two different epitopes on a first HIV target protein, and one epitope on a second HIV target protein, wherein the first and second HIV target proteins are different. In some embodiments, the binding protein is trispecific and capable of specifically binding three different antigen targets. In some embodiments, the binding protein is capable of inhibiting the function of one or more HIV target proteins. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{L1} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ

ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively. In some embodiments, V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{L2} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively. In some embodiments, V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{L3} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively. In some embodiments, V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{H1} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ

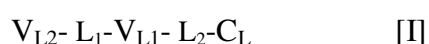
ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively. In some embodiments, V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{H2} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively. In some embodiments, V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{H3} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 266, a CDR-L2 comprising the sequence of SEQ ID NO: 267, and a CDR-L3 comprising the sequence of SEQ ID NO: 268; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 248, a CDR-H2 comprising

the sequence of SEQ ID NO: 497, and a CDR-H3 comprising the sequence of SEQ ID NO: 250. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 512; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 502. In some embodiments, V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 512; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 502. In some embodiments, V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable

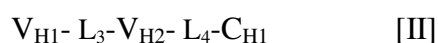
domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503. In some embodiments, V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503. In some embodiments, V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable

domain sequence of SEQ ID NO: 518; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503. In some embodiments, V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503. In some embodiments, at least one of L_1 , L_2 , L_3 , or L_4 is independently 0 amino acids in length. In some embodiments, L_1 , L_2 , L_3 , or L_4 are each independently at least one amino acid in length. In some embodiments, L_1 comprises Asp-Lys-Thr-His-Thr (SEQ ID NO: 525).

[0011] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L₁, L₂, L₃, and L₄ are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1}, V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124, 130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; or

(b) V_{L1}, V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and

wherein:

(a) V_{H1}, V_{H2}, and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 19, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123, 129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242; or

(b) V_{H1}, V_{H2}, and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265.

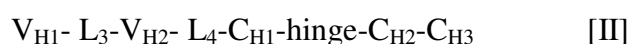
[0012] In some embodiments, the second polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the third polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region

comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

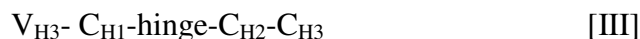
[0013] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124, 130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and

wherein:

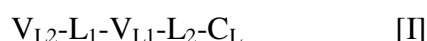
(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 19, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123, 129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265.

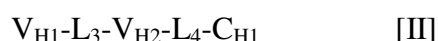
[0014] In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0015] In some embodiments, at least one of L_1 , L_2 , L_3 , or L_4 is independently 0 amino acids in length. In some embodiments, L_1 , L_2 , L_3 , or L_4 are each independently at least one amino acid in length. In some embodiments, L_1 comprises Asp-Lys-Thr-His-Thr (SEQ ID NO: 525).

[0016] In one embodiment, the disclosure provides a trispecific and/or trivalent binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind three different HIV target proteins, wherein a first polypeptide chain has a structure represented by the formula:



and a second polypeptide chain has a structure represented by the formula:



and a third polypeptide chain has a structure represented by the formula:



and a fourth polypeptide chain has a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

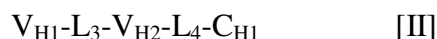
L_1 , L_2 , L_3 and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0017] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain has a structure represented by the formula:



and a second polypeptide chain has a structure represented by the formula:



and a third polypeptide chain has a structure represented by the formula:



and a fourth polypeptide chain has a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124, 130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and

wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 19, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123, 129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265.

[0018] In another embodiment, the disclosure provides a binding protein comprising a first polypeptide chain, a second polypeptide chain, a third polypeptide chain and a fourth polypeptide chain wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 4; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 3 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 3; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 1 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 2;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 12; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 11 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 11; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 9; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 10 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 10;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 20; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 19 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 19; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 17 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 17; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 18 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 18;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 28 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 28; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 27 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 27; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 25 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 25; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 26 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 26;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 36 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 36; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 35 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 35; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 33 or an amino acid sequence that is at least 95% identical to the amino acid sequence of

SEQ ID NO: 33; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 34 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 34;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 44 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 44; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 43 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 43; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 41 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 41; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 42 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 42;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 52 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 52; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 51 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 49 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 49; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 50 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 60 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 60; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 59 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 59; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 57 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 57; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 58 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 58;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 68 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 68; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:

67 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 67; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 65 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 65; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 66 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 66;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 76 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 76; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 75 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 75; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 73 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 73; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 74 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 74;

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 84 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 84; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 83 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 83; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 81 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 81; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 82 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 82;

(l) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 92 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 92; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 91 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 91; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 89 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 89; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 90 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 90;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 100 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 100; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 99 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 99; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 97 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 97; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 98 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 98;

(n) the first polypeptide comprises the amino acid sequence of SEQ ID NO: 108 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 108; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 107; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 105 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 105; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 106;

(o) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 116 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 116; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 115; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 113 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 113; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 114;

(p) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 124 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 124; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 123 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 123; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 121 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 121; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 122 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 122;

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 132 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 132; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 131 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 131; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 129 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 129; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 130 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 130;

(r) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 140 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 140; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 139 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 139; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 137; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 138;

(s) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 148 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 148; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 147 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 147; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 145 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 145; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 146 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 146;

(t) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 156 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 156; the second polypeptide chain comprises the amino acid sequence of SEQ ID

NO: 155 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 155; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 153 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 153; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 154 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 154;

(u) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 164 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 164; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 163 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 163; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 161 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 161; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 162 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 162;

(v) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 172 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 172; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 171 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 171; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 169 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 169; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 170 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 170;

(w) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 180 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 180; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 179 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 179; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 177 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 177; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 178 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 178;

(x) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 188 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 188; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 187 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 187; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 185 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 185; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 186 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 186;

(y) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 196 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 196; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 195 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 195; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 193 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 193; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 194 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 194;

(z) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 204 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 204; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 203 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 203; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 201 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 201; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 202 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 202;

(aa) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 212 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 212; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 211 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 211; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 209 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 209; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 210 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 210;

(bb) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 220 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 220; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 219 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 219; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 217 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 217; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 218 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 218;

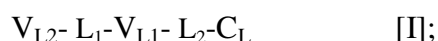
(cc) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 228 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 228; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 227 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 227; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 225 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 225; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 226 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 226;

(dd) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 235 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 235; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 234 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 234; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 232 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 232; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 233 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 233; or

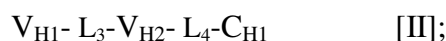
(ee) first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 243 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 243; the second polypeptide chain comprises the amino acid sequence of SEQ ID

NO: 242 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 242; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 240 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 240; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 241 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 241.

[0019] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins and one or more T cell target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



a second polypeptide chain comprises a structure represented by the formula:



a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0020] In some embodiments, the second polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the third polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an

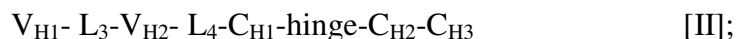
immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0021] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more

HIV target proteins and one or more T cell target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



a second polypeptide chain comprises a structure represented by the formula:



a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0022] In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are

Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0023] In some embodiments, the one or more HIV target proteins are selected from the group consisting of glycoprotein 120, glycoprotein 41 and glycoprotein 160. In some embodiments, the one or more T cell target proteins are CD3 or CD28. In some embodiments, the binding protein is trispecific and capable of specifically binding an HIV target protein and two different epitopes on a single T cell target protein. In some embodiments, the binding protein is trispecific and capable of specifically binding an HIV target protein and two different T cell target proteins. In some embodiments, the binding protein is trispecific and capable of specifically binding a T cell target protein and two different epitopes on a single HIV target protein. In some embodiments, the binding protein is trispecific and capable of specifically binding a T cell target protein and two different HIV target proteins. In some embodiments, the first and second polypeptide chains form two antigen binding sites that specifically target two T cell target proteins, and the third and fourth polypeptide chains form an antigen binding site that specifically binds an HIV target protein. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524. In some embodiments, V_{L1} comprises a light chain variable domain comprising a sequence selected from the group

consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524. In some embodiments, V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively. In some embodiments, V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524. In some embodiments, V_{L2} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524. In some embodiments, V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively. In some embodiments, V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524. In some embodiments, V_{L3} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524. In some embodiments, V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID

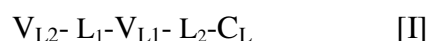
NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively. In some embodiments, V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511. In some embodiments, V_{H1} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511. In some embodiments, V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively. In some embodiments, V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511. In some embodiments, V_{H2} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511. In some embodiments, V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively. In

some embodiments, V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511. In some embodiments, V_{H3} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511. In some embodiments, V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 488, a CDR-L2 comprising the sequence of SEQ ID NO: 489, and a CDR-L3 comprising the sequence of SEQ ID NO: 490; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 494, a CDR-L2 comprising the sequence of SEQ ID NO: 495, and a CDR-L3 comprising the sequence of SEQ ID NO: 496; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 479, a CDR-H2 comprising the sequence of SEQ ID NO: 480, and a CDR-H3 comprising the sequence of SEQ ID NO: 481; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 485, a CDR-H2 comprising the sequence of SEQ ID NO: 486, and a CDR-H3 comprising the sequence of SEQ ID NO: 487; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 522; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 524; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 509; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 511; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503. In some embodiments, V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 522; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 524; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable

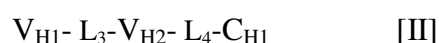
domain comprising the sequence of SEQ ID NO: 509; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 511; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503. In some embodiments, V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 494, a CDR-L2 comprising the sequence of SEQ ID NO: 495, and a CDR-L3 comprising the sequence of SEQ ID NO: 496; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 488, a CDR-L2 comprising the sequence of SEQ ID NO: 489, and a CDR-L3 comprising the sequence of SEQ ID NO: 490; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 485, a CDR-H2 comprising the sequence of SEQ ID NO: 486, and a CDR-H3 comprising the sequence of SEQ ID NO: 487; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 479, a CDR-H2 comprising the sequence of SEQ ID NO: 480, and a CDR-H3 comprising the sequence of SEQ ID NO: 481; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 524; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 522; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 511; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 509; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503. In some embodiments, V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 524; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 522; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 511; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 509; and V_{H3} comprises a heavy

chain variable domain comprising the sequence of SEQ ID NO: 503. In some embodiments, at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length. In some embodiments, L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length. In some embodiments, L₁ is Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299).

[0024] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L₁, L₂, L₃, and L₄ are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1}, V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383, 385, 391, 393, 399, 401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

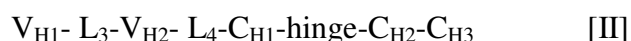
[0025] In some embodiments, the second polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the third polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1} , the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein

the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

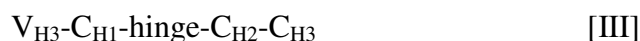
[0026] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L₁, L₂, L₃, and L₄ are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1}, V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383, 385, 391, 393, 399, 401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; or

(b) V_{L1}, V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and
wherein:

(a) V_{H1}, V_{H2}, and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472; or

(b) V_{H1}, V_{H2}, and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

[0027] In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide

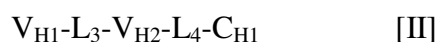
chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W. In some embodiments, the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0028] In some embodiments, at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length. In some embodiments, L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length. In some embodiments, L₁ is Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299).

[0029] In one embodiment, the disclosure provides a binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain has a structure represented by the formula:



and a second polypeptide chain has a structure represented by the formula:



and a third polypeptide chain has a structure represented by the formula:



and a fourth polypeptide chain has a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L₁, L₂, L₃, and L₄ are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383, 385, 391, 393, 399, 401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and

wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

[0030] In another embodiment, the disclosure provides a binding protein comprising a first polypeptide chain, a second polypeptide chain, a third polypeptide chain and a fourth polypeptide chain wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 305 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 305; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 304 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 304; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 302 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 302; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 303 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 303;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 313 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 313; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 312 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 312; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 310 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 310; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 311 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 311;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 321 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 321; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 320 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 320; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 318 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 318; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 319 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 319;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 329 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 329; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 328 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 328; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 326 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 326; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 327 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 327;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 337 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 337; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 336 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 336; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 334 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 334; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 335 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 335;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 345 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 345; the second polypeptide chain comprises the amino acid sequence of SEQ ID

NO: 344 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 344; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 342 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 342; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 343 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 343;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 353 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 353; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 352 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 352; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 350 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 350; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 351 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 351;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 361 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 361; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 360 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 360; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 358 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 358; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 359 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 359;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 369 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 369; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 368 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 368; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 366 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 366; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 367 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 367;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 377 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 377; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 376 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 376; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 374 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 374; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 375 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 375;

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 385 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 385; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 384 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 384; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 382 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 382; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 383 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 383;

(l) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 393 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 393; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 392 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 392; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 390 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 390; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 391 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 391;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 401 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 401; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 400 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 400; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 398 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 398; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 399 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 399;

(n) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 409 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 409; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 408 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 408; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 406 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 406; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 407 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 407;

(p) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 417 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 417; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 416 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 416; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 414 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 414; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 415 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 415;

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 425 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 425; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 424 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 424; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 422 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 422; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 423 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 423;

(r) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 433 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 433; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:

432 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 432; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 430 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 430; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 431 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 431;

(s) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 441 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 441; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 440 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 440; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 438 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 438; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 439 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 439;

(t) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 449 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 449; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 448 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 448; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 446 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 446; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 447 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 447;

(u) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 457 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 457; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 456 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 456; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 454 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 454; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 455 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 455;

(v) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 465 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 465; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 464 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 464; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 462 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 462; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 463 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 463; or

(w) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 473 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 473; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 472 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 472; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 470 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 470; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 471 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 471.

[0031] In one embodiment, the disclosure provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding the binding protein according to any of the above embodiments. In one embodiment, the disclosure provides an expression vector comprising the nucleic acid molecule according to any of the above embodiments. In one embodiment, the disclosure provides an isolated host cell comprising the nucleic acid molecule according to any of the above embodiments. In one embodiment, the disclosure provides an isolated host cell comprising the expression vector according to any of the above embodiments. In some embodiments, the isolated host cell is a mammalian cell or an insect cell. In one embodiment, the disclosure provides a vector system comprising one or more vectors encoding a first, second, third, and fourth polypeptide chain of a binding protein according to any of the above embodiments. In some embodiments, the vector system comprises a first vector encoding the first polypeptide chain of the binding protein, a second vector encoding the second polypeptide chain of the binding protein, a third vector encoding the third polypeptide chain of the binding protein, and a fourth vector encoding the fourth polypeptide chain of the binding protein. In some embodiments, the vector

system comprises a first vector encoding the first and second polypeptide chains of the binding protein, and a second vector encoding the third and fourth polypeptide chains of the binding protein. In some embodiments, the one or more vectors are expression vectors. In one embodiment, the disclosure provides an isolated host cell comprising the vector system according to any of the above embodiments. In some embodiments, the isolated host cell is a mammalian cell or an insect cell. In one embodiment, the disclosure provides a method of producing a binding protein, the method comprising: a) culturing a host cell according to any of the above embodiments under conditions such that the host cell expresses the binding protein; and b) isolating the binding protein from the host cell.

[0032] In one embodiment, the disclosure provides a method of preventing and/or treating HIV infection in a patient comprising administering to the patient a therapeutically effective amount of at least one binding protein according to any of the above embodiments. In some embodiments, the binding protein is co-administered with standard anti-retroviral therapy. In some embodiments, administration of the at least one binding protein results in the neutralization of one or more HIV virions. In some embodiments, administration of the at least one binding protein results in the elimination of one or more latently and/or chronically HIV-infected cells in the patient. In some embodiments, the patient is a human.

[0033] In one embodiment, the disclosure provides a binding protein according to any of the above embodiments for the prevention or treatment of an HIV infection in a patient. In some embodiments, the binding protein is co-administered with standard anti-retroviral therapy. In some embodiments, the binding protein causes the neutralization of one or more HIV virions in the patient. In some embodiments, the binding protein causes the elimination of one or more latently and/or chronically HIV-infected cells in the patient. In some embodiments, the patient is a human.

[0034] Specific embodiments of the invention will become evident from the following more detailed description of certain embodiments and the claims.

[0035] It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present invention. These and other aspects of the invention will become apparent to one of skill in the art.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] **FIGS. 1A-D** show schematic representations of trispecific binding proteins comprising four polypeptide chains that form three antigen binding sites that specifically bind three different epitopes on one or more antigens, wherein a first pair of polypeptides possess dual variable domains having a cross-over orientation forming two antigen binding sites (comprising V_{H1} - V_{L1} and V_{H2} - V_{L2}) and wherein a second pair of polypeptides possess a single antigen binding site (comprising V_{H3} - V_{L3}), in accordance with some embodiments. **FIG. 1A** shows a trispecific binding protein comprising a “knobs-into-holes” modification, wherein the knob is on the first pair of polypeptides. **FIG. 1B** shows a trispecific binding protein comprising a “knobs-into-holes” modification, wherein the knob is on the second pair of polypeptides. **FIG. 1C** shows the orientation of variable domains on the polypeptide chains, and the knob/hole orientation for binding proteins 1-31 shown in Tables 1 and 2. “Heavy chain A” (*e.g.*, a third polypeptide chain of the present disclosure) indicates the variable domain of heavy chain A. “Light chain A” (*e.g.*, a fourth polypeptide chain of the present disclosure) indicates the variable domain of light chain A. “Heavy chain B” (*e.g.*, a second polypeptide chain of the present disclosure) indicates variable domain 1 and variable domain 2 of heavy chain B. “Light chain B” (*e.g.*, a first polypeptide chain of the present disclosure) indicates variable domain 1 and variable domain 2 of light chain B. **FIG. 1D** shows the orientation of variable domains on the polypeptide chains, and the knob/hole orientation for binding proteins 32-53 shown in Tables 1 and 2. “Heavy chain A” (*e.g.*, a third polypeptide chain of the present disclosure) indicates the variable domain of heavy chain A. “Light chain A” (*e.g.*, a fourth polypeptide chain of the present disclosure) indicates the variable domain of light chain A. “Heavy chain B” (*e.g.*, a second polypeptide chain of the present disclosure) indicates variable domain 1 and variable domain 2 of heavy chain B. “Light chain B” (*e.g.*, a first polypeptide chain of the present disclosure) indicates variable domain 1 and variable domain 2 of light chain B.

[0037] **FIGS. 2A-B** show purification of three trispecific binding proteins first using affinity chromatography, and then using preparative size exclusion chromatography. **FIG. 2A** shows the elution profile of the trispecific binding proteins during purification using protein A affinity chromatography. **FIG. 2B** shows purification of monomeric proteins by Superdex200 size exclusion chromatography.

[0038] **FIGS. 3A-B** show purification of the MPER Ab, CD4BS Ab “b”, and V1/V2 directed Ab “a” parental antibodies first using affinity chromatography, and then using

preparative size exclusion chromatography. **FIG. 3A** shows the elution profile of the parental antibodies during purification using protein A affinity chromatography. **FIG. 3B** shows purification of monomeric proteins by Superdex200 size exclusion chromatography.

[0039] **FIGS. 4A-B** show the size exclusion chromatography profiles of bispecific and trispecific binding proteins. **FIG. 4A** shows the size exclusion chromatography profiles of the bispecific binding proteins. **FIG. 4B** shows the size exclusion chromatography profiles of the trispecific binding proteins.

[0040] **FIG. 5** shows the Biacore sensograms of the binding kinetics of three trispecific binding proteins and the parental MPER Ab antibody for an HIV gp41-derived peptide (the MPER binding site), as assessed by the standard Biacore-based kinetic assay.

[0041] **FIG. 6** shows the Biacore sensograms of the binding kinetics of three trispecific binding proteins and the parental CD4BS Ab “b” antibody for recombinant HIV gp120, as assessed by the standard Biacore-based kinetic assay.

[0042] **FIG. 7** shows the results of a pharmacokinetic (PK) study of the indicated proteins after intravenous (IV) injection in rhesus macaques.

[0043] **FIGS. 8A-8B** show schematic representations of trispecific T-cell engagers, in accordance with some embodiments. The binding sites are indicated by the dotted circles.

[0044] **FIG. 9** shows binding properties of the trispecific binding proteins “Binding Protein 32” and “CD3 x CD28 / CD4BS Ab ‘b’” to CD3 (CD3E represents CD3epsilon protein; CD3D represents CD3delta protein), CD28, and Resurfaced Stabilized Core 3 (RSC3) protein of gp120, as well as a negative control (human IgG).

[0045] **FIG. 10** shows CD8 T-cell activation using the trispecific proteins “Binding Protein 32” and “CD3 x CD28 / CD4BS Ab ‘b’” compared to the parental CD4BS IgG4 antibody, as well as a negative control (No mAb).

[0046] **FIG. 11** shows CD4 T-cell activation using the trispecific proteins “Binding Protein 32” and “CD3 x CD28 / CD4BS Ab ‘b’” compared to the parental CD4BS IgG4 antibody, as well as a negative control (No mAb).

[0047] **FIG. 12** shows CD3 downregulation after T cell activation by the trispecific proteins “Binding Protein 32” and “CD3 x CD28 / CD4BS Ab ‘b’” compared to the parental CD4BS IgG4 antibody, as well as a negative control (No mAb).

[0048] **FIGS. 13A-C** show fluorescence-activated cell sorting (FACS)-based cytotoxicity assay results for trispecific binding proteins against latently infected HIV-1⁺ T cells. **FIG. 13A** shows the results for trispecific binding proteins incubated with CEM-BaL

cells. **FIG. 13B** shows the results for trispecific binding proteins incubated with ACH2 cells. **FIG. 13C** shows the results for trispecific binding proteins incubated with J1.1 cells.

DETAILED DESCRIPTION

[0049] The present disclosure provides trispecific and/or trivalent binding proteins comprising four polypeptide chains that form three antigen binding sites that specifically bind to one or more human immunodeficiency virus (HIV) target proteins and/or one or more T-cell receptor target proteins, wherein a first pair of polypeptides forming the binding protein possess dual variable domains having a cross-over orientation and wherein a second pair of polypeptides forming the binding protein possess a single variable domain.

[0050] The following description sets forth exemplary methods, parameters, and the like. It should be recognized, however, that such description is not intended as a limitation on the scope of the present disclosure but is instead provided as a description of exemplary embodiments.

Definitions

[0051] As utilized in accordance with the present disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings. Unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular.

[0052] The term "polynucleotide" as used herein refers to single-stranded or double-stranded nucleic acid polymers of at least 10 nucleotides in length. In certain embodiments, the nucleotides comprising the polynucleotide can be ribonucleotides or deoxyribonucleotides or a modified form of either type of nucleotide. Such modifications include base modifications such as bromuridine, ribose modifications such as arabinoside and 2',3'-dideoxyribose, and internucleotide linkage modifications such as phosphorothioate, phosphorodithioate, phosphoroselenoate, phosphorodiselenoate, phosphoroanilothioate, phosphoraniladate and phosphoroamidate. The term "polynucleotide" specifically includes single-stranded and double-stranded forms of DNA.

[0053] An "isolated polynucleotide" is a polynucleotide of genomic, cDNA, or synthetic origin or some combination thereof, which: (1) is not associated with all or a portion of a polynucleotide in which the isolated polynucleotide is found in nature, (2) is linked to a polynucleotide to which it is not linked in nature, or (3) does not occur in nature as part of a larger sequence.

[0054] An "isolated polypeptide" is one that: (1) is free of at least some other polypeptides with which it would normally be found, (2) is essentially free of other polypeptides from the same source, *e.g.*, from the same species, (3) is expressed by a cell from a different species, (4) has been separated from at least about 50 percent of polynucleotides, lipids, carbohydrates, or other materials with which it is associated in nature, (5) is not associated (by covalent or noncovalent interaction) with portions of a polypeptide with which the "isolated polypeptide" is associated in nature, (6) is operably associated (by covalent or noncovalent interaction) with a polypeptide with which it is not associated in nature, or (7) does not occur in nature. Such an isolated polypeptide can be encoded by genomic DNA, cDNA, mRNA or other RNA, of synthetic origin, or any combination thereof. Preferably, the isolated polypeptide is substantially free from polypeptides or other contaminants that are found in its natural environment that would interfere with its use (therapeutic, diagnostic, prophylactic, research or otherwise).

[0055] Naturally occurring antibodies typically comprise a tetramer. Each such tetramer is typically composed of two identical pairs of polypeptide chains, each pair having one full-length "light" chain (typically having a molecular weight of about 25 kDa) and one full-length "heavy" chain (typically having a molecular weight of about 50-70 kDa). The terms "heavy chain" and "light chain" as used herein refer to any immunoglobulin polypeptide having sufficient variable domain sequence to confer specificity for a target antigen. The amino-terminal portion of each light and heavy chain typically includes a variable domain of about 100 to 110 or more amino acids that typically is responsible for antigen recognition. The carboxy-terminal portion of each chain typically defines a constant domain responsible for effector function. Thus, in a naturally occurring antibody, a full-length heavy chain immunoglobulin polypeptide includes a variable domain (V_H) and three constant domains (C_{H1} , C_{H2} , and C_{H3}), wherein the V_H domain is at the amino-terminus of the polypeptide and the C_{H3} domain is at the carboxyl-terminus, and a full-length light chain immunoglobulin polypeptide includes a variable domain (V_L) and a constant domain (C_L), wherein the V_L domain is at the amino-terminus of the polypeptide and the C_L domain is at the carboxyl-terminus.

[0056] Human light chains are typically classified as kappa and lambda light chains, and human heavy chains are typically classified as mu, delta, gamma, alpha, or epsilon, and define the antibody's isotype as IgM, IgD, IgG, IgA, and IgE, respectively. IgG has several subclasses, including, but not limited to, IgG1, IgG2, IgG3, and IgG4. IgM has subclasses

including, but not limited to, IgM1 and IgM2. IgA is similarly subdivided into subclasses including, but not limited to, IgA1 and IgA2. Within full-length light and heavy chains, the variable and constant domains typically are joined by a "J" region of about 12 or more amino acids, with the heavy chain also including a "D" region of about 10 more amino acids. *See, e.g.*, FUNDAMENTAL IMMUNOLOGY (Paul, W., ed., Raven Press, 2nd ed., 1989), which is incorporated by reference in its entirety for all purposes. The variable regions of each light/heavy chain pair typically form an antigen binding site. The variable domains of naturally occurring antibodies typically exhibit the same general structure of relatively conserved framework regions (FR) joined by three hypervariable regions, also called complementarity determining regions or CDRs. The CDRs from the two chains of each pair typically are aligned by the framework regions, which may enable binding to a specific epitope. From the amino-terminus to the carboxyl-terminus, both light and heavy chain variable domains typically comprise the domains FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

[0057] The term "CDR set" refers to a group of three CDRs that occur in a single variable region capable of binding the antigen. The exact boundaries of these CDRs have been defined differently according to different systems. The system described by Kabat (Kabat *et al.*, SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST (National Institutes of Health, Bethesda, Md. (1987) and (1991)) not only provides an unambiguous residue numbering system applicable to any variable region of an antibody, but also provides precise residue boundaries defining the three CDRs. These CDRs may be referred to as Kabat CDRs. Chothia and coworkers (Chothia and Lesk, 1987, *J. Mol. Biol.* 196: 901-17; Chothia *et al.*, 1989, *Nature* 342: 877-83) found that certain sub-portions within Kabat CDRs adopt nearly identical peptide backbone conformations, despite having great diversity at the level of amino acid sequence. These sub-portions were designated as L1, L2, and L3 or H1, H2, and H3 where the "L" and the "H" designates the light chain and the heavy chain regions, respectively. These regions may be referred to as Chothia CDRs, which have boundaries that overlap with Kabat CDRs. Other boundaries defining CDRs overlapping with the Kabat CDRs have been described by Padlan, 1995, *FASEB J.* 9: 133-39; MacCallum, 1996, *J. Mol. Biol.* 262(5): 732-45; and Lefranc, 2003, *Dev. Comp. Immunol.* 27: 55-77. Still other CDR boundary definitions may not strictly follow one of the herein systems, but will nonetheless overlap with the Kabat CDRs, although they may be shortened or lengthened in light of prediction or experimental findings that particular

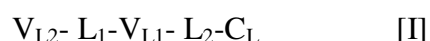
residues or groups of residues or even entire CDRs do not significantly impact antigen binding. The methods used herein may utilize CDRs defined according to any of these systems, although certain embodiments use Kabat or Chothia defined CDRs. Identification of predicted CDRs using the amino acid sequence is well known in the field, such as in Martin, A.C. "Protein sequence and structure analysis of antibody variable domains," *In Antibody Engineering*, Vol. 2. Kontermann R., Dübel S., eds. Springer-Verlag, Berlin, p. 33–51 (2010). The amino acid sequence of the heavy and/or light chain variable domain may be also inspected to identify the sequences of the CDRs by other conventional methods, *e.g.*, by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. The numbered sequences may be aligned by eye, or by employing an alignment program such as one of the CLUSTAL suite of programs, as described in Thompson, 1994, *Nucleic Acids Res.* 22: 4673-80. Molecular models are conventionally used to correctly delineate framework and CDR regions and thus correct the sequence-based assignments.

[0058] The term "Fc" as used herein refers to a molecule comprising the sequence of a non-antigen-binding fragment resulting from digestion of an antibody or produced by other means, whether in monomeric or multimeric form, and can contain the hinge region. The original immunoglobulin source of the native Fc is preferably of human origin and can be any of the immunoglobulins, although IgG1 and IgG2 are preferred. Fc molecules are made up of monomeric polypeptides that can be linked into dimeric or multimeric forms by covalent (*i.e.*, disulfide bonds) and non-covalent association. The number of intermolecular disulfide bonds between monomeric subunits of native Fc molecules ranges from 1 to 4 depending on class (*e.g.*, IgG, IgA, and IgE) or subclass (*e.g.*, IgG1, IgG2, IgG3, IgA1, and IgGA2). One example of a Fc is a disulfide-bonded dimer resulting from papain digestion of an IgG. The term "Fc" as used herein is generic to the monomeric, dimeric, and multimeric forms.

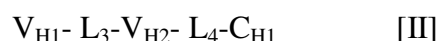
[0059] A F(ab) fragment typically includes one light chain and the V_H and C_{H1} domains of one heavy chain, wherein the V_H-C_{H1} heavy chain portion of the F(ab) fragment cannot form a disulfide bond with another heavy chain polypeptide. As used herein, a F(ab) fragment can also include one light chain containing two variable domains separated by an amino acid linker and one heavy chain containing two variable domains separated by an amino acid linker and a C_{H1} domain.

[0060] A F(ab') fragment typically includes one light chain and a portion of one heavy chain that contains more of the constant region (between the C_{H1} and C_{H2} domains), such that an interchain disulfide bond can be formed between two heavy chains to form a F(ab')₂ molecule.

[0061] The term "binding protein" as used herein refers to a non-naturally occurring (or recombinant or engineered) molecule that specifically binds to at least one target antigen, and which comprises four polypeptide chains that form at least three antigen binding sites, wherein a first polypeptide chain has a structure represented by the formula:



and a second polypeptide chain has a structure represented by the formula:



and a third polypeptide chain has a structure represented by the formula:



and a fourth polypeptide chain has a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L₁, L₂, L₃, and L₄ are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0062] A "recombinant" molecule is one that has been prepared, expressed, created, or isolated by recombinant means.

[0063] One embodiment of the disclosure provides binding proteins having biological and immunological specificity to between one and three target antigens. Another embodiment of the disclosure provides nucleic acid molecules comprising nucleotide sequences encoding polypeptide chains that form such binding proteins. Another

embodiment of the disclosure provides expression vectors comprising nucleic acid molecules comprising nucleotide sequences encoding polypeptide chains that form such binding proteins. Yet another embodiment of the disclosure provides host cells that express such binding proteins (*i.e.*, comprising nucleic acid molecules or vectors encoding polypeptide chains that form such binding proteins).

[0064] The term "swapability" as used herein refers to the interchangeability of variable domains within the binding protein format and with retention of folding and ultimate binding affinity. "Full swapability" refers to the ability to swap the order of both V_{H1} and V_{H2} domains, and therefore the order of V_{L1} and V_{L2} domains, in the polypeptide chain of formula I or the polypeptide chain of formula II (*i.e.*, to reverse the order) while maintaining full functionality of the binding protein as evidenced by the retention of binding affinity. Furthermore, it should be noted that the designations V_H and V_L refer only to the domain's location on a particular protein chain in the final format. For example, V_{H1} and V_{H2} could be derived from V_{L1} and V_{L2} domains in parent antibodies and placed into the V_{H1} and V_{H2} positions in the binding protein. Likewise, V_{L1} and V_{L2} could be derived from V_{H1} and V_{H2} domains in parent antibodies and placed in the V_{H1} and V_{H2} positions in the binding protein. Thus, the V_H and V_L designations refer to the present location and not the original location in a parent antibody. V_H and V_L domains are therefore "swappable."

[0065] The term "antigen" or "target antigen" or "antigen target" as used herein refers to a molecule or a portion of a molecule that is capable of being bound by a binding protein, and additionally is capable of being used in an animal to produce antibodies capable of binding to an epitope of that antigen. A target antigen may have one or more epitopes. With respect to each target antigen recognized by a binding protein, the binding protein is capable of competing with an intact antibody that recognizes the target antigen.

[0066] The term "HIV" as used herein means Human Immunodeficiency Virus. As used herein, the term "HIV infection" generally encompasses infection of a host, particularly a human host, by the human immunodeficiency virus (HIV) family of retroviruses including, but not limited to, HIV I, HIV II, HIV III (also known as HTLV-II, LAV-1, LAV-2). HIV can be used herein to refer to any strains, forms, subtypes, clades and variations in the HIV family. Thus, treating HIV infection will encompass the treatment of a person who is a carrier of any of the HIV family of retroviruses or a person who is diagnosed with active AIDS, as well as the treatment or prophylaxis of the AIDS-related conditions in such persons.

[0067] The term "AIDS" as used herein means Acquired Immunodeficiency Syndrome. AIDS is caused by HIV.

[0068] The terms "CD4bs" or "CD4 binding site" refer to the binding site for CD4 (cluster of differentiation 4), which is a glycoprotein found on the surface of immune cells such as T helper cells, monocytes, macrophages, and dendritic cells.

[0069] The term "CD3" is cluster of differentiation factor 3 polypeptide and is a T-cell surface protein that is typically part of the T cell receptor (TCR) complex.

[0070] "CD28" is cluster of differentiation 28 polypeptide and is a T-cell surface protein that provides co-stimulatory signals for T-cell activation and survival.

[0071] The term "glycoprotein 160" or "gp160 protein" refers to the envelope glycoprotein complex of HIV and which is a homotrimer that is cleaved into gp120 and gp41 subunits.

[0072] The term "MPER" refers to the membrane-proximal external region of glycoprotein 41 (gp41), which is a subunit of the envelope protein complex of retroviruses, including HIV.

[0073] The term "glycan" refers to the carbohydrate portion of a glycoconjugate, such as a glycoprotein, glycolipid, or a proteoglycan. In the disclosed binding proteins, glycan refers to the HIV-1 envelope glycoprotein gp120.

[0074] The term "T-cell engager" refers to binding proteins directed to a host's immune system, more specifically the T cells' cytotoxic activity as well as directed to a HIV target protein.

[0075] The term "trimer apex" refers to apex of HIV-1 envelope glycoprotein gp120.

[0076] The term "monospecific binding protein" refers to a binding protein that specifically binds to one antigen target.

[0077] The term "monovalent binding protein" refers to a binding protein that has one antigen binding site.

[0078] The term "bispecific binding protein" refers to a binding protein that specifically binds to two different antigen targets.

[0079] The term "bivalent binding protein" refers to a binding protein that has two binding sites.

[0080] The term "trispecific binding protein" refers to a binding protein that specifically binds to three different antigen targets.

[0081] The term "trivalent binding protein" refers to a binding protein that has three binding sites. In particular embodiments the trivalent binding protein can bind to one antigen target. In other embodiments, the trivalent binding protein can bind to two antigen targets. In other embodiments, the trivalent binding protein can bind to three antigen targets.

[0082] An "isolated" binding protein is one that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would interfere with diagnostic or therapeutic uses for the binding protein, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In some embodiments, the binding protein will be purified: (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated binding proteins include the binding protein *in situ* within recombinant cells since at least one component of the binding protein's natural environment will not be present.

[0083] The terms "substantially pure" or "substantially purified" as used herein refer to a compound or species that is the predominant species present (*i.e.*, on a molar basis it is more abundant than any other individual species in the composition). In some embodiments, a substantially purified fraction is a composition wherein the species comprises at least about 50% (on a molar basis) of all macromolecular species present. In other embodiments, a substantially pure composition will comprise more than about 80%, 85%, 90%, 95%, or 99% of all macromolecular species present in the composition. In still other embodiments, the species is purified to essential homogeneity (contaminant species cannot be detected in the composition by conventional detection methods) wherein the composition consists essentially of a single macromolecular species.

[0084] A "neutralizing" binding protein as used herein refers to a molecule that is able to block or substantially reduce an effector function of a target antigen to which it binds. As used herein, "substantially reduce" means at least about 60%, preferably at least about 70%, more preferably at least about 75%, even more preferably at least about 80%, still more preferably at least about 85%, most preferably at least about 90% reduction of an effector function of the target antigen.

[0085] The term "epitope" includes any determinant, preferably a polypeptide determinant, capable of specifically binding to an immunoglobulin or T-cell receptor. In certain embodiments, epitope determinants include chemically active surface groupings of molecules such as amino acids, sugar side chains, phosphoryl groups, or sulfonyl groups, and, in certain embodiments, may have specific three-dimensional structural characteristics and/or specific charge characteristics. An epitope is a region of an antigen that is bound by an antibody or binding protein. In certain embodiments, a binding protein is said to specifically bind an antigen when it preferentially recognizes its target antigen in a complex mixture of proteins and/or macromolecules. In some embodiments, a binding protein is said to specifically bind an antigen when the equilibrium dissociation constant is $\leq 10^{-8}$ M, more preferably when the equilibrium dissociation constant is $\leq 10^{-9}$ M, and most preferably when the dissociation constant is $\leq 10^{-10}$ M.

[0086] The dissociation constant (K_D) of a binding protein can be determined, for example, by surface plasmon resonance. Generally, surface plasmon resonance analysis measures real-time binding interactions between ligand (a target antigen on a biosensor matrix) and analyte (a binding protein in solution) by surface plasmon resonance (SPR) using the BIAcore system (Pharmacia Biosensor; Piscataway, NJ). Surface plasmon analysis can also be performed by immobilizing the analyte (binding protein on a biosensor matrix) and presenting the ligand (target antigen). The term " K_D ," as used herein refers to the dissociation constant of the interaction between a particular binding protein and a target antigen.

[0087] The term "specifically binds" as used herein refers to the ability of a binding protein or an antigen-binding fragment thereof to bind to an antigen containing an epitope with an K_d of at least about 1×10^{-6} M, 1×10^{-7} M, 1×10^{-8} M, 1×10^{-9} M, 1×10^{-10} M, 1×10^{-11} M, 1×10^{-12} M, or more, and/or to bind to an epitope with an affinity that is at least two-fold greater than its affinity for a nonspecific antigen.

[0088] The term "linker" as used herein refers to one or more amino acid residues inserted between immunoglobulin domains to provide sufficient mobility for the domains of the light and heavy chains to fold into cross over dual variable region immunoglobulins. A linker is inserted at the transition between variable domains or between variable and constant domains, respectively, at the sequence level. The transition between domains can be identified because the approximate size of the immunoglobulin domains are well understood. The precise location of a domain transition can be determined by locating

peptide stretches that do not form secondary structural elements such as beta-sheets or alpha-helices as demonstrated by experimental data or as can be assumed by techniques of modeling or secondary structure prediction. The linkers described herein are referred to as L₁, which is located on the light chain between the C-terminus of the V_{L2} and the N-terminus of the V_{L1} domain; and L₂, which is located on the light chain between the C-terminus of the V_{L1} and the N-terminus of the C_L domain. The heavy chain linkers are known as L₃, which is located between the C-terminus of the V_{H1} and the N-terminus of the V_{H2} domain; and L₄, which is located between the C-terminus of the V_{H2} and the N-terminus of the C_{H1} domain.

[0089] The term "vector" as used herein refers to any molecule (*e.g.*, nucleic acid, plasmid, or virus) that is used to transfer coding information to a host cell. The term "vector" includes a nucleic acid molecule that is capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid," which refers to a circular double-stranded DNA molecule into which additional DNA segments may be inserted. Another type of vector is a viral vector, wherein additional DNA segments may be inserted into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) can be integrated into the genome of a host cell upon introduction into the host cell and thereby are replicated along with the host genome. In addition, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "recombinant expression vectors" (or simply, "expression vectors"). In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. The terms "plasmid" and "vector" may be used interchangeably herein, as a plasmid is the most commonly used form of vector. However, the disclosure is intended to include other forms of expression vectors, such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses, and adeno-associated viruses), which serve equivalent functions.

[0090] The phrase "recombinant host cell" (or "host cell") as used herein refers to a cell into which a recombinant expression vector has been introduced. A recombinant host cell or host cell is intended to refer not only to the particular subject cell, but also to the progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to

the parent cell, but such cells are still included within the scope of the term "host cell" as used herein. A wide variety of host cell expression systems can be used to express the binding proteins, including bacterial, yeast, baculoviral, and mammalian expression systems (as well as phage display expression systems). An example of a suitable bacterial expression vector is pUC19. To express a binding protein recombinantly, a host cell is transformed or transfected with one or more recombinant expression vectors carrying DNA fragments encoding the polypeptide chains of the binding protein such that the polypeptide chains are expressed in the host cell and, preferably, secreted into the medium in which the host cells are cultured, from which medium the binding protein can be recovered.

[0091] The term "transformation" as used herein refers to a change in a cell's genetic characteristics, and a cell has been transformed when it has been modified to contain a new DNA. For example, a cell is transformed where it is genetically modified from its native state. Following transformation, the transforming DNA may recombine with that of the cell by physically integrating into a chromosome of the cell, or may be maintained transiently as an episomal element without being replicated, or may replicate independently as a plasmid. A cell is considered to have been stably transformed when the DNA is replicated with the division of the cell. The term "transfection" as used herein refers to the uptake of foreign or exogenous DNA by a cell, and a cell has been "transfected" when the exogenous DNA has been introduced inside the cell membrane. A number of transfection techniques are well known in the art. Such techniques can be used to introduce one or more exogenous DNA molecules into suitable host cells.

[0092] The term "naturally occurring" as used herein and applied to an object refers to the fact that the object can be found in nature and has not been manipulated by man. For example, a polynucleotide or polypeptide that is present in an organism (including viruses) that can be isolated from a source in nature and that has not been intentionally modified by man is naturally-occurring. Similarly, "non-naturally occurring" as used herein refers to an object that is not found in nature or that has been structurally modified or synthesized by man.

[0093] As used herein, the twenty conventional amino acids and their abbreviations follow conventional usage. Stereoisomers (*e.g.*, D-amino acids) of the twenty conventional amino acids; unnatural amino acids and analogs such as α -, α -disubstituted amino acids, N-alkyl amino acids, lactic acid, and other unconventional amino acids may also be suitable components for the polypeptide chains of the binding proteins. Examples of

unconventional amino acids include: 4-hydroxyproline, γ -carboxyglutamate, ϵ -N,N,N-trimethyllysine, ϵ -N-acetyllysine, O-phosphoserine, N-acetylserine, N-formylmethionine, 3-methylhistidine, 5-hydroxylysine, σ -N-methylarginine, and other similar amino acids and imino acids (*e.g.*, 4-hydroxyproline). In the polypeptide notation used herein, the left-hand direction is the amino terminal direction and the right-hand direction is the carboxyl-terminal direction, in accordance with standard usage and convention.

[0094] Naturally occurring residues may be divided into classes based on common side chain properties:

- (1) hydrophobic: Met, Ala, Val, Leu, Ile, Phe, Trp, Tyr, Pro;
- (2) polar hydrophilic: Arg, Asn, Asp, Gln, Glu, His, Lys, Ser, Thr ;
- (3) aliphatic: Ala, Gly, Ile, Leu, Val, Pro;
- (4) aliphatic hydrophobic: Ala, Ile, Leu, Val, Pro;
- (5) neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;
- (6) acidic: Asp, Glu;
- (7) basic: His, Lys, Arg;
- (8) residues that influence chain orientation: Gly, Pro;
- (9) aromatic: His, Trp, Tyr, Phe; and
- (10) aromatic hydrophobic: Phe, Trp, Tyr.

[0095] Conservative amino acid substitutions may involve exchange of a member of one of these classes with another member of the same class. Non-conservative substitutions may involve the exchange of a member of one of these classes for a member from another class.

[0096] A skilled artisan will be able to determine suitable variants of the polypeptide chains of the binding proteins using well-known techniques. For example, one skilled in the art may identify suitable areas of a polypeptide chain that may be changed without destroying activity by targeting regions not believed to be important for activity. Alternatively, one skilled in the art can identify residues and portions of the molecules that are conserved among similar polypeptides. In addition, even areas that may be important for biological activity or for structure may be subject to conservative amino acid substitutions without destroying the biological activity or without adversely affecting the polypeptide structure.

[0097] The term "patient" as used herein includes human and animal subjects.

[0098] The terms "treatment" or "treat" as used herein refer to both therapeutic treatment and prophylactic or preventative measures. Those in need of treatment include those having the disorder as well as those prone to have a disorder or those in which the disorder is to be prevented. In particular embodiments, binding proteins can be used to treat humans infected with HIV, or humans susceptible to HIV infection, or ameliorate HIV infection in a human subject infected with HIV. The binding proteins can also be used to prevent HIV in a human patient.

[0099] It should be understood as that treating humans infected with HIV include those subjects who are at any one of the several stages of HIV infection progression, which, for example, include acute primary infection syndrome (which can be asymptomatic or associated with an influenza-like illness with fevers, malaise, diarrhea and neurologic symptoms such as headache), asymptomatic infection (which is the long latent period with a gradual decline in the number of circulating CD4⁺T cells), and AIDS (which is defined by more serious AIDS-defining illnesses and/or a decline in the circulating CD4 cell count to below a level that is compatible with effective immune function). In addition, treating or preventing HIV infection will also encompass treating suspected infection by HIV after suspected past exposure to HIV by e.g., contact with HIV-contaminated blood, blood transfusion, exchange of body fluids, "unsafe" sex with an infected person, accidental needle stick, receiving a tattoo or acupuncture with contaminated instruments, or transmission of the virus from a mother to a baby during pregnancy, delivery or shortly thereafter.

[0100] The terms "pharmaceutical composition" or "therapeutic composition" as used herein refer to a compound or composition capable of inducing a desired therapeutic effect when properly administered to a patient.

[0101] The term "pharmaceutically acceptable carrier" or "physiologically acceptable carrier" as used herein refers to one or more formulation materials suitable for accomplishing or enhancing the delivery of a binding protein.

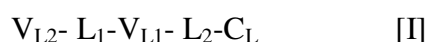
[0102] The terms "effective amount" and "therapeutically effective amount" when used in reference to a pharmaceutical composition comprising one or more binding proteins refer to an amount or dosage sufficient to produce a desired therapeutic result. More specifically, a therapeutically effective amount is an amount of a binding protein sufficient to inhibit, for some period of time, one or more of the clinically defined pathological processes associated with the condition being treated. The effective amount may vary depending on the specific

binding protein that is being used, and also depends on a variety of factors and conditions related to the patient being treated and the severity of the disorder. For example, if the binding protein is to be administered *in vivo*, factors such as the age, weight, and health of the patient as well as dose response curves and toxicity data obtained in preclinical animal work would be among those factors considered. The determination of an effective amount or therapeutically effective amount of a given pharmaceutical composition is well within the ability of those skilled in the art.

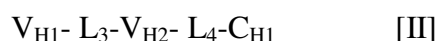
[0103] One embodiment of the disclosure provides a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a binding protein.

Trispecific and/or Trivalent Binding Proteins

[0104] In one embodiment, the binding protein of the disclosure is a trispecific and/or trivalent binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more (e.g., three different) HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain; and

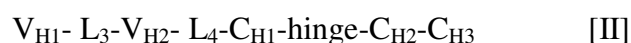
L_1 , L_2 , L_3 and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

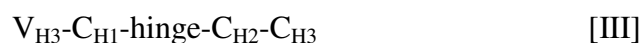
[0105] In one embodiment, the binding protein of the disclosure is a trispecific and/or trivalent binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more (e.g., three different) HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0106] In some embodiments, the first polypeptide chain and the second polypeptide chain have a cross-over orientation that forms two distinct antigen binding sites. In some embodiments, the V_{H1} and V_{L1} form a binding pair and form the first antigen binding site. In some embodiments, the V_{H2} and V_{L2} form a binding pair and form the second antigen binding site. In some embodiments, the third polypeptide and the fourth polypeptide form a third

antigen binding site. In some embodiments, the V_{H3} and V_{L3} form a binding pair and form the third antigen binding site.

[0107] In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124, 130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; and V_{H1} , V_{H2} and V_{H3} , are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 19, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123, 129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242. In other embodiments, V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and V_{H1} , V_{H2} and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265. In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a light chain variable domain comprising a light chain variable domain sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a heavy chain variable domain comprising a heavy chain variable domain sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein. In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a light chain variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a heavy chain variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein.

[0108] In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383,

385, 391, 393, 399, 401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; and V_{H1} , V_{H2} and V_{H3} , are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472. In other embodiments, V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and V_{H1} , V_{H2} and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

[0109] In particular embodiments, the order of the V_{H1} and V_{H2} domains, and therefore the order of V_{L1} and V_{L2} domains, in the polypeptide chain of formula I or the polypeptide chain of formula II (*i.e.*, to reverse the order) are swapped.

[0110] In some embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 4; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 3 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 3; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 1 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 2.

[0111] In some embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 12; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 11 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 11; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 9; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 10 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 10.

[0112] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 20; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 19 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 19; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 17 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 17; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 18 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 18.

[0113] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 28 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 28; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 27 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 27; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 25 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 25; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 26 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 26.

[0114] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 36 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 36; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 35 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 35; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 33 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 33; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 34 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 34.

[0115] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 44 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 44; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 43 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 43; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 41 or an amino acid sequence that is at least 95% identical to

the amino acid sequence of SEQ ID NO: 41; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 42 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 42.

[0116] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 52 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 52; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 51 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 49 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 49; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 50 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50.

[0117] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 60 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 60; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 59 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 59; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 57 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 57; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 58 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 58.

[0118] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 68 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 68; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 67 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 67; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 65 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 65; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 66 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 66.

[0119] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 76 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 76; the second polypeptide chain comprises the amino

acid sequence of SEQ ID NO: 75 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 75; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 73 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 73; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 74 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 74.

[0120] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 84 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 84; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 83 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 83; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 81 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 81; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 82 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 82.

[0121] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 92 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 92; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 91 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 91; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 89 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 89; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 90 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 90.

[0122] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 100 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 100; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 99 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 99; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 97 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 97; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 98 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 98.

[0123] In other embodiments, the first polypeptide comprises the amino acid sequence of SEQ ID NO: 108 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 108; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 107; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 105 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 105; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 106.

[0124] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 116 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 116; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 115; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 113 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 113; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 114.

[0125] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 124 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 124; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 123 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 123; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 121 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 121; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 122 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 122.

[0126] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 132 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 132; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 131 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 131; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 129 or an amino acid sequence that is at least 95%

identical to the amino acid sequence of SEQ ID NO: 129; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 130 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 130.

[0127] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 140 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 140; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 139 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 139; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 137; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 138.

[0128] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 148 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 148; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 147 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 147; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 145 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 145; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 146 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 146.

[0129] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 156 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 156; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 155 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 155; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 153 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 153; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 154 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 154.

[0130] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 164 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 164; the second polypeptide chain comprises the amino

acid sequence of SEQ ID NO: 163 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 163; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 161 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 161; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 162 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 162.

[0131] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 172 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 172; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 171 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 171; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 169 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 169; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 170 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 170.

[0132] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 180 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 180; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 179 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 179; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 177 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 177; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 178 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 178.

[0133] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 188 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 188; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 187 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 187; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 185 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 185; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 186 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 186.

[0134] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 196 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 196; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 195 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 195; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 193 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 193; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 194 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 194.

[0135] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 204 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 204; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 203 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 203; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 201 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 201; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 202 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 202.

[0136] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 212 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 212; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 211 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 211; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 209 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 209; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 210 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 210.

[0137] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 220 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 220; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 219 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 219; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 217 or an amino acid sequence that is at least 95%

identical to the amino acid sequence of SEQ ID NO: 217; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 218 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 218.

[0138] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 228 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 228; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 227 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 227; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 225 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 225; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 226 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 226.

[0139] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 235 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 235; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 234 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 234; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 232 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 232; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 233 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 233.

[0140] In other embodiments, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 243 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 243; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 242 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 242; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 240 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 240; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 241 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 241.

[0141] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 305 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 305; the second polypeptide chain comprises the amino

acid sequence of SEQ ID NO: 304 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 304; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 302 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 302; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 303 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 303.

[0142] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 313 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 313; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 312 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 312; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 310 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 310; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 311 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 311.

[0143] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 321 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 321; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 320 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 320; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 318 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 318; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 319 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 319.

[0144] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 329 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 329; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 328 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 328; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 326 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 326; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 327 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 327.

[0145] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 337 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 337; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 336 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 336; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 334 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 334; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 335 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 335.

[0146] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 345 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 345; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 344 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 344; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 342 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 342; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 343 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 343.

[0147] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 353 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 353; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 352 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 352; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 350 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 350; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 351 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 351.

[0148] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 361 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 361; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 360 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 360; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 358 or an amino acid sequence that is at least 95%

identical to the amino acid sequence of SEQ ID NO: 358; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 359 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 359.

[0149] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 369 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 369; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 368 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 368; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 366 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 366; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 367 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 367.

[0150] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 377 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 377; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 376 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 376; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 374 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 374; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 375 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 375.

[0151] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 385 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 385; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 384 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 384; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 382 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 382; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 383 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 383.

[0152] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 393 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 393; the second polypeptide chain comprises the amino

acid sequence of SEQ ID NO: 392 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 392; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 390 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 390; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 391 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 391.

[0153] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 401 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 401; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 400 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 400; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 398 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 398; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 399 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 399.

[0154] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 409 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 409; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 408 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 408; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 406 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 406; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 407 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 407.

[0155] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 417 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 417; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 416 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 416; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 414 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 414; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 415 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 415.

[0156] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 425 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 425; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 424 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 424; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 422 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 422; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 423 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 423.

[0157] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 433 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 433; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 432 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 432; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 430 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 430; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 431 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 431.

[0158] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 441 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 441; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 440 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 440; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 438 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 438; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 439 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 439.

[0159] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 449 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 449; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 448 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 448; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 446 or an amino acid sequence that is at least 95%

identical to the amino acid sequence of SEQ ID NO: 446; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 447 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 447.

[0160] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 457 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 457; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 456 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 456; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 454 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 454; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 455 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 455.

[0161] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 465 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 465; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 464 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 464; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 462 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 462; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 463 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 463.

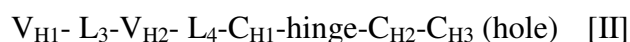
[0162] In another embodiment, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 473 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 473; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 472 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 472; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 470 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 470; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 471 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 471.

[0163] In other embodiments, the binding protein of the disclosure is a trispecific and/or trivalent binding protein comprising four polypeptide chains that form three antigen binding

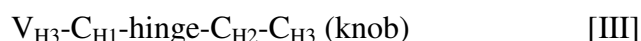
sites that specifically bind one or more (e.g., three) HIV target antigens, wherein a first polypeptide chain has a structure represented by the formula:



and a second polypeptide chain has a structure represented by the formula:



and a third polypeptide chain has a structure represented by the formula:



and a fourth polypeptide chain has a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

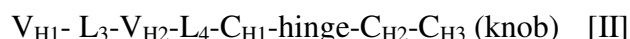
L_1 , L_2 , L_3 and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

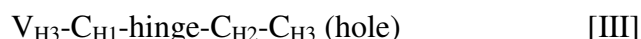
[0164] In other embodiments, the binding protein of the disclosure is a trispecific and/or trivalent binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more (e.g., three) HIV target antigens, wherein a first polypeptide chain has a structure represented by the formula:



and a second polypeptide chain has a structure represented by the formula:



and a third polypeptide chain has a structure represented by the formula:



and a fourth polypeptide chain has a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;
V_{L2} is a second immunoglobulin light chain variable domain;
V_{L3} is a third immunoglobulin light chain variable domain;
V_{H1} is a first immunoglobulin heavy chain variable domain;
V_{H2} is a second immunoglobulin heavy chain variable domain;
V_{H3} is a third immunoglobulin heavy chain variable domain;
C_L is an immunoglobulin light chain constant domain;
C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and
L₁, L₂, L₃ and L₄ are amino acid linkers;
and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

Additional examples of trispecific binding proteins

[0165] In some embodiments, V_{L1}, V_{L2} and V_{L3} are each independently a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{L1}, V_{L2} and V_{L3} are each independently a variable domain comprising an amino acid sequence having at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about 86%, at least about 87%, at least about 88%, at least about 89%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

[0166] In some embodiments, V_{H1}, V_{H2} and V_{H3} are each independently a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{H1}, V_{H2} and V_{H3} are each independently a variable domain comprising an amino acid sequence having at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about 86%, at least about 87%, at least about 88%, at least about 89%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

[0167] In some embodiments, V_{L1} , V_{L2} , and V_{L3} comprise an amino acid sequence as set forth in SEQ ID NOs: 518, 519, and 512, respectively, and V_{H1} , V_{H2} , and V_{H3} comprise an amino acid sequence as set forth in SEQ ID NOs: 504, 506, and 502, respectively. In some embodiments, V_{L1} , V_{L2} , and V_{L3} comprise an amino acid sequence as set forth in SEQ ID NOs: 518, 519, and 513, respectively, and V_{H1} , V_{H2} , and V_{H3} comprises an amino acid sequence as set forth in SEQ ID NOs: 504, 506, and 503, respectively. In some embodiments, V_{L1} , V_{L2} , and V_{L3} comprises an amino acid sequence as set forth in SEQ ID NOs: 519, 518, and 513, respectively, and V_{H1} , V_{H2} , and V_{H3} comprises an amino acid sequence as set forth in SEQ ID NOs: 506, 504, and 503, respectively.

[0168] In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508. In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a light chain variable domain sequence shown in Table C. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a heavy chain variable domain sequence shown in Table C.

[0169] In some embodiments, V_{L1} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 518, V_{L2} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 519, V_{L3} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 512, V_{H1} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 504, V_{H2} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 506, and V_{H3} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 502. In some embodiments, V_{L1} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of

SEQ ID NO: 518, V_{L2} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 519, V_{L3} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 513, V_{H1} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 504, V_{H2} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 506, and V_{H3} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 503. In some embodiments, V_{L1} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 519, V_{L2} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 518, V_{L3} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 513, and V_{H1} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 506, V_{H2} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 504, and V_{H3} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 503.

[0170] In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising: (a) a CDR-L1 comprising a sequence selected from the group consisting of SEQ ID NOs: 266, 269, 275, 278, 281, and 500; (b) a CDR-L2 comprising a sequence selected from the group consisting of SEQ ID NOs: 267, 270, 276, 279, 282, and 501; and/or (c) a CDR-L3 comprising a sequence selected from the group consisting of SEQ ID NOs: 268, 271, 274, 277, 280, and 283. In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 comprising amino acid sequences as shown in Table B. In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively.

[0171] In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising: (a) a CDR-H1 comprising a sequence selected from the group consisting of SEQ ID NOs: 248, 251, 254, 257, 263, and 499; (b) a CDR-H2 comprising a sequence selected from the group consisting of SEQ ID NOs: 252, 255, 258, 261, 264, and 497; and/or (c) a CDR-H3 comprising a sequence selected from the group consisting of SEQ ID NOs: 250, 253, 256, 259, 262, 265, and 498. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 comprising amino acid sequences as shown in Table B. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively.

[0172] In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 500, 501, and 274, respectively; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 275, 276, and 277, respectively; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 266, 267, and 268, respectively; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 254, 255, and 256, respectively; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 257, 258, and 259, respectively; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 248, 497, and 250, respectively. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 500, 501, and 274, respectively; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 275, 276, and 277, respectively; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 269, 270, and 271, respectively; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 254, 255, and 256, respectively; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 257, 258, and 259, respectively; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 251, 252, and 253, respectively. In some embodiments, V_{L1} comprises a CDR-L1,

CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 275, 276, and 277, respectively; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 500, 501, and 274, respectively; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 269, 270, and 271, respectively; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 257, 258, and 259, respectively; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 254, 255, and 256, respectively; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 251, 252, and 253, respectively.

Additional trispecific binding proteins targeting one or more HIV target proteins
and one or more T cell target proteins

[0173] In some embodiments, a binding protein of the present disclosure comprises four polypeptide chains that form three antigen binding sites that specifically bind one or more (*e.g.*, one or two) HIV target proteins and one or more (*e.g.*, one or two) T cell target proteins, wherein a first polypeptide chain has a structure represented by the formula:

$$V_{L2}-L_1-V_{L1}-L_2-C_L \quad [I];$$

a second polypeptide chain has a structure represented by the formula:

$$V_{H1}-L_3-V_{H2}-L_4-C_{H1} \quad [II];$$

a third polypeptide chain has a structure represented by the formula:

$$V_{H3}-C_{H1} \quad [III];$$

and a fourth polypeptide chain has a structure represented by the formula:

$$V_{L3}-C_L \quad [IV];$$

wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain; and

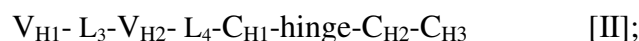
L₁, L₂, L₃, and L₄ are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

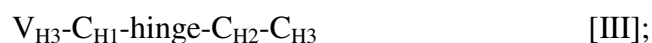
[0174] In some embodiments, a binding protein of the present disclosure comprises four polypeptide chains that form three antigen binding sites that specifically bind one or more (*e.g.*, one or two) HIV target proteins and one or more (*e.g.*, one or two) T cell target proteins, wherein a first polypeptide chain has a structure represented by the formula:



a second polypeptide chain has a structure represented by the formula:



a third polypeptide chain has a structure represented by the formula:



and a fourth polypeptide chain has a structure represented by the formula



wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0175] In some embodiments, the first polypeptide chain and the second polypeptide chain have a cross-over orientation that forms two distinct antigen binding sites. In some embodiments, the V_{H1} and V_{L1} form a binding pair and form the first antigen binding site. In some embodiments, the V_{H2} and V_{L2} form a binding pair and form the second antigen binding site. In some embodiments, the third polypeptide and the fourth polypeptide form a third

antigen binding site. In some embodiments, the V_{H3} and V_{L3} form a binding pair and form the third antigen binding site.

[0176] In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524. In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising an amino acid sequence having at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about 86%, at least about 87%, at least about 88%, at least about 89%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0177] In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising an amino acid sequence having at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about 86%, at least about 87%, at least about 88%, at least about 89%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0178] In some embodiments, V_{L1} , V_{L2} , and V_{L3} comprise an amino acid sequence as set forth in SEQ ID NOs: 522, 524, and 513, respectively, and V_{H1} , V_{H2} , and V_{H3} comprise an amino acid sequence as set forth in SEQ ID NOs: 509, 511, and 503, respectively. In some embodiments, V_{L1} , V_{L2} , and V_{L3} comprise an amino acid sequence as set forth in SEQ ID NOs: 524, 522, and 513, respectively, and V_{H1} , V_{H2} , and V_{H3} comprise an amino acid sequence as set forth in SEQ ID NOs: 511, 509, and 503, respectively.

[0179] In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0180] In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0181] In some embodiments, V_{L1} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 522, V_{L2} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 524, V_{L3} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 513, V_{H1} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 509, V_{H2} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 511, and V_{H3} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 503. In some embodiments, V_{L1} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 524, V_{L2} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence of SEQ ID NO: 522, V_{L3} is a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a light chain variable domain sequence of SEQ ID NO: 513, V_{H1} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 511, V_{H2} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 509, and V_{H3} is a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence of SEQ ID NO: 503.

[0182] In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising: (a) a CDR-L1 comprising a sequence selected from the group consisting of SEQ ID NOs: 266, 269, 275, 278, 281, 488, 491, 494 and 500; (b) a CDR-L2 comprising a sequence selected from the group consisting of SEQ ID NOs: 267, 270, 276, 279, 282, 489, 492, 495, and 501; and (c) a CDR-L3 comprising a sequence selected from the group consisting of SEQ ID NOs: 268, 271, 274, 277, 280, 283, 490, 493, and 496. In some embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 comprising amino acid sequences as shown in Table B. In some

embodiments, V_{L1} , V_{L2} and V_{L3} are each independently a variable domain comprising a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively.

[0183] In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising: (a) a CDR-H1 comprising a sequence selected from the group consisting of SEQ ID NOs: 248, 251, 254, 257, 263, 479, 482, 485, and 499; (b) a CDR-H2 comprising a sequence selected from the group consisting of SEQ ID NOs: 252, 255, 258, 261, 264, 480, 483, 486, and 497; and (c) a CDR-H3 comprising a sequence selected from the group consisting of SEQ ID NOs: 250, 253, 256, 259, 262, 265, 481, 484, 487, and 498. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 comprising amino acid sequences as shown in Table B. In some embodiments, V_{H1} , V_{H2} and V_{H3} are each independently a variable domain comprising a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively.

[0184] In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 488, 489, and 490, respectively; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 494, 495, and 496, respectively; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 269, 270, and 271, respectively; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 479, 480, and 481, respectively; V_{H2}

comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 485, 486, and 487, respectively; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 251, 252, and 253, respectively. In some embodiments, V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 494, 495, and 496, respectively; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 488, 489, and 490, respectively; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising the sequence of SEQ ID NOs: 269, 270, and 271, respectively; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 485, 486, and 487, respectively; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 479, 480, and 481, respectively; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising the sequence of SEQ ID NOs: 251, 252, and 253, respectively.

[0185] In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD28 or CD28_2 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD3 described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein. In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising the six CDRs of antibody CD28 or CD28_2 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising the six CDRs of antibody CD3 described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising the six CDRs of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein.

[0186] In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD28 or CD28_2 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD3 described herein. In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising the six CDRs of antibody CD28 or CD28_2 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains

comprising the six CDRs of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising the six CDRs of antibody CD3 described herein.

[0187] In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD3 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD28 or CD28_2 described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein. In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising the six CDRs of antibody CD3 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising the six CDRs of antibody CD28 or CD28_2 described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising the six CDRs of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein.

[0188] In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD3 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD28 or CD28_2 described herein. In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising the six CDRs of antibody CD3 described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising the six CDRs of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising the six CDRs of antibody CD28 or CD28_2 described herein.

[0189] In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD28 or CD28_2 described herein, and V_{L3} and V_{H3} are

light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD3 described herein. In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising the six CDRs of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising the six CDRs of antibody CD28 or CD28_2 described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising the six CDRs of antibody CD3 described herein.

[0190] In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD3 described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising a light and heavy chain variable sequence of antibody CD28 or CD28_2 described herein. In some embodiments, V_{L1} and V_{H1} are light and heavy chain variable domains comprising the six CDRs of antibody CD4BS “a”, CD4BS “b”, MPER, MPER_100W, V1/V2 directed “a”, V1/V2 directed “b”, or V3 directed described herein, V_{L2} and V_{H2} are light and heavy chain variable domains comprising the six CDRs of antibody CD3 or CD28_2 described herein, and V_{L3} and V_{H3} are light and heavy chain variable domains comprising the six CDRs of antibody CD28 or CD28_2 described herein.

Target Proteins

[0191] In one embodiment, the binding proteins specifically bind to one or more HIV target proteins. In some embodiments, the binding proteins are trispecific and specifically bind to MPER of the HIV-1 gp41 protein, a CD4 binding site of the HIV-1 gp120 protein, a glycan in the V3 loop of the HIV-1 gp120 protein, a trimer apex of the HIV-1 gp120 protein or gp160. In other embodiments, the binding proteins specifically bind to one or more HIV target proteins and one or more target proteins on a T-cell including T cell receptor complex. These T-cell engager binding proteins are capable of recruiting T cells transiently to target cells and, at the same time, activating the cytolytic activity of the T cells. The T-cell engager trispecific antibodies can be used to activate HIV-1 reservoirs and redirect/activate T cells to lyse latently infected HIV-1⁺ T cells. Examples of target proteins on T cells include but are not limited to CD3 and CD28, among others. In some embodiments, the trispecific binding

proteins may be generated by combining the antigen binding domains of two or more monospecific antibodies (parent antibodies) into one antibody. *See* International Publication Nos. WO 2011/038290 A2, WO 2013/086533 A1, WO 2013/070776 A1, WO 2012/154312 A1, and WO 2013/163427 A1, which are hereby incorporated into this disclosure by reference. The binding proteins of the disclosure may be prepared using domains or sequences obtained or derived from any human or non-human antibody, including, for example, human, murine, or humanized antibodies.

[0192] In some embodiments of the disclosure, the trivalent binding protein is capable of binding three different antigen targets. In one embodiment, the binding protein is trispecific and one light chain-heavy chain pair is capable of binding two different antigen targets or epitopes and one light chain-heavy chain pair is capable of binding one antigen target or epitope. In another embodiment, the binding protein is capable of binding three different HIV antigen targets that are located on the HIV envelope glycoprotein structure composed of gp120 and gp41 subunits. In other embodiments, the binding protein is capable of inhibiting the function of one or more of the antigen targets.

[0193] In some embodiments, a binding protein of the present disclosure binds one or more HIV target proteins. In some embodiments, the binding protein is capable of specifically binding three different epitopes on a single HIV target protein. In some embodiments, the binding protein is capable of binding two different epitopes on a first HIV target protein, and one epitope on a second HIV target protein. In some embodiments, the first and second HIV target proteins are different. In some embodiments, the binding protein is capable of specifically binding three different HIV target protein. In some embodiments, the one or more HIV target proteins are one or more of glycoprotein 120, glycoprotein 41, and glycoprotein 160.

[0194] In some embodiments, a binding protein of the present disclosure binds one or more HIV target proteins and one or more T cell target proteins. In some embodiments, the binding protein is capable of specifically binding one HIV target protein and two different epitopes on a single T cell target protein. In some embodiments, the binding protein is capable of specifically binding one HIV target protein and two different T cell target proteins (e.g., CD28 and CD3). In some embodiments, the binding protein is capable of specifically binding one T cell target protein and two different epitopes on a single HIV target protein. In some embodiments, the binding protein is capable of specifically binding one T cell target protein and two different HIV target proteins. In some embodiments, the first and second

polypeptide chains of the binding protein form two antigen binding sites that specifically target two T cell target proteins, and the third and fourth polypeptide chains of the binding protein form an antigen binding site that specifically binds an HIV target protein. In some embodiments, the one or more HIV target proteins are one or more of glycoprotein 120, glycoprotein 41, and glycoprotein 160. In some embodiments, the one or more T cell target proteins are one or more of CD3 and CD28.

Linkers

[0195] In some embodiments, the linkers L₁, L₂, L₃, and L₄ range from no amino acids (length=0) to about 100 amino acids long, or less than 100, 50, 40, 30, 20, or 15 amino acids or less. The linkers can also be 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 amino acids long. L₁, L₂, L₃, and L₄ in one binding protein may all have the same amino acid sequence or may all have different amino acid sequences.

[0196] Examples of suitable linkers include a single glycine (Gly) residue; a diglycine peptide (Gly-Gly); a tripeptide (Gly-Gly-Gly); a peptide with four glycine residues (Gly-Gly-Gly-Gly; SEQ ID NO: 285); a peptide with five glycine residues (Gly-Gly-Gly-Gly-Gly; SEQ ID NO: 286); a peptide with six glycine residues (Gly-Gly-Gly-Gly-Gly-Gly; SEQ ID NO: 287); a peptide with seven glycine residues (Gly-Gly-Gly-Gly-Gly-Gly-Gly; SEQ ID NO: 288); a peptide with eight glycine residues (Gly-Gly-Gly-Gly-Gly-Gly-Gly-Gly; SEQ ID NO: 289). Other combinations of amino acid residues may be used such as the peptide Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 290), the peptide Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 291) and the peptide Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Ser (SEQ ID NO: 292). Other suitable linkers include a single Ser, and Val residue; the dipeptide Arg-Thr, Gln-Pro, Ser-Ser, Thr-Lys, and Ser-Leu; Thr-Lys-Gly-Pro-Ser (SEQ ID NO: 293), Thr-Val-Ala-Ala-Pro (SEQ ID NO: 294), Gln-Pro-Lys-Ala-Ala (SEQ ID NO: 295), Gln-Arg-Ile-Glu-Gly (SEQ ID NO: 296); Ala-Ser-Thr-Lys-Gly-Pro-Ser (SEQ ID NO: 297), Arg-Thr-Val-Ala-Ala-Pro-Ser (SEQ ID NO: 298), Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299), and His-Ile-Asp-Ser-Pro-Asn-Lys (SEQ ID NO: 300). The examples listed above are not intended to limit the scope of the disclosure in any way, and linkers comprising randomly selected amino acids selected from the group consisting of valine, leucine, isoleucine, serine, threonine, lysine, arginine, histidine, aspartate, glutamate, asparagine, glutamine, glycine, and proline have been shown to be suitable in the binding proteins.

[0197] The identity and sequence of amino acid residues in the linker may vary depending on the type of secondary structural element necessary to achieve in the linker. For example, glycine, serine, and alanine are best for linkers having maximum flexibility. Some combination of glycine, proline, threonine, and serine are useful if a more rigid and extended linker is necessary. Any amino acid residue may be considered as a linker in combination with other amino acid residues to construct larger peptide linkers as necessary depending on the desired properties.

[0198] In some embodiments, the length of L_1 is at least twice the length of L_3 . In some embodiments, the length of L_2 is at least twice the length of L_4 . In some embodiments, the length of L_1 is at least twice the length of L_3 , and the length of L_2 is at least twice the length of L_4 . In some embodiments, L_1 is 3 to 12 amino acid residues in length, L_2 is 3 to 14 amino acid residues in length, L_3 is 1 to 8 amino acid residues in length, and L_4 is 1 to 3 amino acid residues in length. In some embodiments, L_1 is 5 to 10 amino acid residues in length, L_2 is 5 to 8 amino acid residues in length, L_3 is 1 to 5 amino acid residues in length, and L_4 is 1 to 2 amino acid residues in length. In some embodiments, L_1 is 7 amino acid residues in length, L_2 is 5 amino acid residues in length, L_3 is 1 amino acid residue in length, and L_4 is 2 amino acid residues in length.

[0199] In some embodiments, L_1 , L_2 , L_3 , and/or L_4 comprise the sequence Asp-Lys-Thr-His-Thr (SEQ ID NO: 525). In some embodiments, L_1 comprises the sequence Asp-Lys-Thr-His-Thr (SEQ ID NO: 525). In some embodiments, L_3 comprises the sequence Asp-Lys-Thr-His-Thr (SEQ ID NO: 525).

[0200] In some embodiments, L_1 , L_2 , L_3 , and/or L_4 comprise the sequence Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299). In some embodiments, L_1 comprises the sequence Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299). In some embodiments, L_1 comprises the sequence Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299), L_2 comprises the sequence Thr-Lys-Gly-Pro-Ser-Arg (SEQ ID NO: 526), L_3 comprises the sequence Ser, and L_4 comprises the sequence Arg-Thr. In some embodiments, L_3 comprises the sequence Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299). In some embodiments, L_1 comprises the sequence Ser, L_2 comprises the sequence Arg-Thr, L_3 comprises the sequence Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299) and L_4 comprises the sequence Thr-Lys-Gly-Pro-Ser-Arg (SEQ ID NO: 526).

Fc regions and constant domains

[0201] In some embodiments, a binding protein of the present disclosure comprises a second polypeptide chain further comprising an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, a binding protein of the present disclosure comprises a third polypeptide chain further comprising an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains. In some embodiments, a binding protein of the present disclosure comprises a second polypeptide chain further comprising an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and a third polypeptide chain further comprising an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0202] To improve the yields of the binding proteins, in some embodiments, the C_{H3} domains can be altered by the "knob-into-holes" technology which is described in detail with several examples in, for example, International Publication No. WO 96/027011, Ridgway *et al.*, 1996, *Protein Eng.* 9: 617-21; and Merchant *et al.*, 1998, *Nat. Biotechnol.* 16: 677-81. Specifically, the interaction surfaces of the two C_{H3} domains are altered to increase the heterodimerisation of both heavy chains containing these two C_{H3} domains. Each of the two C_{H3} domains (of the two heavy chains) can be the "knob," while the other is the "hole." The introduction of a disulfide bridge further stabilizes the heterodimers (Merchant *et al.*, 1998; Atwell *et al.*, 1997, *J. Mol. Biol.* 270: 26-35) and increases the yield. In particular embodiments, the knob is on the second pair of polypeptides with a single variable domain. In other embodiments, the knob is on the first pair of polypeptides having the cross-over orientation. In yet other embodiments, the C_{H3} domains do not include a knob in hole.

[0203] In some embodiments, a binding protein of the present disclosure comprises a "knob" mutation on the second polypeptide chain and a "hole" mutation on the third polypeptide chain. In some embodiments, a binding protein of the present disclosure comprises a "knob" mutation on the third polypeptide chain and a "hole" mutation on the second polypeptide chain. In some embodiments, the "knob" mutation comprises substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index. In some embodiments, the amino acid substitutions are S354C and T366W. In some embodiments, the "hole" mutation comprises substitutions at positions corresponding to

positions 349, 366, 368, and 407 of human IgG1 according to EU Index. In some embodiments, the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V. In some embodiments, the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

[0204] In some embodiments, a binding protein of the present disclosure comprises one or more mutations to improve serum half-life (*See e.g.*, Hinton, P.R. *et al.* (2006) *J. Immunol.* 176(1):346-56). In some embodiments, the mutation comprises substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S. In some embodiments, the binding protein comprises a second polypeptide chain further comprising a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and a third polypeptide chain further comprising a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first and second Fc

regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S. In some embodiments, a binding protein of the present disclosure comprises knob and hole mutations and one or more mutations to improve serum half-life.

[0205] In some embodiments, C_{H1}, C_{H2}, C_{H3} and C_L of the trispecific binding proteins described herein may comprise any of C_{H1}, C_{H2}, C_{H3} and C_L sequences of binding proteins 1-53.

Nucleic acids

[0206] Standard recombinant DNA methodologies are used to construct the polynucleotides that encode the polypeptides which form the binding proteins, incorporate these polynucleotides into recombinant expression vectors, and introduce such vectors into host cells. *See e.g.*, Sambrook *et al.*, 2001, MOLECULAR CLONING: A LABORATORY MANUAL (Cold Spring Harbor Laboratory Press, 3rd ed.). Enzymatic reactions and purification techniques may be performed according to manufacturer's specifications, as commonly accomplished in the art, or as described herein. Unless specific definitions are provided, the nomenclature utilized in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well-known and commonly used in the art. Similarly, conventional techniques may be used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, delivery, and treatment of patients.

[0207] Other aspects of the present disclosure relate to isolated nucleic acid molecules comprising a nucleotide sequence encoding any of the binding proteins described herein. In some embodiments, the isolated nucleic acid is operably linked to a heterologous promoter to direct transcription of the binding protein-coding nucleic acid sequence. A promoter may refer to nucleic acid control sequences which direct transcription of a nucleic acid. A first nucleic acid sequence is operably linked to a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence of a binding protein if the promoter affects the transcription or expression of the coding sequence. Examples of promoters may include, but are not limited to, promoters obtained from the genomes of viruses (such as polyoma virus, fowlpox virus, adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B

virus, Simian Virus 40 (SV40), and the like), from heterologous eukaryotic promoters (such as the actin promoter, an immunoglobulin promoter, from heat-shock promoters, and the like), the CAG-promoter (Niwa et al., *Gene* 108(2):193-9, 1991), the phosphoglycerate kinase (PGK)-promoter, a tetracycline-inducible promoter (Masui et al., *Nucleic Acids Res.* 33:e43, 2005), the lac system, the trp system, the tac system, the trc system, major operator and promoter regions of phage lambda, the promoter for 3-phosphoglycerate kinase, the promoters of yeast acid phosphatase, and the promoter of the yeast alpha-mating factors. Polynucleotides encoding binding proteins of the present disclosure may be under the control of a constitutive promoter, an inducible promoter, or any other suitable promoter described herein or other suitable promoter that will be readily recognized by one skilled in the art.

[0208] In some embodiments, the isolated nucleic acid is incorporated into a vector. In some embodiments, the vector is an expression vector. Expression vectors may include one or more regulatory sequences operatively linked to the polynucleotide to be expressed. The term "regulatory sequence" includes promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Examples of suitable enhancers may include, but are not limited to, enhancer sequences from mammalian genes (such as globin, elastase, albumin, α -fetoprotein, insulin and the like), and enhancer sequences from a eukaryotic cell virus (such as SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, adenovirus enhancers, and the like). Examples of suitable vectors may include, for example, plasmids, cosmids, episomes, transposons, and viral vectors (e.g., adenoviral, vaccinia viral, Sindbis-viral, measles, herpes viral, lentiviral, retroviral, adeno-associated viral vectors, etc.). Expression vectors can be used to transfect host cells, such as, for example, bacterial cells, yeast cells, insect cells, and mammalian cells. Biologically functional viral and plasmid DNA vectors capable of expression and replication in a host are known in the art, and can be used to transfect any cell of interest.

[0209] Other aspects of the present disclosure relate to a vector system comprising one or more vectors encoding a first, second, third, and fourth polypeptide chain of any of the binding proteins described herein. In some embodiments, the vector system comprises a first vector encoding the first polypeptide chain of the binding protein, a second vector encoding the second polypeptide chain of the binding protein, a third vector encoding the third polypeptide chain of the binding protein, and a fourth vector encoding the fourth polypeptide chain of the binding protein. In some embodiments, the vector system comprises a first vector

encoding the first and second polypeptide chains of the binding protein, and a second vector encoding the third and fourth polypeptide chains of the binding protein. In some embodiments, the vector system comprises a first vector encoding the first and third polypeptide chains of the binding protein, and a second vector encoding the second and fourth polypeptide chains of the binding protein. In some embodiments, the vector system comprises a first vector encoding the first and fourth polypeptide chains of the binding protein, and a second vector encoding the second and third polypeptide chains of the binding protein. In some embodiments, the vector system comprises a first vector encoding the first, second, third, and fourth polypeptide chains of the binding protein. The one or more vectors of the vector system may be any of the vectors described herein. In some embodiments, the one or more vectors are expression vectors.

Host cells

[0210] Other aspects of the present disclosure relate to a host cell (*e.g.*, an isolated host cell) comprising one or more isolated polynucleotides, vectors, and/or vector systems described herein. In some embodiments, an isolated host cell of the present disclosure is cultured *in vitro*. In some embodiments, the host cell is a bacterial cell (*e.g.*, an *E. coli* cell). In some embodiments, the host cell is a yeast cell (*e.g.*, an *S. cerevisiae* cell). In some embodiments, the host cell is an insect cell. Examples of insect host cells may include, for example, *Drosophila* cells (*e.g.*, S2 cells), *Trichoplusia ni* cells (*e.g.*, High FiveTM cells), and *Spodoptera frugiperda* cells (*e.g.*, Sf21 or Sf9 cells). In some embodiments, the host cell is a mammalian cell. Examples of mammalian host cells may include, for example, human embryonic kidney cells (*e.g.*, 293 or 293 cells subcloned for growth in suspension culture), Expi293TM cells, CHO cells, baby hamster kidney cells (*e.g.*, BHK, ATCC CCL 10), mouse sertoli cells (*e.g.*, TM4 cells), monkey kidney cells (*e.g.*, CV1 ATCC CCL 70), African green monkey kidney cells (*e.g.*, VERO-76, ATCC CRL-1587), human cervical carcinoma cells (*e.g.*, HELA, ATCC CCL 2), canine kidney cells (*e.g.*, MDCK, ATCC CCL 34), buffalo rat liver cells (*e.g.*, BRL 3A, ATCC CRL 1442), human lung cells (*e.g.*, W138, ATCC CCL 75), human liver cells (*e.g.*, Hep G2, HB 8065), mouse mammary tumor cells (*e.g.*, MMT 060562, ATCC CCL51), TRI cells, MRC 5 cells, FS4 cells, a human hepatoma line (*e.g.*, Hep G2), and myeloma cells (*e.g.*, NS0 and Sp2/0 cells).

[0211] Other aspects of the present disclosure relate to a method of producing any of the binding proteins described herein. In some embodiments, the method includes a) culturing a host cell (*e.g.*, any of the host cells described herein) comprising an isolated nucleic acid,

vector, and/or vector system (*e.g.*, any of the isolated nucleic acids, vectors, and/or vector systems described herein) under conditions such that the host cell expresses the binding protein; and b) isolating the binding protein from the host cell. Methods of culturing host cells under conditions to express a protein are well known to one of ordinary skill in the art. Methods of isolating proteins from cultured host cells are well known to one of ordinary skill in the art, including, for example, by affinity chromatography (*e.g.*, two step affinity chromatography comprising protein A affinity chromatography followed by size exclusion chromatography).

Use for Binding Proteins

[0212] The binding proteins can be employed in any known assay method, such as competitive binding assays, direct and indirect sandwich assays, and immunoprecipitation assays for the detection and quantitation of one or more target antigens. The binding proteins will bind the one or more target antigens with an affinity that is appropriate for the assay method being employed.

[0213] For diagnostic applications, in certain embodiments, binding proteins can be labeled with a detectable moiety. The detectable moiety can be any one that is capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety can be a radioisotope, such as ^3H , ^{14}C , ^{32}P , ^{35}S , ^{125}I , ^{99}Tc , ^{111}In , or ^{67}Ga ; a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin; or an enzyme, such as alkaline phosphatase, β -galactosidase, or horseradish peroxidase.

[0214] The binding proteins are also useful for *in vivo* imaging. A binding protein labeled with a detectable moiety can be administered to an animal, *e.g.*, into the bloodstream, and the presence and location of the labeled antibody in the host assayed. The binding protein can be labeled with any moiety that is detectable in an animal, whether by nuclear magnetic resonance, radiology, or other detection means known in the art.

[0215] The disclosure also relates to a kit comprising a binding protein and other reagents useful for detecting target antigen levels in biological samples. Such reagents can include a detectable label, blocking serum, positive and negative control samples, and detection reagents. In some embodiments, the kit comprises a composition comprising any binding protein, polynucleotide, vector, vector system, and/or host cell described herein. In some embodiments, the kit comprises a container and a label or package insert on or associated with the container. Suitable containers include, for example, bottles, vials, syringes, IV solution bags, etc. The containers may be formed from a variety of materials such as glass or

plastic. The container holds a composition which is by itself or combined with another composition effective for treating, preventing and/or diagnosing a condition (*e.g.*, HIV infection) and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). In some embodiments, the label or package insert indicates that the composition is used for preventing, diagnosing, and/or treating the condition of choice. Alternatively, or additionally, the article of manufacture or kit may further comprise a second (or third) container comprising a pharmaceutically-acceptable buffer, such as bacteriostatic water for injection (BWFI), phosphate-buffered saline, Ringer's solution and dextrose solution. It may further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, and syringes.

[0216] Therapeutic or pharmaceutical compositions comprising binding proteins are within the scope of the disclosure. Such therapeutic or pharmaceutical compositions can comprise a therapeutically effective amount of a binding protein, or binding protein-drug conjugate, in admixture with a pharmaceutically or physiologically acceptable formulation agent selected for suitability with the mode of administration.

[0217] Acceptable formulation materials are nontoxic to recipients at the dosages and concentrations employed.

[0218] The pharmaceutical composition can contain formulation materials for modifying, maintaining, or preserving, for example, the pH, osmolarity, viscosity, clarity, color, isotonicity, odor, sterility, stability, rate of dissolution or release, adsorption, or penetration of the composition. Suitable formulation materials include, but are not limited to, amino acids (such as glycine, glutamine, asparagine, arginine, or lysine), antimicrobials, antioxidants (such as ascorbic acid, sodium sulfite, or sodium hydrogen-sulfite), buffers (such as borate, bicarbonate, Tris-HCl, citrates, phosphates, or other organic acids), bulking agents (such as mannitol or glycine), chelating agents (such as ethylenediamine tetraacetic acid (EDTA)), complexing agents (such as caffeine, polyvinylpyrrolidone, beta-cyclodextrin, or hydroxypropyl-beta-cyclodextrin), fillers, monosaccharides, disaccharides, and other carbohydrates (such as glucose, mannose, or dextrans), proteins (such as serum albumin, gelatin, or immunoglobulins), coloring, flavoring and diluting agents, emulsifying agents, hydrophilic polymers (such as polyvinylpyrrolidone), low molecular weight polypeptides, salt-forming counterions (such as sodium), preservatives (such as benzalkonium chloride, benzoic acid, salicylic acid, thimerosal, phenethyl alcohol, methylparaben, propylparaben,

chlorhexidine, sorbic acid, or hydrogen peroxide), solvents (such as glycerin, propylene glycol, or polyethylene glycol), sugar alcohols (such as mannitol or sorbitol), suspending agents, surfactants or wetting agents (such as pluronics; PEG; sorbitan esters; polysorbates such as polysorbate 20 or polysorbate 80; triton; tromethamine; lecithin; cholesterol or tyloxapal), stability enhancing agents (such as sucrose or sorbitol), tonicity enhancing agents (such as alkali metal halides – *e.g.*, sodium or potassium chloride – or mannitol sorbitol), delivery vehicles, diluents, excipients and/or pharmaceutical adjuvants (*see, e.g.*, REMINGTON'S PHARMACEUTICAL SCIENCES (18th Ed., A.R. Gennaro, ed., Mack Publishing Company 1990), and subsequent editions of the same, incorporated herein by reference for any purpose).

[0219] The optimal pharmaceutical composition will be determined by a skilled artisan depending upon, for example, the intended route of administration, delivery format, and desired dosage. Such compositions can influence the physical state, stability, rate of *in vivo* release, and rate of *in vivo* clearance of the binding protein.

[0220] The primary vehicle or carrier in a pharmaceutical composition can be either aqueous or non-aqueous in nature. For example, a suitable vehicle or carrier for injection can be water, physiological saline solution, or artificial cerebrospinal fluid, possibly supplemented with other materials common in compositions for parenteral administration. Neutral buffered saline or saline mixed with serum albumin are further exemplary vehicles. Other exemplary pharmaceutical compositions comprise Tris buffer of about pH 7.0-8.5, or acetate buffer of about pH 4.0-5.5, which can further include sorbitol or a suitable substitute. In one embodiment of the disclosure, binding protein compositions can be prepared for storage by mixing the selected composition having the desired degree of purity with optional formulation agents in the form of a lyophilized cake or an aqueous solution. Further, the binding protein can be formulated as a lyophilizate using appropriate excipients such as sucrose.

[0221] The pharmaceutical compositions of the disclosure can be selected for parenteral delivery or subcutaneous. Alternatively, the compositions can be selected for inhalation or for delivery through the digestive tract, such as orally. The preparation of such pharmaceutically acceptable compositions is within the skill of the art.

[0222] The formulation components are present in concentrations that are acceptable to the site of administration. For example, buffers are used to maintain the composition at

physiological pH or at a slightly lower pH, typically within a pH range of from about 5 to about 8.

[0223] When parenteral administration is contemplated, the therapeutic compositions for use can be in the form of a pyrogen-free, parenterally acceptable, aqueous solution comprising the desired binding protein in a pharmaceutically acceptable vehicle. A particularly suitable vehicle for parenteral injection is sterile distilled water in which a binding protein is formulated as a sterile, isotonic solution, properly preserved. Yet another preparation can involve the formulation of the desired molecule with an agent, such as injectable microspheres, bio-erodible particles, polymeric compounds (such as polylactic acid or polyglycolic acid), beads, or liposomes, that provides for the controlled or sustained release of the product which can then be delivered via a depot injection. Hyaluronic acid can also be used, and this can have the effect of promoting sustained duration in the circulation. Other suitable means for the introduction of the desired molecule include implantable drug delivery devices.

[0224] In one embodiment, a pharmaceutical composition can be formulated for inhalation. For example, a binding protein can be formulated as a dry powder for inhalation. Binding protein inhalation solutions can also be formulated with a propellant for aerosol delivery. In yet another embodiment, solutions can be nebulized.

[0225] It is also contemplated that certain formulations can be administered orally. In one embodiment of the disclosure, binding proteins that are administered in this fashion can be formulated with or without those carriers customarily used in the compounding of solid dosage forms such as tablets and capsules. For example, a capsule can be designed to release the active portion of the formulation at the point in the gastrointestinal tract where bioavailability is maximized and pre-systemic degradation is minimized. Additional agents can be included to facilitate absorption of the binding protein. Diluents, flavorings, low melting point waxes, vegetable oils, lubricants, suspending agents, tablet disintegrating agents, and binders can also be employed.

[0226] Another pharmaceutical composition can involve an effective quantity of binding proteins in a mixture with non-toxic excipients that are suitable for the manufacture of tablets. By dissolving the tablets in sterile water, or another appropriate vehicle, solutions can be prepared in unit-dose form. Suitable excipients include, but are not limited to, inert diluents, such as calcium carbonate, sodium carbonate or bicarbonate, lactose, or calcium

phosphate; or binding agents, such as starch, gelatin, or acacia; or lubricating agents such as magnesium stearate, stearic acid, or talc.

[0227] Additional pharmaceutical compositions of the disclosure will be evident to those skilled in the art, including formulations involving binding proteins in sustained- or controlled-delivery formulations. Techniques for formulating a variety of other sustained- or controlled-delivery means, such as liposome carriers, bio-erodible microparticles or porous beads and depot injections, are also known to those skilled in the art. Additional examples of sustained-release preparations include semipermeable polymer matrices in the form of shaped articles, *e.g.* films, or microcapsules. Sustained release matrices can include polyesters, hydrogels, polylactides, copolymers of L-glutamic acid and gamma ethyl-L-glutamate, poly(2-hydroxyethyl-methacrylate), ethylene vinyl acetate, or poly-D(-)-3-hydroxybutyric acid. Sustained-release compositions can also include liposomes, which can be prepared by any of several methods known in the art.

[0228] Pharmaceutical compositions to be used for *in vivo* administration typically must be sterile. This can be accomplished by filtration through sterile filtration membranes. Where the composition is lyophilized, sterilization using this method can be conducted either prior to, or following, lyophilization and reconstitution. The composition for parenteral administration can be stored in lyophilized form or in a solution. In addition, parenteral compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

[0229] Once the pharmaceutical composition has been formulated, it can be stored in sterile vials as a solution, suspension, gel, emulsion, solid, or as a dehydrated or lyophilized powder. Such formulations can be stored either in a ready-to-use form or in a form (*e.g.*, lyophilized) requiring reconstitution prior to administration.

[0230] The disclosure also encompasses kits for producing a single-dose administration unit. The kits can each contain both a first container having a dried protein and a second container having an aqueous formulation. Also included within the scope of this disclosure are kits containing single and multi-chambered pre-filled syringes (*e.g.*, liquid syringes and lyosyringes).

[0231] The effective amount of a binding protein pharmaceutical composition to be employed therapeutically will depend, for example, upon the therapeutic context and objectives. One skilled in the art will appreciate that the appropriate dosage levels for

treatment will thus vary depending, in part, upon the molecule delivered, the indication for which the binding protein is being used, the route of administration, and the size (body weight, body surface, or organ size) and condition (the age and general health) of the patient. Accordingly, the clinician can titer the dosage and modify the route of administration to obtain the optimal therapeutic effect.

[0232] Dosing frequency will depend upon the pharmacokinetic parameters of the binding protein in the formulation being used. Typically, a clinician will administer the composition until a dosage is reached that achieves the desired effect. The composition can therefore be administered as a single dose, as two or more doses (which may or may not contain the same amount of the desired molecule) over time, or as a continuous infusion via an implantation device or catheter. Further refinement of the appropriate dosage is routinely made by those of ordinary skill in the art and is within the ambit of tasks routinely performed by them. Appropriate dosages can be ascertained through use of appropriate dose-response data.

[0233] The route of administration of the pharmaceutical composition is in accord with known methods, *e.g.*, orally; through injection by intravenous, intraperitoneal, intracerebral (intraparenchymal), intracerebroventricular, intramuscular, intraocular, intraarterial, intraportal, or intralesional routes; by sustained release systems; or by implantation devices. Where desired, the compositions can be administered by bolus injection or continuously by infusion, or by implantation device.

[0234] The composition can also be administered locally via implantation of a membrane, sponge, or other appropriate material onto which the desired molecule has been absorbed or encapsulated. Where an implantation device is used, the device can be implanted into any suitable tissue or organ, and delivery of the desired molecule can be via diffusion, timed-release bolus, or continuous administration.

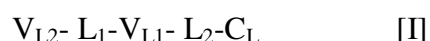
[0235] The pharmaceutical compositions can be used to prevent and/or treat HIV infection. The pharmaceutical compositions can be used as a standalone therapy or in combination with standard anti-retroviral therapy.

[0236] In some embodiments, the present disclosure relates to a method of preventing and/or treating HIV infection in a patient. In some embodiments, the method comprises administering to the patient a therapeutically effective amount of at least one of the binding proteins described herein. In some embodiments, the at least one binding protein is administered in combination with an anti-retroviral therapy (*e.g.*, an anti-HIV therapy). In

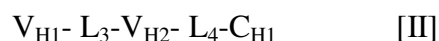
some embodiments, the at least one binding protein is administered before the anti-retroviral therapy. In some embodiments, the at least one binding protein is administered concurrently with the anti-retroviral therapy. In some embodiments, the at least one binding protein is administered after the anti-retroviral therapy. In some embodiments, the at least one binding protein is co-administered with any standard anti-retroviral therapy known in the art. In some embodiments, administration of the at least one binding protein results in neutralization of one or more HIV virions. In some embodiments, administration of the at least one binding protein results in elimination of one or more latently and/or chronically HIV-infected cells in the patient. In some embodiments, administration of the at least one binding protein results in neutralization of one or more HIV virions and results in elimination of one or more latently and/or chronically HIV-infected cells in the patient. In some embodiments, the patient is a human.

[0237] Without limiting the present disclosure, a number of embodiments of the present disclosure are described below for purpose of illustration.

[0238] Item 1: A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

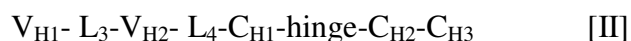
L₁, L₂, L₃, and L₄ are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

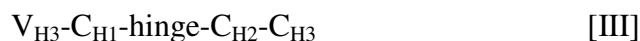
[0239] Item 2: A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L₁, L₂, L₃ and L₄ are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0240] Item 3: The binding protein of item 1 or item 2, wherein the one or more HIV target proteins is selected from the group consisting of glycoprotein 120, glycoprotein 41 and glycoprotein 60.

[0241] Item 4: The binding protein of item 1 or item 2, wherein the binding protein is trispecific and capable of specifically binding three different epitopes on a single HIV target protein.

[0242] Item 5: The binding protein of item 1 or item 2, wherein the binding protein is trispecific and capable of specifically binding two different epitopes on a first HIV target protein, and one epitope on a second HIV target protein, wherein the first and second HIV target proteins are different.

[0243] Item 6: The binding protein of item 1 or item 2, wherein the binding protein is trispecific and capable of specifically binding three different antigen targets.

[0244] Item 7: The binding protein of item 1 or item 2, wherein the binding protein is capable of inhibiting the function of one or more HIV target proteins.

[0245] Item 8: The binding protein of any one of items 1-7, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively.

[0246] Item 9: The binding protein of any one of items 1-7, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

[0247] Item 10: The binding protein of any one of items 1-9, wherein V_{L1} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

[0248] Item 11: The binding protein of any one of items 1-10, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively.

[0249] Item 12: The binding protein of any one of items 1-10, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

[0250] Item 13: The binding protein of any one of items 1-12, wherein V_{L2} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

[0251] Item 14: The binding protein of any one of items 1-13, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively.

[0252] Item 15: The binding protein of any one of items 1-13, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

[0253] Item 16: The binding protein of any one of items 1-15, wherein V_{L3} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

[0254] Item 17: The binding protein of any one of items 1-16, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively.

[0255] Item 18: The binding protein of any one of items 1-16, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

[0256] Item 19: The binding protein of any one of items 1-18, wherein V_{H1} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

[0257] Item 20: The binding protein of any one of items 1-19, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively.

[0258] Item 21: The binding protein of any one of items 1-19, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

[0259] Item 22: The binding protein of any one of items 1-21, wherein V_{H2} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

[0260] Item 23: The binding protein of any one of items 1-22, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively.

[0261] Item 24: The binding protein of any one of items 1-22, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

[0262] Item 25: The binding protein of any one of items 1-24, wherein V_{H3} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

[0263] Item 26: The binding protein of any one of items 1-25, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence

of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 266, a CDR-L2 comprising the sequence of SEQ ID NO: 267, and a CDR-L3 comprising the sequence of SEQ ID NO: 268; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 248, a CDR-H2 comprising the sequence of SEQ ID NO: 497, and a CDR-H3 comprising the sequence of SEQ ID NO: 250.

[0264] Item 27: The binding protein of any one of items 1-25, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 512; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 502.

[0265] Item 28: The binding protein of any one of items 1-27, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 512; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 502.

[0266] Item 29: The binding protein of any one of items 1-25, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence

of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

[0267] Item 30: The binding protein of any one of items 1-25, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

[0268] Item 31: The binding protein of any one of items 1-25 and 29-30, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

[0269] Item 32: The binding protein of any one of items 1-25, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence

of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

[0270] Item 33: The binding protein of any one of items 1-25, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

[0271] Item 34: The binding protein of any one of items 1-25 and 32-33, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

[0272] Item 35: The binding protein of item 1, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0273] Item 36: The binding protein of item 1, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0274] Item 37: The binding protein of item 1, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0275] Item 38: The binding protein of item 1, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

[0276] Item 39: The binding protein of any one of items 1, 37, and 38, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and

C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0277] Item 40: The binding protein of item 2, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0278] Item 41: The binding protein of item 2, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

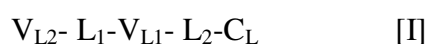
[0279] Item 42: The binding protein of any one of items 2, 40, and 41, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0280] Item 43: The binding protein of item 1 or item 2, wherein at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length.

[0281] Item 44: The binding protein of item 1 or item 2, wherein L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length.

[0282] Item 45: The binding protein of any one of items 1-44, wherein L₁ comprises Asp-Lys-Thr-His-Thr (SEQ ID NO: 525).

[0283] Item 46: A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:

$$V_{H1}-L_3-V_{H2}-L_4-C_{H1} \quad [II]$$

and a third polypeptide chain comprises a structure represented by the formula:

$$V_{H3}-C_{H1} \quad [III]$$

and a fourth polypeptide chain comprises a structure represented by the formula:

$$V_{L3}-C_L \quad [IV]$$

wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124, 130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and

wherein:

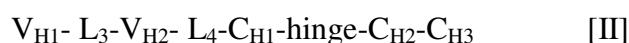
(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 10, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123, 129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265.

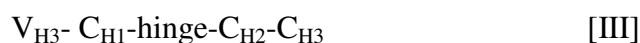
[0284] Item 47: A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124,

130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and
wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 10, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123, 129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265.

[0285] Item 48: The binding protein of item 46, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0286] Item 49: The binding protein of item 46, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0287] Item 50: The binding protein of item 46, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1} , the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0288] Item 51: The binding protein of item 46, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an

immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

[0289] Item 52: The binding protein of any one of items 46, 50, and 51, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0290] Item 53: The binding protein of item 47, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0291] Item 54: The binding protein of item 47, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

[0292] Item 55: The binding protein of any one of items 47, 53, and 54, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0293] Item 56: The binding protein of item 46 or item 47, wherein at least one of L₁, L₂, L₃ or L₄ is independently 0 amino acids in length.

[0294] Item 57: The binding protein of item 46 or item 47, wherein L₁, L₂, L₃ or L₄ are each independently at least one amino acid in length.

[0295] Item 58: The binding protein of any one of items 46-57, wherein L₁ comprises Asp-Lys-Thr-His-Thr (SEQ ID NO: 525).

[0296] Item 59: A binding protein comprising a first polypeptide chain, a second polypeptide chain, a third polypeptide chain and a fourth polypeptide chain wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 4; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 3 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 3; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 1 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 2;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 12; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 11 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 11; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 9; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 10 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 10;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 20; the second polypeptide chain comprises the amino acid sequence of SEQ

ID NO: 19 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 19; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 17 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 17; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 18 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 18;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 28 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 28; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 27 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 27; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 25 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 25; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 26 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 26;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 36 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 36; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 35 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 35; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 33 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 33; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 34 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 34;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 44 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 44; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 43 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 43; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 41 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 41; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 42 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 42;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 52 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 52; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 51 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 49 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 49; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 50 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 60 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 60; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 59 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 59; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 57 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 57; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 58 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 58;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 68 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 68; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 67 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 67; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 65 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 65; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 66 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 66;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 76 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 76; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 75 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 75; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 73 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 73; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 74 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 74;

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 84 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 84; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 83 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 83; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 81 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 81; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 82 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 82;

(l) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 92 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 92; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 91 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 91; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 89 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 89; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 90 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 90;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 100 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 100; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 99 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 99; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 97 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 97; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 98 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 98;

(n) the first polypeptide comprises the amino acid sequence of SEQ ID NO: 108 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 108; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:

107 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 107; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 105 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 105; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 106;

(o) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 116 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 116; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 115; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 113 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 113; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 114;

(p) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 124 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 124; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 123 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 123; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 121 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 121; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 122 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 122;

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 132 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 132; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 131 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 131; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 129 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 129; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 130 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 130;

(r) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 140 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 140; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 139 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 139; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 137; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 138;

(s) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 148 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 148; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 147 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 147; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 145 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 145; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 146 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 146;

(t) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 156 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 156; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 155 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 155; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 153 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 153; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 154 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 154;

(u) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 164 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 164; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 163 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 163; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 161 or an amino acid sequence that is at least 95% identical to the

amino acid sequence of SEQ ID NO: 161; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 162 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 162;

(v) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 172 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 172; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 171 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 171; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 169 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 169; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 170 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 170;

(w) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 180 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 180; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 179 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 179; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 177 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 177; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 178 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 178;

(x) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 188 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 188; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 187 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 187; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 185 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 185; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 186 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 186;

(y) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 196 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 196; the second polypeptide chain comprises the amino acid sequence of SEQ

ID NO: 195 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 195; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 193 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 193; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 194 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 194;

(z) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 204 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 204; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 203 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 203; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 201 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 201; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 202 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 202;

(aa) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 212 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 212; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 211 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 211; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 209 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 209; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 210 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 210;

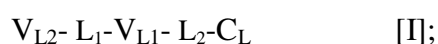
(bb) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 220 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 220; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 219 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 219; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 217 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 217; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 218 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 218;

(cc) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 228 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 228; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 227 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 227; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 225 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 225; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 226 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 226;

(dd) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 235 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 235; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 234 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 234; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 232 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 232; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 233 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 233; or

(ee) first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 243 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 243; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 242 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 242; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 240 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 240; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 241 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 241.

[0297] Item 60: A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins and one or more T cell target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



a second polypeptide chain comprises a structure represented by the formula:

$$V_{H1}-L_3-V_{H2}-L_4-C_{H1} \quad [II];$$

a third polypeptide chain comprises a structure represented by the formula:

$$V_{H3}-C_{H1} \quad [III];$$

and a fourth polypeptide chain comprises a structure represented by the formula:

$$V_{L3}-C_L \quad [IV];$$

wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0298] Item 61: A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins and one or more T cell target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:

$$V_{L2}-L_1-V_{L1}-L_2-C_L \quad [I];$$

a second polypeptide chain comprises a structure represented by the formula:

$$V_{H1}-L_3-V_{H2}-L_4-C_{H1}-\text{hinge}-C_{H2}-C_{H3} \quad [II];$$

a third polypeptide chain comprises a structure represented by the formula:

$$V_{H3}-C_{H1}-\text{hinge}-C_{H2}-C_{H3} \quad [III];$$

and a fourth polypeptide chain comprises a structure represented by the formula:

$$V_{L3}-C_L \quad [IV];$$

wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;
 V_{H3} is a third immunoglobulin heavy chain variable domain;
 C_L is an immunoglobulin light chain constant domain;
 C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;
 C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;
 C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;
hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and
 L_1 , L_2 , L_3 , and L_4 are amino acid linkers;
and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

[0299] Item 62: The binding protein of item 60 or item 61, wherein the one or more HIV target proteins are selected from the group consisting of glycoprotein 120, glycoprotein 41 and glycoprotein 160.

[0300] Item 63: The binding protein of item 60 or item 61, wherein the one or more T cell target proteins are CD3 or CD28.

[0301] Item 64: The binding protein of item 60 or item 61, wherein the binding protein is trispecific and capable of specifically binding an HIV target protein and two different epitopes on a single T cell target protein.

[0302] Item 65: The binding protein of item 60 or item 61, wherein the binding protein is trispecific and capable of specifically binding an HIV target protein and two different T cell target proteins.

[0303] Item 66: The binding protein of item 60 or item 61, wherein the binding protein is trispecific and capable of specifically binding a T cell target protein and two different epitopes on a single HIV target protein.

[0304] Item 67: The binding protein of item 60 or item 61, wherein the binding protein is trispecific and capable of specifically binding a T cell target protein and two different HIV target proteins.

[0305] Item 68: The binding protein of item 60 or item 61, wherein the first and second polypeptide chains form two antigen binding sites that specifically target two T cell target proteins, and the third and fourth polypeptide chains form an antigen binding site that specifically binds an HIV target protein.

[0306] Item 69: The binding protein of any one of items 60-68, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266,

267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively.

[0307] Item 70: The binding protein of any one of items 60-68, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0308] Item 71: The binding protein of any one of items 60-70, wherein V_{L1} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0309] Item 72: The binding protein of any one of items 60-71, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively.

[0310] Item 73: The binding protein of any one of items 60-71, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0311] Item 74: The binding protein of any one of items 60-73, wherein V_{L2} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0312] Item 75: The binding protein of any one of items 60-74, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271,

respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively.

[0313] Item 76: The binding protein of any one of items 60-74, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0314] Item 77: The binding protein of any one of items 60-76, wherein V_{L3} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

[0315] Item 78: The binding protein of any one of items 60-77, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively.

[0316] Item 79: The binding protein of any one of items 60-77, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0317] Item 80: The binding protein of any one of items 60-79, wherein V_{H1} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0318] Item 81: The binding protein of any one of items 60-80, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253,

respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively.

[0319] Item 82: The binding protein of any one of items 60-80, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0320] Item 83: The binding protein of any one of items 60-82, wherein V_{H2} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0321] Item 84: The binding protein of any one of items 60-83, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively.

[0322] Item 85: The binding protein of any one of items 60-83, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0323] Item 86: The binding protein of any one of items 60-85, wherein V_{H3} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

[0324] Item 87: The binding protein of any one of items 60-86, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 488, a CDR-L2 comprising the sequence

of SEQ ID NO: 489, and a CDR-L3 comprising the sequence of SEQ ID NO: 490; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 494, a CDR-L2 comprising the sequence of SEQ ID NO: 495, and a CDR-L3 comprising the sequence of SEQ ID NO: 496; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 479, a CDR-H2 comprising the sequence of SEQ ID NO: 480, and a CDR-H3 comprising the sequence of SEQ ID NO: 481; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 485, a CDR-H2 comprising the sequence of SEQ ID NO: 486, and a CDR-H3 comprising the sequence of SEQ ID NO: 487; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

[0325] Item 88: The binding protein of any one of items 60-86, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 522; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 524; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 509; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 511; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

[0326] Item 89: The binding protein of any one of items 60-88, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 522; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 524; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 509; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 511; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

[0327] Item 90: The binding protein of any one of items 60-86, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 494, a CDR-L2 comprising the sequence

of SEQ ID NO: 495, and a CDR-L3 comprising the sequence of SEQ ID NO: 496; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 488, a CDR-L2 comprising the sequence of SEQ ID NO: 489, and a CDR-L3 comprising the sequence of SEQ ID NO: 490; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 485, a CDR-H2 comprising the sequence of SEQ ID NO: 486, and a CDR-H3 comprising the sequence of SEQ ID NO: 487; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 479, a CDR-H2 comprising the sequence of SEQ ID NO: 480, and a CDR-H3 comprising the sequence of SEQ ID NO: 481; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

[0328] Item 91: The binding protein of any one of items 60-86, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 524; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 522; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 511; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 509; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

[0329] Item 92: The binding protein of any one of items 60-86 and 90-91, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 524; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 522; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 511; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 509; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

[0330] Item 93: The binding protein of item 60, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0331] Item 94: The binding protein of item 60, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0332] Item 95: The binding protein of item 60, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0333] Item 96: The binding protein of item 60, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

[0334] Item 97: The binding protein of any one of items 60, 95, and 96, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and

C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0335] Item 98: The binding protein of item 61, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0336] Item 99: The binding protein of item 61, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

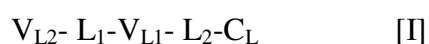
[0337] Item 100: The binding protein of any one of items 61, 98, and 99, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0338] Item 101: The binding protein of item 60 or item 61, wherein at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length.

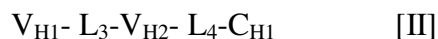
[0339] Item 102: The binding protein of item 60 or item 61, wherein L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length.

[0340] Item 103: The binding protein of any one of items 60-102, wherein L₁ is Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299).

[0341] Item 104: A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383, 385, 391, 393, 399, 401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and

wherein:

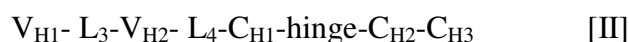
(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

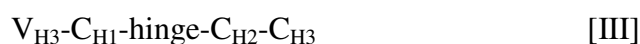
[0342] Item 105: A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383, 385, 391, 393, 399,

401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

[0343] Item 106: The binding protein of item 104, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0344] Item 107: The binding protein of item 104, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

[0345] Item 108: The binding protein of item 104, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1} , the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0346] Item 109: The binding protein of item 104, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an

immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

[0347] Item 110: The binding protein of any one of items 104, 108, and 109, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0348] Item 111: The binding protein of item 105, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

[0349] Item 112: The binding protein of item 105, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

[0350] Item 113: The binding protein of any one of items 105, 111, and 112, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

[0351] Item 114: The binding protein of item 104 or item 105, wherein at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length.

[0352] Item 115: The binding protein of item 104 or item 105, wherein L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length.

[0353] Item 116: The binding protein of any one of items 104-115, wherein L₁ is Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299).

[0354] Item 117: A binding protein comprising a first polypeptide chain, a second polypeptide chain, a third polypeptide chain and a fourth polypeptide chain wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 305 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 305; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 304 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 304; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 302 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 302; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 303 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 303;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 313 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 313; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 312 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 312; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 310 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 310; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 311 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 311;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 321 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 321; the second polypeptide chain comprises the amino acid sequence of SEQ ID

NO: 320 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 320; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 318 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 318; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 319 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 319;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 329 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 329; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 328 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 328; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 326 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 326; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 327 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 327;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 337 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 337; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 336 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 336; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 334 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 334; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 335 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 335;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 345 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 345; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 344 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 344; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 342 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 342; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 343 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 343;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 353 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 353; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 352 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 352; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 350 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 350; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 351 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 351;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 361 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 361; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 360 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 360; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 358 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 358; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 359 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 359;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 369 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 369; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 368 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 368; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 366 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 366; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 367 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 367;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 377 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 377; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 376 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 376; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 374 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 374; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 375 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 375;

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 385 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 385; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 384 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 384; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 382 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 382; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 383 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 383;

(l) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 393 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 393; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 392 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 392; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 390 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 390; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 391 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 391;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 401 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 401; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 400 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 400; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 398 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 398; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 399 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 399;

(n) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 409 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 409; the second polypeptide chain comprises the amino acid sequence of SEQ ID

NO: 408 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 408; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 406 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 406; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 407 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 407;

(p) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 417 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 417; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 416 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 416; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 414 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 414; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 415 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 415;

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 425 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 425; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 424 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 424; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 422 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 422; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 423 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 423;

(r) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 433 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 433; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 432 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 432; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 430 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 430; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 431 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 431;

(s) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 441 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 441; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 440 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 440; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 438 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 438; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 439 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 439;

(t) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 449 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 449; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 448 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 448; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 446 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 446; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 447 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 447;

(u) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 457 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 457; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 456 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 456; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 454 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 454; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 455 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 455;

(v) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 465 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 465; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 464 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 464; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 462 or an amino acid sequence that is at least 95% identical to the

amino acid sequence of SEQ ID NO: 462; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 463 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 463; or

(w) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 473 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 473; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 472 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 472; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 470 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 470; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 471 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 471.

[0355] Item 118: An isolated nucleic acid molecule comprising a nucleotide sequence encoding the binding protein of any one of items 1-117.

[0356] Item 119: An expression vector comprising the nucleic acid molecule of item 118.

[0357] Item 120: An isolated host cell comprising the nucleic acid molecule of item 118.

[0358] Item 121: An isolated host cell comprising the expression vector of item 119.

[0359] Item 122: The isolated host cell of item 120 or item 121, wherein the host cell is a mammalian cell or an insect cell.

[0360] Item 123: A vector system comprising one or more vectors encoding a first, second, third, and fourth polypeptide chain of a binding protein of any one of items 1-117.

[0361] Item 124: The vector system of item 123, wherein the vector system comprises a first vector encoding the first polypeptide chain of the binding protein, a second vector encoding the second polypeptide chain of the binding protein, a third vector encoding the third polypeptide chain of the binding protein, and a fourth vector encoding the fourth polypeptide chain of the binding protein.

[0362] Item 125: The vector system of item 123, wherein the vector system comprises a first vector encoding the first and second polypeptide chains of the binding protein, and a second vector encoding the third and fourth polypeptide chains of the binding protein.

[0363] Item 126: The vector system of any one of items 123-125, wherein the one or more vectors are expression vectors.

[0364] Item 127: An isolated host cell comprising the vector system of any one of items 123-126.

[0365] Item 128: The isolated host cell of item 127, wherein the host cell is a mammalian cell or an insect cell.

[0366] Item 129: A method of producing a binding protein, the method comprising:
a) culturing a host cell of any one of items 120-122 and items 127-128 under conditions such that the host cell expresses the binding protein; and
b) isolating the binding protein from the host cell.

[0367] Item 130: A method of preventing and/or treating HIV infection in a patient comprising administering to the patient a therapeutically effective amount of at least one binding protein of any one of items 1-117.

[0368] Item 131: The method of item 130, wherein the binding protein is co-administered with standard anti-retroviral therapy.

[0369] Item 132: The method of item 130 or item 131, wherein administration of the at least one binding protein results in the neutralization of one or more HIV virions.

[0370] Item 133: The method of any one of items 130-132, wherein administration of the at least one binding protein results in the elimination of one or more latently and/or chronically HIV-infected cells in the patient.

[0371] Item 134: The method of any one of items 130-133, wherein the patient is a human.

[0372] Item 135: The binding protein of any one of items 1-117 for the prevention or treatment of an HIV infection in a patient.

[0373] Item 136: The binding protein of item 135, wherein the binding protein is co-administered with standard anti-retroviral therapy.

[0374] Item 137: The binding protein of item 135 or item 136, wherein the binding protein causes the neutralization of one or more HIV virions in the patient.

[0375] Item 138: The binding protein of any one of items 135-137, wherein the binding protein causes the elimination of one or more latently and/or chronically HIV-infected cells in the patient.

[0376] Item 139: The binding protein of any one of items 135-138, wherein the patient is a human.

EXAMPLES

[0377] The Examples that follow are illustrative of specific embodiments of the disclosure, and various uses thereof. They are set forth for explanatory purposes only, and should not be construed as limiting the scope of the invention in any way.

Example 1: production of trispecific binding proteins targeting the HIV-1 Env glycoprotein.

[0378] The HIV-1 envelope glycoprotein (Env/gp160) is located on the surface of the virus particle, and is composed of a homo-trimer comprising three non-covalently-linked transmembrane gp41 and gp120 complexes. Env enables viral entry into target cells by the binding of gp120 to HIV's main receptor (CD4) and co-receptor (CCR5 or CXCR4), followed by the induction of viral/cellular membrane fusion facilitated by conformational changes in gp41, resulting in entry of the viral capsid and delivery of the viral genome into the host cell. Additionally, Env is expressed on the surface of infected cells.

[0379] Env acts as the only target for neutralizing antibodies on the HIV-1 virion. Binding of neutralizing antibodies to viral Env inhibits viral attachment/entry. Moreover, binding of neutralizing antibodies to HIV-1 infected, Env expressing cells leads to their destruction by Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) and Complement Dependent Cytotoxicity (CDC), resulting in reduction of the latent viral reservoir. Thus, neutralizing antibodies targeting Env are an attractive area for anti-viral therapy development. However, because of the high sequence diversity and mutation rate of the HIV-1 virus, developing neutralizing antibodies targeting Env has proven challenging due to the high likelihood that a given HIV-1 strain either lacks the epitope of any given neutralizing antibody, or the strain has evolved a mutation to become resistant to the antibody. Strategies must be developed to mitigate the breakthrough of viral strains when developing novel neutralizing antibodies targeting HIV-1. The studies described herein explore the development of novel trispecific binding proteins comprising four polypeptides forming three antigen binding sites that specifically bind three different epitopes on the HIV Env glycoprotein, and use of these novel trispecific binding proteins in neutralizing HIV-1.

Methods

Binding protein production and purification

[0380] The vectors expressing the trispecific binding proteins were constructed by inserting the designed heavy and light chain genes into a mammalian expression vector.

Corresponding heavy and light chain pairing occurred spontaneously, and heterodimer formation was promoted by Knob-in-Hole mutations engineered in the Fc region.

[0381] Binding proteins were produced in Expi293 cells by cotransfection of four expression plasmids (Life Technologies, Expi293TM Expression System Kit, Cat. No. A14635). Binding proteins were purified using a two-step purification scheme. First, binding proteins were captured on protein A affinity chromatography resin, washed, and then eluted in glycine at pH 3.0. The eluted proteins were then dialyzed in PBS, concentrated, and filtered. The filtered antibodies were further purified using a Superdex 200 SEC column to obtain monomeric binding proteins.

Affinity measurements of the binding proteins

[0382] Binding affinities of anti-HIV trispecific binding proteins were measured by surface plasmon resonance (SPR) using a Biacore3000 instrument (GE Healthcare). The assay buffer used was HBS-EP (GE Healthcare).

[0383] The affinity of the indicated proteins for the MPER binding site on the HIV-1 protein gp41 was measured by surface plasmon resonance (SPR) analysis using a Biacore Instrument as follows: binding proteins were first captured on a CM5 chip coupled with anti-human Fc antibody, followed by flow through of varying concentrations (100 nM – 6.25 nM) of the MPER binding peptide (Acetyl-

RRRNEQEELLELDKWASLWNWFDITNWLWYIRRR-Ttds-Lys-(Biotin)-NH₂) (SEQ ID NO: 284) at 30 µL per minute, and binding was detected by measurement of association for 240 seconds, and dissociation for 300 seconds on a Biacore 3000 at 25°C. HBS-EP buffer was used for sample dilution, as well as running buffer. Regeneration of the chip was done with 3 M MgCl₂ at 30 µL per minute. For data analysis the BIAevaluation software v.4.1 (GE Healthcare) was used. Data were fit globally using a 1:1 Langmuir model with mass transfer. After software-based curve fitting, the ON and OFF rates at each concentration of MPER binding peptide was calculated and used to obtain a binding affinity for each binding protein.

[0384] The affinity of the indicated proteins for the CD4BS binding site on the HIV-1 protein gp120 was measured by SPR as follows: recombinant HIV-1 gp120 (Thr27-Arg498) protein (HIV-1 /Clade B/C (CN54), ARCO Biosystems (Cat. # GP4-V15227)) was captured on a CM5 chip, followed by flow through of varying concentrations (100 nM – 6.25 nM) of the binding proteins, and binding was detected by measurement of association for 240 seconds, and dissociation for 300 seconds on a Biacore 3000 at 25°C. HBS-EP buffer was used for sample dilution, as well as running buffer. Regeneration of the chip was done with 3

M MgCl₂ at 30 µL per minute. For data analysis the BIAevaluation software v.4.1 (GE Healthcare) was used. Data were fit globally using a 1:1 Langmuir model with mass transfer. After software-based curve fitting, the ON and OFF rates at each concentration of Binding Protein was calculated and used to obtain a binding affinity for each binding protein.

Conformational stability and aggregation assays

[0385] Conformational stability of the trispecific binding proteins was assessed by determining the melting point T_m and aggregation onset temperature (T_{agg}).

[0386] Melting point T_m measurements were performed by differential scanning fluorimetry (DSF). Samples were diluted in D-PBS buffer (Invitrogen) to a final concentration of 0.2 µg/µL including a 4X concentration solution of SYPRO-Orange dye (Invitrogen, 5000X stock in DMSO) in D-PBS in white semi-skirt 96-well plates (BIORAD). All measurements were done in duplicate using a MyiQ2 real time PCR instrument (BIORAD). Negative first derivative curves ($-d(RFU)/dT$) of the melting curves were generated in the iQ5 software v2.1 (BIORAD). Data were then exported into Excel for T_m determination and graphical display.

[0387] Melting Point T_m and aggregation onset temperature (T_{agg}) were also measured by static light scattering (SLS) using a Unit instrument (Unchained Labs). 9µL of each sample was loaded undiluted into a multicuvette array. The samples were then heated from 20°C to 95°C at a heating rate of 0.3°C/minute. The barycentric mean (BCM) of the tryptophan fluorescence spectra was used to measure the protein melting curve, and determine the T_m values. The 266 nm static light scattering (SLS) signal was used to measure the aggregation curve and determine the T_{agg} . Data analysis was performed using the Unit analysis software v2.1.

Results

[0388] A novel strategy was developed for improving neutralizing antibody efficacy against HIV-1, while concomitantly limiting the likelihood of viral breakthrough due to high sequence diversity and/or viral mutation. This strategy involved the generation of trispecific binding proteins comprising four polypeptides that formed three antigen binding sites that specifically bind three different epitopes on the HIV Env glycoprotein (**FIG. 1**). Each antigen binding site comprised the V_H and V_L domain from a different HIV-1 neutralizing antibody that targeted a distinct epitope on the Env glycoprotein. The trispecific binding proteins contained a first pair of polypeptides that possessed dual variable domains having a cross-over orientation forming two distinct antigen binding sites (called the CODV Ig format), and

a second pair of polypeptides, each with a single variable domain that formed a third antigen binding site (**FIGS. 1A and 1B**).

[0389] The first pair of polypeptides (that possessed the dual variable domains) comprised a first polypeptide having the structure V_{L2} -Linker- V_{L1} -Linker-Immunoglobulin light chain constant domain, and a second polypeptide having the structure V_{H1} -Linker- V_{H2} -Linker-Immunoglobulin C_{H1} , hinge, C_{H2} , and C_{H3} heavy chain constant domains, resulting in a pair of polypeptides which had a cross over orientation that formed two distinct antigen binding sites: V_{H1} - V_{L1} and V_{H2} - V_{L2} (**FIGS. 1C and 1D**, see light and heavy chains B). The second pair of polypeptides (that each possessed a single variable domain) comprised a first polypeptide having the structure V_{H3} -Immunoglobulin C_{H1} , hinge, C_{H2} , and C_{H3} heavy chain constant domains, and a second polypeptide having the structure V_{L3} -Immunoglobulin light chain constant domain, resulting in a pair of polypeptides that formed a third antigen binding site: V_{H3} - V_{L3} (**FIGS. 1C and 1D**, see light and heavy chains A). In addition, the trispecific binding proteins were constructed to include an LS mutation. Furthermore, the trispecific binding proteins were constructed such that within one binding protein, one C_{H3} domain included a knob mutation and the other C_{H3} domain included a hole mutation to facilitate heterodimerization of the heavy chains (**FIG. 1**).

[0390] Using the above described approach for trivalent binding protein design, three trispecific binding proteins (Binding Proteins 2, 3, and 24) were generated. These trispecific binding proteins were created by grafting onto a trispecific binding protein framework the V_H and V_L domains isolated from antibodies targeting three distinct epitopes on the HIV-1 Env glycoprotein: MPER Ab (targeting the MPER epitope on gp41), CD4BS Ab “b” (targeting the CD4 Binding Site on gp120), and V1/V2 directed Ab “a” (targeting the V1/V2 domain on gp120). Binding Protein 2 was constructed such that the first pair of polypeptides (which formed two antigen binding sites) targeted the HIV-1 Env glycoprotein epitopes MPER and V1/V2, and the second pair of polypeptides (which formed the single antigen binding site) targeted the HIV-1 Env glycoprotein epitope CD4BS (Binding Protein 2 = MPER x V1/V2 / CD4BS). Binding Protein 3 was constructed such that the first pair of polypeptides (which formed two antigen binding sites) targeted the HIV-1 Env glycoprotein epitopes V1/V2 and MPER, and the second pair of polypeptides (which formed the single antigen binding site) targeted the HIV-1 Env glycoprotein epitope CD4BS (Binding Protein 3 = V1/V2 x MPER / CD4BS). Binding Protein 24 was constructed such that the first pair of polypeptides (which formed two antigen binding sites) targeted the HIV-1 Env glycoprotein epitopes V1/V2 and

CD4BS, and the second pair of polypeptides (which formed the single antigen binding site) targeted the HIV-1 Env glycoprotein epitope MPER (Binding Protein 24 = V1/V2 x CD4BS / MPER). The three trispecific binding proteins, as well as their parental antibodies, were purified over protein A affinity resin (**FIGS. 2A and 3A**) followed by size exclusion chromatography (**FIGS. 2B and 3B**) to obtain monomeric proteins suitable for further characterization. All three trispecific binding proteins were stable and formed monomers at high frequency.

[0391] To test the potential for developing binding proteins targeting two different HIV-1 Env protein epitopes (instead of three), bispecific binding proteins were designed based upon the above described CODV Ig format (*See* WO 2012/135345), using two different V_H and V_L domains from the same parental antibodies used to create the trispecific binding proteins. However, the bispecific binding proteins with these specific variable domains did not purify well as monomers, showing significantly increased aggregate formation when compared to the corresponding trispecific binding proteins (**FIG. 4A and 4B**).

[0392] Next, the binding affinity of the purified trispecific binding proteins (and their parental antibodies) was measured for the HIV-1 Env glycoprotein epitopes on gp41 and gp120. First, the binding affinity for gp41 was measured for the three trispecific binding proteins, as well as the parental MPER antibody, by Biacore assay using the MPER binding peptide (**FIG. 5**). The binding affinity for the MPER antibody was calculated to be 18.7 nM. Surprisingly, the three trispecific binding proteins all had a higher affinity for the MPER binding peptide than did the parental antibody (**Table 3**), with Binding Protein 2 having an approximately 3.1 fold higher affinity than the MPER antibody (6.05 nM vs. 18.7 nM, respectively).

Table 3: Affinity measurements for the MPER binding peptide

Antibody	Analyte	k _a (1/Ms)	k _d (1/s)	R _{max} (RU)	K _A (1/M)	K _D (M)	Chi2	MW MPER (kDa)
MPER Ab	Gp41-MPER JPT	5.85E+04	1.09E-03	47.5	5.35E+07	1.87E-08	0.55	5.25
Binding Protein 2	Gp41-MPER JPT	1.15E+05	6.97E-04	29.0	1.65E+08	6.05E-09	0.27	2.29
Binding Protein 3	Gp41-MPER JPT	4.67E+04	7.79E-04	38.5	6.00E+07	1.67E-08	0.41	5.14
Binding Protein 24	Gp41-MPER JPT	6.28E+04	8.06E-04	35.5	7.80E+07	1.28E-08	0.48	5.24

[0393] Similarly, the binding affinity for the CD4 Binding Site on gp120 was measured for the three trispecific binding proteins, as well as the parental CD4BS antibody, by Biacore

assay (**FIG. 6**). The three trispecific binding proteins all had a similar affinity for the CD4 Binding Site when compared to the parental antibody (**Table 4**).

Table 4: Affinity measurements for the CD4BS binding site

Antibody	k_a (1/Ms)	k_d (1/s)	Rmax (RU)	KD (M)	Chi2
CD4BS Ab “b”	2.79E+05	2.32E-04	31.4	8.30E-10	1.17
Binding Protein 2	2.31E+05	2.41E-04	34.0	1.04E-09	0.74
Binding Protein 3	7.58E+04	2.75E-04	38.2	3.63E-09	0.19
Binding Protein 24	1.46E+05	2.52E-04	41.6	1.73E-09	0.38

[0394] Thus, the trispecific binding proteins were able to bind both of the tested target epitopes on the HIV-1 Env glycoprotein (**Table 5**). Moreover, all three trispecific binding proteins bound the target epitopes with affinities approximately equal to or exceeding those of their parental antibodies. Binding affinity of the V1/V2 directed Ab “a”, as well as of the V1/V2 directed Ab “a” binding sites within the three trispecific binding proteins 2, 3, and 24 could not be determined by Biacore analysis because this required a specific gp120 protein antigen which was unavailable.

Table 5: Summary of binding capabilities of tested binding proteins

Sample	Binding on gp120?	Binding on gp41?
MPER Ab	No	Yes
CD4BS Ab “b”	Yes	No
V1/V2 directed Ab “a”	No	No
Binding Protein 2	Yes	Yes
Binding Protein 3	Yes	Yes
Binding Protein 24	Yes	Yes

[0395] The biophysical properties were tested for the trispecific binding proteins and parental antibodies (**Table 6**). All of the tested proteins had similar stabilities and limited propensities to form aggregates.

Table 6: Conformational stability/aggregation of the binding proteins

Sample	DSF T_m (°C)	Intrinsic AA Fluo T_m (°C)	SLS at 266nm T_{agg} (°C)
MPER Ab	69/75	68	71
CD4BS Ab “b”	69	66	68
V1/V2 directed Ab “a”	69	64	67
Binding Protein 2	60/70	54	58

Binding Protein 3	57/70	55	56
Binding Protein 24	56/71	53	54

[0396] These experiments indicated that stable, monomeric, trispecific binding proteins targeting three distinct epitopes on the HIV-1 Env glycoprotein could be constructed and efficiently purified. Furthermore, the trispecific binding proteins retained their ability to bind their target epitopes, having similar or improved affinity relative to their parental antibodies. Finally, the trispecific binding proteins had suitable biophysical properties, and showed significantly less aggregation than the corresponding bispecific binding proteins.

Example 2: characterization of the Binding Proteins

[0397] Due to the success of developing three trispecific binding proteins with appropriate biophysical properties and binding abilities (as described in Example 1), 21 additional trispecific binding proteins were developed and tested. The experiments described herein explored the ability of the 24 trispecific binding proteins to neutralize HIV-1 *in vitro*, and the pharmacokinetic properties of a number of these trispecific binding proteins *in vivo*.

[0398] Neutralization assays were performed using the TZM-bl assay which measures neutralization as a function of reductions in HIV-1 Tat-regulated firefly luciferase (Luc) reporter gene expression after a single round of infection with Env-pseudotyped viruses. The assays were performed as described in Marcella Sarzotti-Kelsoe et al., J. Immunological Methods, 409:131-146 (2014). The neutralization results of various antibodies are shown in **Tables 8-10**.

Methods

Production of Env-pseudotyped viruses

[0399] Assay stocks of Env-pseudotyped viruses were produced in 293T/17 cells by co-transfection with two plasmids: an Env expression plasmid and a plasmid expressing the entire HIV-1 genome except for Env. Co-transfection of these plasmids produced infectious pseudovirus particles which were capable of delivering the Tat gene into target cells, but infections with these pseudovirions could not themselves produce infectious viral progeny.

Viral neutralization assay

[0400] Neutralization of HIV infection using TZM-bl cells (also known as JC53BL-13 cells) was performed as described previously (Marcella Sarzotti-Kelsoe et al., J. Immunological Methods, 409:131-146 (2014)). Briefly, a single round of infection using the Env-pseudotyped HIV-1 virions was carried out in TZM-bl cells (a CXCR-4-positive HeLa

cell clone). TZM-b1 cells were engineered to express CD4 and CCR5, and to contain integrated reporter genes for firefly luciferase and *E. coli* β -galactosidase under the control of an HIV long-terminal repeat. Reporter gene expression was induced *in trans* by viral Tat protein (delivered by the pseudotyped viruses) soon after single cycle infection. Luciferase activity was quantified as relative luminescence units (RLU), and was directly proportional to the number of infectious virus particles present in the initial inoculum over a wide range of values. Neutralization was measured as a function of decreased Tat-regulated Firefly luciferase (Luc) reporter gene expression after administration of varying concentrations of the indicated binding proteins. Neutralization titers were identified as the protein dilution at which RLUs were reduced by 80% compared to virus control wells after subtraction of background RLUs. The assay was performed in 96-well plates for high throughput capacity, and well-characterized reference strains were utilized for uniformity across studies.

Pharmacokinetic (PK) measurements

[0401] Female Indian rhesus macaques weighing between 3 and 6 kg were randomly assigned to groups according to body weight (two macaques per group) and were intravenously injected with the indicated concentration of binding proteins. Blood was collected from the animals before the injection on day 0, and 30 minutes, 6 hours, 1 day, 2 days, 4 days, 7 days, 14 days, 21 days and 28 days after injection. The serum concentration of each binding protein was quantified in the plasma from the collected blood using an RSC3-based ELISA assay.

Results

[0402] 21 additional trispecific binding proteins targeting three distinct HIV-1 Env glycoprotein epitopes were generated and purified as described in Example 1. These 21 additional trispecific binding proteins (Binding Proteins 1 and 4-23) were created by grafting onto a trispecific binding protein framework the V_H and V_L domains isolated from antibodies targeting distinct HIV-1 epitopes on the HIV-1 Env glycoprotein: the anti-MPER antibodies *MPER Ab “a”* and *MPER Ab “b”* (targeting the MPER epitope on gp41), the anti-CD4BS antibodies *CD4BS Ab “a”* and *CD4BS Ab “b”* (targeting the CD4 Binding Site on gp120), the anti-V1/V2 antibodies *V1/V2 directed Ab “a”* and *V1/V2 directed Ab “b”* (targeting the V1/V2 domain on gp120), and the anti-V3 antibody *V3 directed Ab* (targeting the V3 loop on gp120) (Table 7).

Table 7: Epitope binding site composition of the trispecific binding proteins

Binding Protein:	Epitope Binding Site:
1	MPER x V1/V2 directed / CD4BS

2	MPER x V1/V2 directed / CD4BS
3	V1/V2 directed x MPER / CD4BS
4	MPER x V1/V2 directed / CD4BS
5	MPER x V3 directed / CD4BS
6	V1/V2 directed x MPER / CD4BS
7	V3 directed x V1/V2 directed / CD4BS
8	MPER x V1/V2 directed / CD4BS
9	MPER x V1/V2 directed / CD4BS
10	V1/V2 directed x MPER / CD4BS
11	MPER x V1/V2 directed / CD4BS
12	MPER x V3 directed / CD4BS
13	MPER x V3 directed / V1/V2 directed
14	V1/V2 directed x MPER / CD4BS
15	MPER x V3 directed / V1/V2 directed
16	MPER x V3 directed / CD4BS
17	V1/V2 directed x V3 directed / CD4BS
18	V3 directed x MPER / CD4BS
19	V3 directed x V1/V2 directed / MPER
20	V3 directed x V1/V2 directed / CD4BS
21	MPER x CD4BS / V1/V2 directed
22	CD4BS x MPER / V1/V2 directed
23	CD4BS x V1/V2 directed / MPER
24	V1/V2 directed x CD4BS / MPER

[0403] The viral neutralization capabilities of five of the trispecific binding proteins (and their parental antibodies) at varying concentrations were tested against a panel of 208 different HIV-1 Env-pseudotyped viruses (**Table 8**). Binding protein-mediated neutralization of the pseudotyped HIV-1 isolates was measured using the TZM-b1 luciferase reporter gene assay. The inhibitory dose for each binding protein was calculated for each pseudotyped virus as the dilution that caused an 80% reduction in luminescence (IC₈₀) after infection. Surprisingly, the IC₈₀ geometric means calculated for each of the tested trispecific binding proteins was lower than the parental antibodies, suggesting that these trispecific binding proteins were more potent at neutralizing pseudotyped HIV-1 than their parental neutralizing antibodies.

Table 8: IC₈₀ measurements from viral neutralization assay

	Binding Protein:						Parental Antibody:				
	15	1	2	19	20	3	MPER Ab	V1/V2 directed Ab "a"	V3 directed Ab	CD4BS Ab "b"	CD4BS Ab "a"
# Viruses	208	208	208	208	208	208	208	208	208	208	208
Total VS Neutralized:											
IC ₈₀ <50 µg/mL	190	202	206	198	206	206	203	151	113	202	183
IC ₈₀ <10 µg/mL	180	199	206	180	206	206	193	149	109	200	175

IC ₈₀ <1.0 µg/mL	166	169	191	145	188	186	61	133	98	184	108
IC ₈₀ <0.1 µg/mL	122	109	136	80	144	123	10	99	72	79	10
IC ₈₀ <0.01 µg/mL	74	7	70	22	54	47	5	24	26	6	0
% VS Neutralized:											
IC ₈₀ <50 µg/mL	91	97	99	95	99	99	98	73	54	97	88
IC ₈₀ <10 µg/mL	87	96	99	87	99	99	93	72	52	96	84
IC ₈₀ <1.0 µg/mL	80	81	92	70	90	89	29	64	47	88	52
IC ₈₀ <0.1 µg/mL	59	52	65	38	69	59	5	48	35	38	5
IC ₈₀ <0.01 µg/mL	36	3	34	11	26	23	2	12	13	3	0
Median IC ₈₀	0.033	0.088	0.026	0.164	0.029	0.045	1.69	0.037	0.054	0.149	0.780
Geometric Mean	0.033	0.135	0.028	0.199	0.034	0.051	1.34	0.063	0.057	0.144	0.814

[0404] Next, the viral neutralization capabilities of a larger panel of trispecific binding proteins (and their parental antibodies) at varying concentrations were tested against 20 pseudotyped viruses representing 10 different HIV-1 clades (**Table 9**). The trispecific binding proteins provided robust protection against infection with these 20 viruses (**Table 10**).

Table 9: 20 representative viruses used for viral neutralization assay

Virus	Clade
KER2008.12.SG3	A
620345.c1.SG3	AE
DJ263.8.SG3	AG
T266-60.SG3	AG
T278-50.SG3	AG
BL01.DG.SG3	B
BR07.DG.SG3	B
CNE57.SG3	B
H086.8.SG3	B
QH0692.42.SG3	B
SS1196.01.SG3	B
CNE21.SG3	BC
6471.V1.C16.SG3	C
CAP210.E8.SG3	C
DU156.12.SG3	C
DU422.01.SG3	C
TV1.29.SG3	C
ZM106.9.SG3	C
3817.v2.c59.SG3	CD
X2088.c9.SG3	G

Table 10: IC₈₀ measurements from viral neutralization assay of 20 representative viruses

	# Viruses	Total VS Neutralized		% VS Neutralized		Median IC ₈₀	Geometric Mean
		IC ₈₀ <50 µg/mL	IC ₈₀ <1 µg/mL	IC ₈₀ <50 µg/mL	IC ₈₀ <1 µg/mL		
Binding Protein 4	20	17	11	85	55	0.474	0.398
Binding Protein 5	20	14	11	70	55	0.199	0.324
Binding Protein 6	20	16	9	80	45	0.453	0.449
Binding Protein 7	20	16	9	80	45	0.523	0.312
Binding Protein 8	20	17	12	85	60	0.578	0.488
Binding Protein 9	20	14	9	70	45	0.836	0.531

Binding Protein 10	20	16	12	80	60	0.222	0.173
Binding Protein 11	20	18	15	90	75	0.310	0.181
Binding Protein 12	20	17	12	85	60	0.526	0.566
Binding Protein 13	20	19	12	95	60	0.202	0.189
Binding Protein 14	20	17	15	85	75	0.208	0.088
Binding Protein 15	20	17	10	85	50	0.345	0.378
Binding Protein 16	20	18	11	90	55	0.228	0.314
Binding Protein 17	20	17	12	85	60	0.086	0.180
Binding Protein 18	20	15	10	75	50	0.536	0.501
Binding Protein 19	20	18	11	90	55	0.563	0.538
Binding Protein 20	20	18	14	90	70	0.224	0.229
Binding Protein 21	20	15	9	75	45	0.627	0.501
Binding Protein 2	20	18	13	90	65	0.375	0.222
Binding Protein 22	20	13	8	65	40	0.856	0.634
Binding Protein 23	20	17	6	85	30	1.930	1.129
Binding Protein 3	20	18	12	90	60	0.469	0.287
Binding Protein 24	20	16	7	80	35	2.130	1.054
MPER Ab “a”	20	16	8	80	40	1.007	0.981
MPER Ab “b”	20	16	16	80	80	0.071	0.024
CD4BS Ab “b”	20	15	9	75	45	0.181	0.399
V1/V2 directed Ab “a”	20	11	9	55	45	0.060	0.094
V3 directed Ab	20	12	10	60	50	0.183	0.136
CD4BS Ab “a”	20	10	1	50	5	1.530	1.811
V1/V2 directed Ab “b”	20	9	9	45	45	0.051	0.039

[0405] Finally, the pharmacokinetics (PK) of a subset of the trispecific binding proteins and parental antibodies were tested in rhesus macaques. Briefly, 10 or 20 mg/kg of the proteins were intravenously injected into female rhesus macaques, and ELISA assays were performed on the plasma from blood samples taken prior to injection, and on the plasma from blood samples taken at many time points after the injection (up to 42 days) (**FIG. 7**). All of the trispecific binding proteins could be detected at least 14 days after IV administration, with Binding Protein 1 remaining detectable at least 35 days after injection, showing that the binding proteins were stable *in vivo*.

[0406] Taken together, this data suggested that broadly neutralizing trispecific binding proteins could be constructed which targeted three distinct epitopes on the HIV-1 Env glycoprotein. These binding proteins showed similar or increased potency/much improved neutralizing capabilities (breadth) relative to the parental neutralizing antibodies. Furthermore, these trispecific binding proteins appeared to be well tolerated *in vivo*. Without wishing to be bound by theory, the development of broadly neutralizing trispecific binding proteins targeting multiple epitopes on HIV may allow for improved anti-viral therapy relative to monospecific or bispecific antibodies, as HIV viral particles are less likely to be resistant to all three antigen binding sites on the neutralizing trispecific binding proteins than

the single or dual antigen binding sites on monospecific or bispecific neutralizing antibodies, respectively.

Example 3: characterization of T-cell engagers.

[0407] As noted above, Env is expressed on the surface of HIV-infected cells. Because of this, Env can act as an antibody target to identify infected cells, and induce Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) and Complement Dependent Cytotoxicity (CDC), resulting in reduction of the latent viral reservoir. The studies described herein explore the development of novel trispecific binding proteins (termed “T cell engagers”) that contain three antigen binding sites targeting three different antigens (HIV-1 Env glycoprotein, CD3, and CD28). These novel proteins not only include antigen binding sites from neutralizing antibodies, but also the ability to bind effector T cells, bringing them into close proximity to infected target cells, thus inducing HIV-infected cell lysis.

Methods

Binding properties of T-cell engagers

[0408] The binding properties of the T-cell engagers was measured by ELISA assay using a horse radish peroxidase-conjugated anti-Fab probe to detect T-cell engager binding to the surface of ELISA plates coated with CD3, CD28, or Resurfaced Stabilized Core 3 (RSC3) protein of gp120. Human CD3ge-hIgG4 (KIH) (Cat. No: 03-01-0051) from Cambridge Biologics, MA, USA; Human CD28-hIgG4 (Cat. No: 03-01-0303) from Cambridge Biologics, MA, USA.

T-cell activation assay

[0409] CD4 and CD8 T cell activation were measured as follows: peripheral blood mononuclear cells (PBMCs) were enriched from buffy coats obtained from naïve donors (NIH blood bank) using magnetic beads (Miltenyi Biotec). These cells were co-cultured for 14-16 hours with either uninfected or HIV-1 infected CEM cells in the presence of increasing concentrations of the binding proteins (0.01-1.0 µg/mL) with brefeldin A. The cells were then stained for surface expression of T-cell markers (CD3, CD4, and CD8) and activation markers (CD25 and CD69), followed by intracellular staining for cytokines (IFN-γ, TNF-α, and IL-2) using fluorescently conjugated antibodies (BD Biosciences, eBiosciences, Biolegend). The number of CD4 and CD8 T cells expressing each cytokine or activation marker was determined by running the samples on an LSRII flow cytometer and analyzing the data with Flowjo software (Treestar).

CD3 downregulation

[0410] CD3 downregulation after T cell activation by the T-cell engagers was measured by staining activated PBMCs with non-competing mouse anti-human CD3 antibody and quantitated using flow cytometry.

Cytotoxicity assay

[0411] Cytotoxicity of the T-cell engagers to CEM-BaL, ACH2, and J1.1 cells was monitored by flow cytometry as follows: latent cell lines (ACH2, J1.1, OM10) were obtained from the NIH AIDS Reagent Program. The activation of these cells was performed by culturing the cells in the presence or absence of TNF- α (10 ng/mL) for 14-16 hours. Activation was measured by determining the expression of cell surface HIV envelope glycoprotein by flow cytometry using an allophycocyanin-conjugated anti-HIV Env antibody (2G12). The CEM-IIIb, ACH2, J1.1 and OM10 cells were labeled with the membrane dye PKH-26 (Sigma) and used as target cells in a cytotoxicity assay. These labeled target cells were co-cultured for 14-16 hours at an E:T ratio of 10:1 with enriched human T cells as effector cells in the presence of increasing amounts of the binding proteins. The extent of cell lysis in the target cells was determined by staining with a live/dead cell marker (Life technologies) and measuring the number of dead cells in the labeled target cell population by running the samples on an LSRII flow cytometer followed by analysis using Flowjo software (Treestar).

Results

[0412] The capacity to develop T cell engagers with antigen binding sites targeting both T cell surface proteins and neutralizing epitopes on HIV-1 was explored. T cell engagers were constructed which contained two antigen binding sites targeting two different T cell surface receptors (CD3 and CD28), and a third antigen binding site targeting the HIV-1 Env glycoprotein (**FIGS. 8A and 8B**). In addition, the T cell engagers were constructed to include an LS mutation. Furthermore, the T cell engagers were constructed such that within one binding protein, one C_{H3} domain included a knob mutation and the other C_{H3} domain included a hole mutation to facilitate heterodimerization of the heavy chains (**FIGS. 8A and 8B**).

[0413] Using this approach, two T cell engagers were constructed which targeted both T cell surface proteins and the HIV-1 Env glycoprotein (Binding Protein 32 and CD3 x CD28 / CD4BS “b” Ab). These two T cell engagers were created by grafting onto a trispecific binding protein framework the V_H and V_L domains isolated from parental antibodies targeting the T cell surface proteins CD3 and CD28, and the anti-HIV-1 antibody CD4BS Ab “b”

(targeting the CD4 Binding Site on gp120). Binding Protein 32 was constructed such that the first pair of polypeptides (which formed two antigen binding sites) targeted the T cell surface receptors CD28 and CD3, and the second pair of polypeptides (which formed the single antigen binding site) targeted the HIV-1 antigen CD4BS (Binding Protein 32 = CD28 x CD3 / CD4BS). The CD3 x CD28 / CD4BS “b” Ab trispecific binding protein was constructed such that the first pair of polypeptides (which formed two antigen binding sites) targeted the T cell surface receptors CD3 and CD28, and the second pair of polypeptides (which formed the single antigen binding site) targeted the HIV-1 antigen CD4BS (**Table 11**).

Table 11: Format of T-cell engagers

Format	Name of Construct	Arm 1 Antigen	Arm 2 Antigen	Arm 3 Antigen
T cell engagers, trispecific	CD3 x CD28 / CD4BS Ab “b”	CD4BS	CD3	CD28
T cell engagers, trispecific	Binding Protein 32	CD4BS	CD28	CD3
Monospecific	CD4BS IgG4	CD4BS	CD4BS	-

[0414] The ability of the two T cell engagers to bind to each of their three target antigens was tested by ELISA assay. The T cell engagers were capable of binding both the CD3 and CD28 T cell surface proteins with the CD3 and CD28 antigen binding sites in either orientation in the bispecific arms of the T cell engagers (*i.e.*, CD3 x CD28 for CD3 x CD28 / CD4BS Ab “b” or CD28 x CD3 for Binding Protein 32). Both T cell engagers were also capable of binding to gp120 (as measured using the HIV-1 RSC3 protein, a gp120 variant lacking the V1, V2, and V3 variable regions) (**FIG. 9**).

[0415] The effect on T cell activity was next tested for both of the T cell engagers. Incubation of the T cell engagers with monocytes revealed that the T cell engagers induced robust CD8⁺ T cell activation (**FIG. 10**). Similarly, the T cell engagers were capable of inducing significant CD4⁺ T cell activation on PBMCs alone, or PBMCs incubated with either of the HIV-1 infected T cell lines CEM-NKr cells or CEM-BaL cells (**FIG. 11**). Additionally, both of the T cell engagers reduced cell surface expression of CD3 on activated T cells (**FIG. 12**).

[0416] Finally, the ability of the T cell engagers to induce lysis of HIV-infected cells was tested. The T cell engagers (and positive and negative control bispecific binding proteins targeting CD3 and an HIV antigen) were incubated with the HIV-1 infected T cell line CEM-BaL cells. Incubation of the T cell engagers with the infected cells induced robust cell lysis over a wide range of concentrations (**FIG. 13A**). Likewise, incubation of these T cell engagers induced lysis of the latently infected T cell line ACH2 cells (**FIG. 13B**), as well as

J1.1 cells (**FIG. 13C**). Surprisingly, the T cell engagers showed comparable or better cytotoxic activity against chronic and latent HIV-infected cell lines when compared to the bispecific binding proteins.

[0417] Taken together, the novel T cell engagers described herein retained the ability from their parental antibodies to bind their target antigens on the HIV-1 Env glycoprotein gp120 on HIV-infected cells, as well as the cell-surface exposed T cell proteins CD3 and CD28. The T cell engagers induced robust CD4⁺ and CD8⁺ T cell activation, and diminished CD3 surface expression. Finally, these T cell engagers induced significant lysis of HIV-1 infected T cells. Without wishing to be bound by theory, these T cell engagers may provide a novel strategy for anti-viral therapeutics by reducing/eliminating the latent viral reservoir through T cell engagement in HIV/AIDS patients.

[0418] While the present disclosure includes various embodiments, it is understood that variations and modifications will occur to those skilled in the art. Therefore, it is intended that the appended claims cover all such equivalent variations that come within the scope of the disclosure. In addition, the section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

[0419] Each embodiment herein described may be combined with any other embodiment or embodiments unless clearly indicated to the contrary. In particular, any feature or embodiment indicated as being preferred or advantageous may be combined with any other feature or features or embodiment or embodiments indicated as being preferred or advantageous, unless clearly indicated to the contrary.

[0420] All references cited in this application are expressly incorporated by reference herein.

SEQUENCES

Table 1: Heavy and light chain SEQ ID NOs for binding proteins 1-53 and the target antigens to which the binding proteins are directed.

Binding Protein	SEQ ID NOs	Target
1	4, 3, 1, 2	MPER x V1/V2 directed / CD4BS
2	12, 11, 9, 10	MPER x V1/V2 directed / CD4BS
3	20, 19, 17, 18	V1/V2 directed x MPER / CD4BS
4	28, 27, 25, 26	MPER x V1/V2 directed / CD4BS
5	36, 35, 33, 34	MPER x V3 directed / CD4BS
6	44, 43, 41, 42	V1/V2 directed x MPER / CD4BS
7	52, 51, 49, 50	V3 directed x V1/V2 directed / CD4BS
8	60, 59, 57, 58	MPER x V1/V2 directed / CD4BS
9	68, 67, 65, 66	MPER x V1/V2 directed / CD4BS
10	76, 75, 73, 74	V1/V2 directed x MPER / CD4BS
11	84, 83, 81, 82	MPER x V1/V2 directed / CD4BS
12	92, 91, 89, 90	MPER x V3 directed / CD4BS
13	100, 99, 97, 98	MPER x V3 directed / V1/V2 directed
14	108, 107, 105, 106	V1/V2 directed x MPER / CD4BS
15	116, 115, 113, 114	MPER x V3 directed / V1/V2 directed
16	124, 123, 121, 122	MPER x V3 directed / CD4BS
17	132, 131, 129, 130	V1/V2 directed x V3 directed / CD4BS
18	140, 139, 137, 138	V3 directed x MPER / CD4BS
19	148, 147, 145, 146	V3 directed x V1/V2 directed / MPER
20	156, 155, 153, 154	V3 directed x V1/V2 directed / CD4BS
21	164, 163, 161, 162	MPER x CD4BS / V1/V2 directed
22	172, 171, 169, 170	CD4BS x MPER / V1/V2 directed
23	180, 179, 177, 178	CD4BS x V1/V2 directed / MPER
24	188, 187, 185, 186	V1/V2 directed x CD4BS / MPER
25	196, 195, 193, 194	MPER x V1/V2 directed / CD4BS
26	204, 203, 201, 202	MPER x V1/V2 directed / CD4BS
27	212, 211, 209, 210	MPER x V1/V2 directed / CD4BS
28	220, 219, 217, 218	MPER x V1/V2 directed / CD4BS
29	228, 227, 225, 226	MPER x V1/V2 directed / CD4BS
30	235, 234, 232, 233	MPER x V1/V2 directed / CD4BS
31	243, 242, 240, 241	MPER x V1/V2 directed / CD4BS
32	305, 304, 302, 303	CD28 x CD3 / CD4BS
33	313, 312, 310, 311	CD28 x CD3 / CD4BS
34	321, 320, 318, 319	CD28 x CD3 / V1/V2 directed
35	329, 328, 326, 327	CD28 x CD3 / V1/V2 directed
36	337, 336, 334, 335	CD28 x CD3 / CD4BS
37	345, 344, 342, 343	CD28 x CD3 / CD4BS
38	353, 352, 350, 351	CD4BS x CD3 / CD28
39	361, 360, 358, 359	CD4BS x CD3 / CD28
40	369, 368, 366, 367	CD3 x CD4BS / CD28
41	377, 376, 374, 375	CD3 x CD4BS / CD28
42	385, 384, 382, 383	CD4BS x CD3 / CD28
43	393, 392, 390, 391	CD4BS x CD3 / CD28
44	401, 400, 398, 399	CD3 x CD4BS / CD28
45	409, 408, 406, 407	CD3 x CD4BS / CD28
46	417, 416, 414, 415	V1/V2 directed x CD3 / CD28

47	425, 424, 422, 423	V1/V2 directed x CD3 / CD28
48	433, 432, 430, 431	CD3 x V1/V2 directed / CD28
49	441, 440, 438, 439	CD3 x V1/V2 directed / CD28
50	449, 448, 446, 447	V1/V2 directed x CD3 / CD28
51	457, 456, 454, 455	V1/V2 directed x CD3 / CD28
52	465, 464, 462, 463	CD3 x V1/V2 directed / CD28
53	473, 472, 470, 471	CD3 x V1/V2 directed / CD28

Table 2: Heavy and light chain sequences of binding proteins. CDR sequences are bolded and italicized.

Binding Protein 1 Amino Acid Sequences		
Heavy chain A	Qvqlvqsggqmkkpgesmriscrasgyefidctlnwirlapgkrpewmgwlkp <i>rggavnyarplqgr</i> vmtmrdvysdtaflelrsltvddtavvfctrgkncdynwdfeh wgrgtpvivssastkgpsvfplapsskstsggtaalgclvkdyfpepvtvswngalt <u>sgvhtfpavllqssglyslssvvtvpssslgtqtyicvnhkpsntkvdkkvepkscd</u> <u>kthtcppcpapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnw</u> <u>yvdgvevhnaktkpreeqynstyrvvsvltvlhqdwlngkeyckvsnkalpapi</u> <u>ektiskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpe</u> <u>nnykttpvldsdgsfflyskltvdksrwqqgnvfscsvlhealthshytqkslsisp</u>	SEQ ID NO: 1
Light chain A	Eivltqspgtlsispgetaiiscrtsqygslawyqqrpgqaprlviysgstraagipdrf sgsrwgpdyntisnlesgdfgvyycqgyeffgqgatkvdikrtvaapsvfifpps <u>deqlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdsksdstylsst</u> <u>ltlskadyekkhkvyacevthqglsspvtksfnrgec</u>	SEQ ID NO: 2
Heavy chain B	Evrivesggglvkpggsrlscsasgfdfnawmtwvrppgkglewvgritpgg <i>egws</i> vdyaesvkgrftisrdntkntlylemnnvrtedtggyfcartgkyydfwsgyp <i>pgeeyfqd</i> wgqgtlvivssdkthtqvhltsqgpevrkpgtsvkvsckapgnltkyd lhwrvsvpgqlqwmngwishegdkkvi verfkakvtidwdrstntaylqlsgltsg dtavyy <i>cakgskhrlrdyalydddgalnwavdvdylnlefw</i> gqgtavtvssdk htastkgpsvfplapsskstsggtaalgclvkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgtqtyicvnhkpsntkvdkkvepkscdkthtcppcp apellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevh naktkpreeqynstyrvvsvltvlhqdwlngkeyckvsnkalpapiektiskakg qprepqvylppcrdeltknqvsllwclvkgfypsdiavewesngqpennykttp vldsdgsfflyskltvdksrwqqgnvfscsvlhealthshytqkslsisp	SEQ ID NO: 3
Light chain B	Dfvltqspshlsvtptgesasisckssshlihgdrnnylawyvqkprspqliylas rasgvpdrfsgsgsdktlksirvetedvgttyy <i>cmqgrespwtf</i> gqgatkvdikdkt ht aseltqdpavsvalkqtvtitcrgdslrshyaswyqkpgqapvllfygknnrpsgi pdrfsgsasgnrasltitgaqaeadyycssrdksgsrslsvfgggtklvldkthtrtv aapsvfifppsdeqlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteq dskdstylsstltlskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 4
Binding Protein 1 Nucleotide Sequences		
Heavy chain A	cagggtgcagctggtgcagctctggcggccagatgaagaaacccggcgagagcatgcg gatcagctgcagagccagcggctacgagttcatcgactgcaccctgaactggatcaga ctggcccctggcaagcggcctgagtgatgggatggctgaagcctagaggcggagc cgtgaactacgccagacctctgcagggcagatgaccatgaccgggacgtgtacag	SEQ ID NO: 5

	<p>cgataccgccttctggaactgcggagcctgaccgtggatgataccgccgtgtacttct gcacccggggcaagaactgcgactacaactgggacttcgagcactggggcagaggc accctgtgatctgtcaagcgcgtcgaccaaggggccccagcgtgtccctctggccc ctagcagcaagagcacatctggcggaacagccgcctgggctgcctcgtgaaggact actttccgagcccgtagccgtgtcctggaattctggcgccctgaccagcggcgtgca cacctttccagctgtgctgcagtccagcggcctgtacagcctgagcagcgtcgtgaca gtgccagcagctctctgggcacccagacctacatctgcaacgtgaaccacaagccca gcaacaccaagggtggacaagaagggtggaaccaagagctgcgacaagaccacac ctgtccccctgtctctgccccgaactgctgggaggcccttccgtgttctgttcccc aaagcccaaggacacctgatgatcagccggacccccgaagtgcctgctgtgtgt ggatgtgtcccacgaggacctgaagtgaagtcaattgtgtacgtggacggcgtggaa gtgcacaacgccaagaccaagccaagagaggaaacagtacaacagcacctaccgggt gggtgtcctgtgtgacctgtgtgcaccaggactggctgaacggcaaaagagtacaagt caaggtgtccaacaaggccctgctgcccccatcgagaaaaccatcagcaaggccaa gggccagccccgcgaacccaggtgtgcacactgccccaaagcaggacgagctg accaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccctccgatatgc cgtggaatgggagagcaacggccagcccagaaacaactacaagaccacccccctg tgctggacagcgacggctcatttctctggtgtccaagctgacagtggacaagtcggg tggcagcagggaacgtgttcagctgctcgtgtgcacgaggccctgcacagccact acaccagaagtcctgagcctgagccccggc</p>	
Light chain A	<p>Gagatcgtgctgacacagagccctggcacccctgagcctgtctccagcgcagacagc catcatcagctgccggacaagccagtacggcagcctggcctggtatcagcagaggcc tggacaggccccagactcgtgatctacagcggcagcacaagagccgccggaatcc ccgatagattcagcggctccagatggggccctgactacaacctgacctcagcaacct ggaaagcggcgacttcggcgtgtactactgccagcagtagtcttctggccagggc accaaggtgcaggtggacatcaagcgtacgggtggcgcctcccagcgtgtcatcttcc cacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaa cttctacccccgcgaggccaaagtgcagtggagggtggacaacgccctgcagagcg gcaacagccaggaaagcgtgaccgagcaggacagcaaggactccacctacagcctg agcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctg cgaagtgaccaccagggcctgtctagccccgtgaccaagagcttaaccggggcga gtgt</p>	SEQ ID NO: 6
Heavy chain B	<p>gaggttagactggtagcagcaggagggggcctgtgaagcccgggtgggtctctccgc ctgagctgttctgcctccggctttgatttcgataacgcctggatgacctgggtcaggcag cctccaggtaaaggactggagtgggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaatctgttaaaggcggtttacaatctcaagggacaatacca agaatacctgtatttggagatgaacaacgtgagaactgaagacaccggaatacttct gtgccagaacaggcaatactacgacttctgtccggctatccccctggcgaggaaat tttaagactgggtcagggaaccctgttatcgtgtcctccgacaaaaccataccag gtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaagtg tctgtcaaggccccctggacaacacctgaaaacctacgacctgactgggtgcgcagc gtgccaggacagggactgcagtgggtggatcagccacgagggcgacaaga aagtgatctgtgaacggttaaggccaaagtgacctcactgggacagaagcacca acaccgctacctgcagctgagcggcctgacctctggcgataccgccgtgtactactg cgccaagggcagcaagcaccggctgagagactacgcctgtacgacgatgacggcg ccctgaactgggcccgtgatgtggactacctgagcaacctggaattctggggccaggg cacagccgtgacctgtcatctgataagaccacaccgcttccaccaaggggccatcg gtttccccctggcacctctctcaagagcacctctgggggcacagcggccctgggt gcctgtgaaggactacttccccgaaccgggtgacgggtgctgtggaactcaggcgcct gaccagcggcgtgcacaccttcccggctgtcctacagtctcaggactctactcctca gcagcgtggtgacctgccctccagcagcttgggcacccagacctacatctgcaacgt gaatcacaagcccagcaacaccaaggtggacaagaaagttagcccaaatctgtga caaaactcacatgccaccgtgccagcactgaactcctgggggggaccgtcagt</p>	SEQ ID NO: 7

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Light chain B	gacttcgtgctgacccagagccctcacagcctgagcgtgacacctggcgagagcgcc agcatcagctgcaagagcagccactccctgatccacggcgaccggaacaactacctg gcttggtacgtgcagaagccccggcagatccccccagctgctgatctacctggccagca gcagagccagcggcgtgcccgatagatttctggcagcggcagcgacaaggacttca ccctgaagatcagccgggtggaaaccgaggacgtgggcacctactactgtatgcagg gcagagagagccccctggaccttggccaggggcaccaaggtggacatcaaggacaaa accataaccgcatccgaactgactcaggaccctgccgtctctgtggcactgaagcaga ctgtgactattacttccgagggcactactgcggagccactacgttctctggtatcaga agaaacccggccagcagcctgtgctgtgttctacggaaagaacaataggccatctgg catccccgaccgcttcttggcagtgatcagggaaccgagccagtctgaccattaccg gcgcccaggtgaggacgaagccgattactattgcagctccgggataagagcggct ccagactgagcgtgttcggaggaggaactaaactgaccgtctcgataagaccatac ccgtacggtggcgcctccagcgtgttcatcttccacctagcgacgagcagctgaagt ccggcacagcctctgtcgtgtgcctgtgaacaacttctacccccgcgaggccaaaagt gcagtggaaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtgacc gagcaggacagcaaggactccacctacagcctgagcagcaccctgacactgagcaa ggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccaggggcctgt ctagccccgtgaccaagagctcaaccggggcgagtg	SEQ ID NO: 8
Binding Protein 2 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkgp gasvr vscqtsgyftahilfwfrqapgrglewvgwikipqy gavnfgggfrdrvltlrdvyreiaymdirglkpdtdavyyacardrsygdsswalda wgqgttvvsaastkgpsvfplapsskstsggtaalglvkdyfpepvtvswnsal tsghvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscd kthtccppcpapellggpsvflfppkpkdtlmsirtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapi ektiskakgqprepqvctlppsrdektknqvsclscavkgfypsdiavewesngqpe nnykttppvldsdgsfflvskltvdksrwqqgnvfscsvlhealthshytqkslslspg	SEQ ID NO: 9
Light chain A	yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkgpgrapklhihtssvedgv psrfsqsgfhtsfnltsdlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsde qlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslsstlts kadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 10
Heavy chain B	Evrlvesggglvkpggsrlscsasgfdnawmtwvrqppgkglewvgr itgpgegwsvdyaesvkgrftisrdntkntlylemnnvrtdtgyyfcartgk yydfwsgyppeeyfqdwgqgtlvivssdkthtqvhltsqsgpevrkpgtsv kvsckapgnltktydlhwrvspgqlqwmgwishedgkdviverfkak vtidwdrstntaylqlsgltsgdavyyacgskhrlrdyalydddgalnwav dvdylnlefwgqgtavtvssdkthtastkgpsvfplapsskstsggtaalgl vkdyfpepvtvswnsalstgsvhtfpavlqssglyslssvvtvpssslgtqtyi cnvnhkpsntkvdkkvepkscdkthtccppcpapellggpsvflfppkpkdt lmsirtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynsty	SEQ ID NO: 11

	rvvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepqvyltp pcrdeltknqvsllwclvkgfypsdiavewesngqpennykttppvldsdgs fflyskltvdksrwqqgnvfscsvlhealthshytqkslsisp	
Light chain B	dfvltqspshsvtpgesasiscksshlihgdrnnylawyvqkprspqlliylasr asgvprdfsgsgsdldfklisrvetdvgttycmqgrespwtfgqgtkvdkdkth taseltqdpavsvalkqvtitcrdslrshyaswyqkpgqapvllfygknnpdsg pdrfsgsasgnrasltitgaqaedeaddyccssrdksgrlsfvgggtklvldkthrtv aapsvfifppsdeqlksgrtasvcllnnfypreakvqwkvdnalqsgnsqesvteq dskdstylsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 12
Binding Protein 2 Nucleotide Sequences		
Heavy chain A	agagcccacgtggtgcagtctggcaccgccatgaagaaccaggcgcctctgtgcgg gtgtcctgtcagacaaggcgtacaccttcaccgcccacatcctgttctggtccggcag gcccctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtg aacttcggcggaggcttcgggatagagtaccctgacccgggacgtgtaccgcgag atcgctcatatggacatccggggcctgaagcccgatgacaccgcccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtgggtgtctgccgcctctacaaaggggccccagcgtgtccctctggcccc tagcagcaagagcacatctggcggaacagccgcctgggctgcctcgtgaaggacta cttcccagagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtgcac accttccagctgtgctgcagtcacggcctgtacagcctgagcagcgtcgtgacagt gcccagcagctctctgggcacccagacctacatctgcaacgtgaaccacaagcccag caacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccacacct gtccccctgtcctgccccgaactgctgggaggcccttcgtgttctgttcccccaa agcccagacaccctgatgatcagccggacccccgaagtacctgcgtggtggtgg atgtgtccacgaggaccctgaagtgaagtcaattggtacgtggacggcgtggaagt gcacaacgccaagaccaagccaagagaggaacagtacaacagcacctaccgggtg gtgtccgtgctgaccgtgctgcaccaggactggctgaacggcgaagagtacaagtgc aaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaaggccaag ggccagccccgcgaaccccaggtgtgcacactgccccaaagcaggggacgagctga ccaagaaccaggtgtcctgagctgtgccgtgaaaggcttaccctccgatatcgcc gtggaatgggagagcaacggccagcccagaaactacaagaccacccccctgt gctggacagcgacggctcattctcctggtgtccaagctgacagtggacaagtcccgt ggcagcagggaacgtgttcagctgtcctgctgcacgaggccctgcacagccact acaccagaagtccctgagcctgagccccggc	SEQ ID NO: 13
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Heavy chain B	gaggttagactggtggagtcaggagggggcgtgtgaagcccggtgggtctctccgc ctgagctgttctgcctccggctttagttcgataacgcctggatgacctgggtcaggcag cctccaggaaggagctggagtggtgggaagaatcacaggtccaggcgagggtg gtcctgtgactacgcgaatctgttaaggcggtttacaatctcaagggacaatacca agaatacctgtatttggagatgaacaacgtgagaactgaagacaccggatattctct gtgccagaacaggcaataactacgacttctgttcggctatccccctggcgaggaatat tttaagactggggtcagggaaccctgttatcgtgtcctccgacaaaaccataccag	SEQ ID NO: 15

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Light chain B	gacttcgtgctgacccagagccctcacagcctgagcgtgacacctggcgagagcgc agcatcagctgcaagagcagccactcctgatccacggcgaccggaacaaactactg gcttggtacgtgcagaagcccgagatccccccagctgctgatctactggccagca gcagagccagcggcgtgcccgatagatttctggcagcggcagcgacaaggacttca ccctgaagatcagccgggtggaaccgaggacgtgggcacctactactgtatgcagg gcagagagagcccctggaccttggccagggcaccaaggtggacatcaaggacaaa accataaccgatccgaactgactcaggaccctgccgtctctgtggcactgaagcaga ctgtgactattactgccgagcgactactgcggagccactacgttctctggtatcaga agaaacccggccaggcacctgtgctgctgtttctacggaaagaacaataggccatctgg catccccgaccgcttttctggcagtgcatcagggaaccgagccagctgaccattaccg gcgcccaggtgaggacgaagccgattactattgcagctcccggaagagcgggt ccagactgagcgtgttcggaggaggaactaaactgaccgtcctcgataagaccatac ccgtacggtggccgctcccagcgtgttcatttccacctagcgacgagcagctgaagt ccggcacagcctctgtcgtgtgctgctgaacaacttctacccccgcgaggccaaagt gcagtggaaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtgacc gagcaggacagcaaggactccactacagcctgagcagcaccctgacactgagcaa ggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcctgt ctagccccgtgaccaagagcttcaaccggggcgaggtg	SEQ ID NO: 16
Binding Protein 3 Amino Acid Sequences		
Heavy chain A	rahlvqsgtamkkpgasvrscqtsgytftahilfwfrqapgrglewvwigpqyg avnfgggfrdrvlttrdvireiaymdirglkpddtavvyccardsygdsswaldaw ggqgtvvvsaastkgpsvfplapsskstsggtaalgclvkdyfepvvtvswngalts gvhtfpavllqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscdk htcpcpapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyv dgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapiekt iskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpenny kttpvldsdgsfflvskltvdksrwqqgnvfscsvlhealthshytqkslsisp	SEQ ID NO: 17
Light chain A	yihvtqspsslsvsigdrvtincqtsqvggsdlhwyqhkpgrapkllihhtssvedgv psrfsfgsfhtsfnltsldlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsde	SEQ ID NO: 18

	qlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslsstlts kadyekhkvyacevthqglsspvtksfnrgec	
Heavy chain B	Qvhlqtsgpevrkpgtsvkvsckapgnltktydlhwvrsvpqgqlqwmg wishegdkkviverfkakvtidwdrstntaylqlsgltsgdtavyycakgsk hrlrdyalydddgalnwavdvdylnlefwgqgtavtvssdkthtevrives ggglvkpggslrlscsasgfdfdnawmtwvrpppgklewvgritgpgeg wsvdyaesvkgrftisrdntkntlylemnnvrtdetgyyfcartgkyydfws gyppgeeyfqdwgqgtlvivssdkthtastkgpsvflapsskstsggtaalg clvkdyfpepvtvswngaltsgvhtfpavlqssgylssvvtvpssslgtqt yicnvnhkpsntkvdkkvepkscdkthtccppcpapellggpsvflfppkpk dtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqyns tyrvvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepvyt lppcrdeltknqvsllwclvkgyfypsdiavewesngqpennykttppvlds gsfflyskltvdksrwqqgnvfscsvlhealthshytqkslsisp	SEQ ID NO: 19
Light chain B	aseltqdpavsvalkqtvtitergdsrlshyaswyqkpgqapvllfygknnrpsgip drfsgsasgnrsltitgaqaeadyycssrdksgrlsvfgggtklvldkthtdfvt qsphslsvtpgesasisckssshlihgdrnnylawyvqkprspqliylasrasgv pdrfsgsgskdftlkisrvetedvgttycmqgrespwtfgggtkvdkdkthtrva apsvfifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqds kdstyslsstltskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 20
Binding Protein 3 Nucleotide Sequences		
Heavy chain A	agagcccacctggtgcagtctggcaccgccatgaagaaccaggcgctctgtgcgg gtgtcctgtcagacaagcggtacacctaccgcccacatcctgttctggttcggcag gcccctggcagaggactggaatgggtggatggatcaagcccagtatggcgccgtg aacttcggcgaggcttcgggatagagtaccctgaccgggacgtgtaccgcgag atcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtggtgtgtctgccgcctctacaaaggccccagcgtgtccctctggcccc tagcagcaagagcacatctggcggaacagccgcttgggtgcctcgtgaaggacta cttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtgcac accttccagctgtgtgcagtccagcgccctgtacagcctgagcagcgtcgtgacagt gcccagcagctcttgggcacccagacctacatctgcaactgaaccacaagcccag caacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccacacct gtccccctgtcctgccccgaactgctgggaggcccttcgtgttctgttcccccaa agccccagacacacctgatgacagccggacccccgaagtgcctgctggtggtgg atgtgtccacgaggaccctgaagtgaagtcaattgtacgtggacggcgtggaagt gcacaacgccaaagaccaagcaagagaggaacagtacaacagcacctaccgggtg gtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaagagtacaagtgc aaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaaggccaag ggccagccccgcgaaccccaggtgtgcacactgcccccaagcaggacgagctga ccaagaaccaggtgtccctgagctgtgccgtgaaaggttctacccctccgatatgcc gtggaatgggagagcaacggccagcccagaaacaactacaagaccacccccctgt gctggacagcagcggtcatttctctggtgtccaagctgacagtggacaagtccgggt ggcagcagggcaactgttcagctgtccgtgctgcacgagccctgcacagccact acaccagaagtccctgagcctgagccccggc	SEQ ID NO: 21
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	<p>agcagactgcacatcaagcgtacggtggccgctcccagcgtgttcatttcccacctag cgacgagcagctgaagtcggcacagcctctgtcgtgtgctgtgaacaacttctacc cccgcgaggccaaagtgcagtggaaagtggaacgccttcagagcggcaacag ccaggaaagcgtgaccgagcaggacagcaaggactccacctacagcctgagcagca ccctgacactgagcaaggccgactacgagaagcacaaggtgtacgctgcgaagtga cccaccaggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt</p>	
Heavy chain B	<p>caggtgcacctgacacagagcggaccggaagtgcggaagcctggcacctct gtgaaggtgtcctgcaaggccctggcaacacctgaaaacctacgacctgca ctgggtgcgcagcgtgccaggacagggactgcagtggatgggctggatcag ccacgagggcgacaagaaagtatcgtggaacggttcaaggccaaagtac catcactgggacagaagcaccacaccgcctacctgcagctgagcggcctg accttggcgataccgccgtgtactactgcgccaaggcgagcaagcaccggc tgagagactacgccctgtacgacgatgacggcgcctgaactgggcccgtgga tgtggactacctgagcaacctggaattctggggccagggcacagccgtgacc gtgtcatctgacaaaaccataccgaggttagactggtggagtcaggaggggg gcttgtgaagcccggtgggtctctccgctgagctgttctgctccggctttgatt tcgataacgcctggatgacctgggtcaggcagcctccagtaagggaactgga gtgggtgggaagaatcacaggtccaggcgagggtggtccgtggactacgc ggaatctgttaaaggcggtttacaatctcaagggacaataccaagaatacttg tatttggagatgaacaacgtgagaactgaagacaccgataattacttctgtcca gaacaggcgaatactacgacttctggtccggctatccccctggcgagggaattt tcaagactggggtcagggaaccctgttatcgtgtcctccgataagaccacac cgcttccaccaaggggcccatcgggttccccctggcacctcctccaagagcac ctctgggggcacagcggccctgggctgctgtgtaaggactacttcccgaac cggtgacggtgtcgtggaactcaggcgcctgaccagcggcgtgcacactt cccggctgtctacagtctcaggactctactccctcagcagcgtggtgacct gccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagc ccagcaacaccaaggtggacaagaaagttgagccaaatcttgtgacaaaact cacacatgccaccgtgccagcacctgaactcctggggggaccgtcagttt ccttctcccccaaaacccaaggacaccctcatgatctccggaccctgaggt cacatgcgtggtggtggacgtgagccacgaagacctgaggtcaagtcaact ggtatgttgacggcgtggaggtgcataatgccaagacaaagccgcgggagga gcagtacaacagcacgtaccgtgtgtcagcgtctcaccgtcctgcaccagg actggctgaatggcaaggagtagaagtgcaaggctccaacaagccctccca gccccatcgagaaaaccatctccaaagccaaagggcagccccgagaacca caggtgtacacctgccccatgccgggatgagctgaccaagaatcaagtcag cctgtggtgctgtgtaaaaggcttctatcccagcgacatcgccgtggagtggga gagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctgga ctccgacggctccttctctactcaaaactcaccgtggacaagagcaggtg gcagcaggggaacgttctctatgctccgtgctgcatgaggctctgcacagcc actacacgcagaagagcctctccctgtctccgggt</p>	SEQ ID NO: 23

Light chain B	gcacccgaactgactcaggaccctgccgtctctgtggcactgaagcagactgtgactat tacttggcaggcgactcactgcggagccactacgcttctggtatcagaagaaaccc ggccaggcacctgtgctgctgttctacggaaagaacaataggccatctggcatccccg accgcttttctggcagtgcacagggaaaccagccagctgaccattaccggcgcca ggctgaggacgaagccgattactattgcagctcccgataagagcggctccagact gagcgtgttcggaggaggaactaaactgaccgtcctcgacaaaaccataccgacttc gtgctgaccagagccctcacagcctgagcgtgacacctggcgagagcggcagatc agctgcaagagcagccactccctgatccacggcgaccggaacaactacctggcttggt acgtgcagaagcccggcagatccccccagctgctgatctacctggccagcagcagag ccagcggcgtgcccgatagattttctggcagcggcagcgacaaggacttcacctgaa gatcagccgggtggaaaccgaggacgtgggcacctactactgtatgcagggcagag agagcccctggacctttggccagggcaccaaggtggacatcaaggataagaccata cccgtacggtggccgctcccagcgtgttcattctccacctagcagcagcagctgaa gtccggcacagcctctgtcgtgtgctgctgaacaacttctacccccgcaggccaaa gtgcagtggaaaggtggacaacgcctgcagagcggcaacagccaggaaagcgtga ccgagcaggacagcaaggactccacctacagcctgagcagcaccctgacactgagc aaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcct gtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 24
Binding Protein 4 Amino Acid Sequences		
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Light chain A	Eivltqspgtlspsgetaiisrctsqygsllawyqqrpgqaprlviysgstraagipdrf sgsrwgpdyntlislesgdfgyycqqyeffgqgktvqvdikrtvaapsvfifpps deqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsksdstylsst ltlskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 26
Heavy chain B	evrlvesggglvkpggslrlscsasgfdfdnawmtwvrqppgkglewvgri tgpgegwsvdyaesvkgrftisrdntkntlylemnnvrtdtgyyfcartgk yydfwwgyppgeeyfqdwgqgtlvivssdkthtqvhltsqgpevrkpgts kvvscapgentlktlydlhwrvsvpgqlqwmngwishegdkkviverfka kvtidwdrstntaylqlsgltsgdtavyycakgskhrlrdyaldddgalnwa vvdylsnlefwgqgtavtvssdkthtastkgpsvfplapsskstsggtaalg clvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvtpssslgtq tyicnvnhkpntkvdkkvepkscdkhtcpccpapellggpsvflfppkpk dtlmsirtpevtcvvvdvshedpevkfnwyvvdgvevhnaktkpreeqyns tyrvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepqvvt lppcrdeltknqvsclwclvkgfypsdiavewesngqpennykttppvlds gsfflyskltvdksrwqqgnvfscsvmhcalhnhytqkslspsg	SEQ ID NO: 27
Light chain B	dfvltqspshslsvtpgesasiscksshlihgdrnylawyqkprspqliylasr asgvpdrfsgsgsdktlktisrvetedvgtyycmqgrespwtfqgktvdikdkth taseltqdpavsvalkqvtitcrdslrshyaswyqkkgqapvllfygknnrpsgi pdrfsgsasgnrasltitgaqaeadyycssrdksgsrlsvfgggtklvldkthrtv aapsvfifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteq dsksdstylsstltlskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 28
Binding Protein 4 Nucleotide Sequences		
Heavy chain A	caggtgcagctggtgcagctctggcggccagatgaagaaacccggcgagagcatcg gatcagctgcagagccagcggctacgagttcatcgactgcaccctgaactggatcaga	SEQ ID NO: 29

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Binding Protein 5 Amino Acid Sequences		
Heavy chain A	Qvqlvqsggqmkkpgesmriscrasgyefidctlnwirlapgkrpewmgwlkpr ggavnyarplqgrvtmtrdvydtaflelrsltdtavycftrgkncdynwdfew grgtpvivssastkgpsvfplapsskstsggtaalglvkdyfpepvtvswngalts gvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscdk htcppepapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyv dgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapiekt iskakgqpprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpenny kttppvldsdgsfflvskltvdksrwqqgnvfscsvmhealhnhytqkslspsg	SEQ ID NO: 33
Light chain A	Eivltqspgtlspsgetaiisrtsyqgslawyqqrpgqaprlviysgstraagipdrfs gsrwgpdynltisnlesgdfgyyycqqyeffgqtkvqvdkrtvaapsvfifppsd eqlksgtasvvcllnnfybreakvqwkvdnalqsgnsqesvteqdskdstyslsstlt lskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 34
Heavy chain B	Evrivesggglvkpgslrlscsasgfdfdnawmtwvrpppgkglewvgr itgpgegwsvdyaesvkgrftisrdntkntlylemnnvrtdtgyyfcartgk yydfwwgyppgeeyfqdwgqgtlvivssdkthtqmqlqesgpglvkpse tllstcsvsgasisdsywswirrspgkglewigyvshksgdtnyspslksrvnl sldtsknqvslslvaataadsgkyycartlhgrriygivafnewftyfymdvw ngtqvtvssdkthtastkgpsvfplapsskstsggtaalglvkdyfpepvtv swngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntk vdkkvepkscdkthtcppepapellggpsvflfppkpkdtlmisrtpevtcv	SEQ ID NO: 35

	vvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeyckvsnkalpapiektiskakgqprepvytlppcrdeltnqvslwclvkgfypsdiavewesngqpennykttppvldsdsfflyskltvdksrwqqgnvfscsvmhealhnhytqkslsisp	
Light chain B	Sdisvapgetariscgekslgsravqwyqhraqapsliiynndrpsgiperfsgspdspfgttatlitsveagdeadyychiwdsrvtkwvfgggtltvldkhtaseltqdpavsvalkqvtitcrgdsrlrshyaswyqkpgqapvllfygknrpsgipdrfsgsasgnrasltitgaqaedeaddyccsrksgsrlsvfgggtklvldkthtrtvaapsvfifp psdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstysls stltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 36
Binding Protein 5 Nucleotide Sequences		
Heavy chain A	Caggtgcagctggtgcagctctggcggccagatgaagaaacccggcgagagcatcgggatcagctgcagagccagcggctacgagttcatcactgcaccctgaactggatcagactggccccctggcaagcggcctgagtggtggatggatggctgaagcctagaggcggagccgtgaactacgccagacctgcagggcagagtaccatgacccgggacgtgtacagcgataccgccttctggaactcggagcctgaccgtggatgataccgccgtgtacttc tgcacccggggcaagaactgcgactacaactgggacttcgagcactggggcagaggcaccctgtgatcgtgtcaagc gcgtcgaccaagggccccagcgtgtccctctggccccctagcagcaagagcacatctggcggaacagccgcctgggctgcctcgtgaaggactacttcccagccccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtgcacaccttccagctgtgtgcatccagcggcctgtacagcctgagcagcgtcgtgacagtgccagcagctctctgggcacccagacctacatctgcaacgtgaaccacaagcccagcaacaccaaggtggacaa gaaggtggaaccaagagctgcgacaagaccacacctgtccccctgtctctgccccgaactgctgggagggcccttccgtgttctgttcccccaagcccaaggacacctgatgatcagccggacccccgaagtacctgcgtggtggtggtggtgtgtccacgaggac cctgaagtgaagttcaattgttacgtggacggcgtggaagtgcacaacccaagaccaagccaagagaggaacagtacaacagcacctaccgggtggtgtccgtgtgaccgtgtgcaccaggactggctgaacggcaagagtacaagtgaaggtgtccaacaaggccc tgctgtcccccatcgagaaacctacagcaaggccaaggggccagccccgcgaacccaggtgtgcacactgcccccaagcagggacgagctgaccaagaaccaggtgtccctgagctgtgccgtgaaaggcttctacccctccgatatgccgtggaatgggagagcaacggccagcccgagaacaactacaagaccacccccctgtgctggacagcgacggctcat tcttctggtgtccaagctgacagtggacaagtcccggtggcagcagggcaacgtgttcagctgtccgtgatgcacgaggccctgcacaaccactacaccagaagtccctgagcctgagccccggc	SEQ ID NO: 37
Light chain A	Gagatcgtgctgacacagagccctggcaccctgagcctgtctccaggcgagacagccatcatcagctgccggacaagccagtacggcagcctggcctggtatcagcagaggcc tggaagggccccagactcgtgatctacagcggcagcacaagagccgccgaatcccgatagattcagcggctccagatggggccctgactacaacctgacctacagcaacct ggaaagcggcgacttcggcgtgtactactgccagcagtagagttcttcggccagggc accaaggtgcaggtggacatcaagcgtacgggtggcgtccagcgtgttcattctccacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaa cttctacccccgcgagggcaagtgacgtggaaggtggacaacgccctgcagagcggcaacagccaggaagcgtgaccgagcaggacagcaaggactccacctacagcctg agcagcaccctgacctgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccaggggcctgtctagccccgtgaccaagagcttcaaccggggcga gtgt	SEQ ID NO: 38
Heavy chain B	gaggttagactggtggagtcaggagggggcctgtgaagccccgtgggtctctccgc ctgagctgttctgcctccggctttgatttcgataacgcctggatgacctgggtcaggcag	SEQ ID NO: 39

	cctccaggttaagggactggagtggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaatctgttaaagggcggttacaatctcaaggacaatacca agaataccttgatttgagatgaacaacgtgagaactgaagacaccggatattacttct gtgccagaacaggcaatactacgacttctgtggggctatccccctggcgaggaata tttcaagactggggtcagggaaccctgttatctgtctctccgacaaaaccataacca gatgcagctgcaggagagcgccctggactcgtgaagcccagcgagaccctgagcc tgacatgcagctgagcggcgccagcatcagcgacagctactggagctggatcagga ggagccctggcaaggcgctggagtggatcggtacgtgcacaagagcggcgacacc aactacagccctccctgaagtccagggtgaacctgtccctggacaccagcaagaacc aggtgagcctgtccctgtggctgccacagctgctgacagcggcaagtactactgtgc caggaccctgcacggcaggaggtatctacggcatcgtggcctcaacagtggttacc tacttctacatggacgtgtggggcaacggcaccaggtgaccgtgagctccgataaga cccacaccgttccaccaaggggccatcggcttccccctggcacctctccaagag cacctctgggggcacagcggccctgggtgctggtcaaggactacttccccgaacc ggtgacggtgtcgtggaactcaggcggccctgaccagcggcgtgcacacctcccggc tgtcctacagtcctcaggacttactccctcagcagcgtggtgaccgtgccctccagca gcttgggcacccagacctacatctgcaacgtgaatcacaagcccagcaacaccaaggt ggacaagaaagttagcccaaatctgtgacaaaactcacacatgccaccgtgccca gcacctgaactcctggggggaccgtcagtcttcttcccccaaaaccaaggaca ccctcatgatctcccgaccctgaggtcacatgcgtggtggtggacgtgagccacga agaccctgaggtcaagtcaactggtatgttgacggcgtggaggtgcataatgcaaga caaagccgaggaggagcagtacaacagcacgtaccgtgtggtcagcgtcctacc gtctgcaccaggactggctgaatggcaaggagtacaagtcaaggctccaacaaa gccctcccagccccatcgagaaaaccatctccaaagccaaaggcgagccccgaga accacaggtgtacaccctgccccatgccgggatgagctgaccaagaatcaagttag cctgtggtgctgtgtaaaaggcttctatcccagcgacatcgccgtggagtgggagagc aatgggcagccggagaaactacaagaccacgcctcccgctgctggactccgacgg ctccttctctactcaaaactcaccgtggacaagagcaggtggcagcaggggaac gtcttctcatgctccgtgatgcatgaggctctgcacaaccactacacgcagaagagcct ctcctgtctccgggt	
Light chain B	tccgacatcagcgtggccccggagagacagccaggatctctgcggcgagaagag cctgggaagcagggtgtgtagtggtaccaacacagggccggacaggtcccagcc tgatcatctacaacaaccaggacagggccagcggcatccctgagaggttcagcggaa gccccgacagcccttcggaaccacagccaccctgaccatcacaagcgtggaagcc ggcgacgagggcgactactactgccacatctgggacagcaggggtgccaccaagtg ggtgtttggcggcgccaccaccctgaccgtgctggacaaaaccataaccgcatccga actgactcaggaccctgcccgtctgtggtgactgaagcagactgtgactattacttggcg aggcgactcactcggagccactacgcttctgttatcagaagaaccggccaggc acctgtgctgctgttctacggaaagaacaataggccatctggcatccccgaccgttttc tggcagtgcatcagggaaccgagccagtctgaccattaccggcgcccaggctgagga cgaagccgattactattgcagctcccgggataagagcggctccagactgagcgtgttc ggaggaggaactaaactgaccgtctcgataagaccatacccgtaggtggccgct cccagcgtgttctatctccacctagcgacgagcagctgaagtccggcacagcctctgt cgtgtgctgctgaacaacttctacccccgcgaggccaaagtgcagtggaaggtggac aacgccctgcagagcggcaacagccaggaaagcgtgaccgagcaggacagcaag gactccacctacagcctgagcagcaccctgacactgagcaaggccgactacgagaag cacaaggtgtacgcctgcgaagtgacccaccagggcctgtctagccccgtgaccaag agcttcaaccggggcgagtg	SEQ ID NO: 40
Binding Protein 6 Amino Acid Sequences		
Heavy chain A	Qvqlvqsggqmkkpgesmriscrasgyefidctlnwirlapgkrpewmgwlkpr ggavnyarplqgrvtmtrdvysdaflelrsltvddtavfyctrkncdynwdfew grgtpvivssastkgpsvfplapsskstsggtaalglvkdyfpepvtvswnsгалts gvhtfpavqlssglylssvvtpssslgtqtyicnvnhkpsntkvdkkvepkscdk	SEQ ID NO: 41

	htppcpapellggpsvflfppkpkdtlmsrtpevtcvvvdvshedpevkfnwyv dgvevhnaktkpreeqynstyrsvsvltvlhqdwlngkeykckvsnkalpapiekt iskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpenny kttppvldsdsfflvskltvdksrwqqgnvfscsvmhealhnhytqkslspsg	
Light chain A	Eivltqspgtlspsgetaiisrtsqygslawyqqrpgqaprlviysgstraagipdrfs gsrwgpdynltisnlesgdfgvyyccqyeffggqtkvqvdkrtvaapsvfifppsd eqlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdskdstyslsstlt lskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 42
Heavy chain B	Qvhltsqsgpevrkpgtsvkvsckapgnltktydlhwrvsvpggqlqwmg wishegdkkviverfkakvtidwdrstntaylqlsglsgdtavyycaakgsk hrlrdyalydddgalnwavdvdylnlefwgqgtavtvssdkthtevrives ggglvkpggslrlscsasgfdfnawmtwvrpppgklewvgritgpgeg wsvdyaesvkgrftisrdntkntlylemnnvrtedgyyfcartgkydfw wgyppeeyfqdwgqgtlvivssdkthtastkgpsvflapsskstsggtaa lgclvkdyfepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgt qyicvnkhkpsntkvdkkvepkscdkthtppcpapellggpsvflfppk pkdtlmsrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqy nstyrsvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepq vytlppcrdeltnqvsllwclvkgfypsdiavewesngqpennykttpvvl dsdgsfflyskltvdksrwqqgnvfscsvmhealhnhytqkslspsg	SEQ ID NO: 43
Light chain B	Aseltqdpavsvalkqtvtitcrgdsrlshyaswyqkkpgqapvllfygknrrpsgi pdrfsgsasgnrasltitgaqaeadyycssrdksgrlsvfgggkltvldkthtdfv ltqspshsvtpgesasiscksshlihgdrnnylawyvqkpgrspqliylassrasg vpdrfsgsgskdftlkisrvetedvgttycmqgrespwtfggqtkvdikdkthtrtv aapsvfifppsdeqlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteq dskdstyslsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 44
Binding Protein 6 Nucleotide Sequences		
Heavy chain A	caggtgcagctggtgcagctctggcggccagatgaagaaacccggcgagagcatgcg gatcagctgcagagccagcggctacaggtcatcactgcacccgaactggatcaga ctggccctggcaagcggcctgagtgatgggatggctgaagcctagaggcggagc cgtgaactacgccagacctctgcagggcagagtaccatgacccgggacgtgtacag cgataccgccttctggaactgcggagcctgaccgtggatgataccgccgtgtacttct gcacccggggcaagaactcgactacaactgggacttcgagcactggggcagaggc accctgtgatcgtgtcaagcgcgtcgaccaaggccccagcgtgtccctctggccc ctagcagcaagagcacatctggcggaacagccgcctgggctgcctcgtgaaggact actttccgagcccgtagcgtgtcctgaattctggcgccctgaccagcggcgtgca cacctttccagctgtgctgcagtcagcggcctgtacagcctgagcagcgtcgtgaca gtgccagcagctctctgggcacccagacctacatctgcaacgtgaaccacaagccca gcaacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccacac ctgtccccctgtcctgccccgaactgctgggaggccctccgtgttctgttcccc aaagcccaaggacaccctgatgatcagccggacccccgaagtacctgcgtggtgt ggatgtgtcccacgaggaccctgaagtgaagtcaattgttacgtggacggcgtggaa gtgcacaacgccaagaccaagccaagagaggaacagtacaacagcacctaccgggt gggtgtcctgctgaccgtgctgcaccaggactggctgaacggcaagagtagaagt caaggtgtccaacaaggccctgctgccccatcgagaaaaccatcagcaaggccaa gggccagccccgcgaacccaggtgtgcacactgccccaaagcaggacgagctg accaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccctccgatacgc cgtggaatgggagagcaacggccagcccagaaacaactacaagaccacccccctg tgctggacagcgacggctattcttctggtgtccaagctgacagtggacaagtcggg tggcagcagggaacgtgttcagctgctcgtgatgcagaggccctgcacaaccact acaccagaagtcctgagcctgagccccggc	SEQ ID NO: 45

Light chain A	gagatcgtgtgacacagagccctggcacccctgagcctgtctccaggcgagacagcc atcatcagctgccggacaagccagtagcggcagcctggcctggtatcagcagaggcct ggacaggccccagactcgtgatctacagcggcagcacaagagccgccggaatccc cgatagattcagcggctccagatggggccctgactacaacctgacctcagcaacctg gaaagcggcgacttcggcgtgtactactgccagcagtagagttctcgccaggggca ccaaggtgcaggtggacatcaagcgtacggtggcgcctccagcgtgttcatctccc acctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaac tttaccctccggaggccaaagtgcagtggaaggtggacaacgccctgcagagcgg caacagccaggaaagcgtgaccgagcaggacagcaaggactccacctacagcctga gcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgc gaagtgaccaccaggcctgtctagccccgtgaccaagagcttcaaccggggcgga gtgt	SEQ ID NO: 46
Heavy chain B	caggtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaa ggtgtcctgcaaggccccctggcaacacctgaaaacctacgacctgactgggtgcg cagcgtgccaggacaggactgcagtggtgggctggatcagccacgaggggcagc aagaaagtgtcgtggaacggttcaaggccaaagtaccatcgactgggacagaagc accaacaccgcctacctgcagctgagcggcctgacctctggcgataccgccgtgtact actgcgccaaaggcagcaagcaccggctgagagactacgccctgtacgacgatgac ggcgccctgaactgggcccgtggatgtggactacctgagcaacctggaattctggggcc agggcacagccgtgaccgtgtcatctgacaaaaccataccgaggttagactggtgga gtcaggaggggggctgtgaagcccgtgggtctctccgctgagctgttctgctcc ggctttgatttcgataacgcctggatgacctgggtcaggcagcctccaggtgaagggact ggagtgggtgggaagaatcacaggtccaggcgagggtggtccgtggactacggg aatctgttaaaggcggtttacaatctcaagggacaataccaagaatacttgtatttga gatgaacaacgtgagaactgaagacaccggatattactctgtgccagaacaggcaaa tactacgacttctgtggggtatccccctggcgaggaatattttcaagactggggtcag ggaaccttgttatcgtgtcctccgataagaccacaccgctccaccaaggggccatc ggcttccccctggcacctctccaagagcacctctgggggcacagcggccctggg ctgcctgtcaaggactactccccgaaccggtgacggtgtcgtggaactcaggcgcc ctgaccagcggcgtgcacacctccccggctgtctacagtctcaggactctactccct cagcagcgtggtgacctgccccccagcagctggggcacccagacctacatctgcaac gtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagcccaaatctgtg acaaaactcacatgcccaccgtgccagcacctgaactcctggggggaccgtcag tcttctcttcccccaaaacccaaggacacctcatgatctccggacccctgagggtca catgctggtggtggagcgtgagccacgaagacctgaggtaagttcaactggtatgtt gacggcgtggaggtgcataatgccaagacaaagccgaggagagcagtacaaca gcacgtaccgtgtgtcagcgtcctcaccgtctgcaccaggactggctgaattggcaa ggagtacaagtgaaggtctccaacaaagccctccagccccatcgagaaaacct ctccaaagccaaagggcagccccgagaaccacaggtgtacacctgccccatgcc gggatgagctgaccaagaatcaagtcagcctgtggtgcctggtaaaaggcttctatccc agcgacatgccgtggagtgaggagcaatgggcagccggagaaactacaaga ccacgcctccgtgtgactccgacggctccttctctactcaaaactaccgtgg acaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgatgaggctct gcacaaccactacacgcagaagagcctctccctgtctccgggt	SEQ ID NO: 47
Light chain B	Gcatccgaactgactcaggaccctgccgtctctgtggcactgaagcagactgt gactattactgccgagcgactactgcggagccactacgcttctggtatca gaagaaacccggccaggcacctgtgctgctgtttctacggaaagaacaatagg ccatctggcatccccgaccgctttctggcagtgcatcagggaaccgagccagt ctgaccattaccggcgcccaggctgaggacgaagccgattactattgcagctc ccgggataagagcggctccagactgagcgtgttcggaggaggaactaaactg accgtctcgcacaaaaccataccgacttcgtgctgaccagagccctcacag cctgagcgtgacacctggcgagagcgccagcatcagctgcaagagcagcca	SEQ ID NO: 48

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Binding Protein 7 Amino Acid Sequences		
Heavy chain A	Qvqlvqsggqmkkpgesmriscrasgyefidctlnwirlapgkrpewmgwlkpr ggavnyarplqgrvtmtrdvysdaflelrsltdtavycftrgkncdynwdfew grgtpvivssastkgpsvfplapsskstsggtaalglvkdyfpepvtvswngalts gvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscdk htcppcpapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyv dgvevhnaktkpreeqynstyrsvsvltvlhqdwlngkeykckvsnkalspapiet iskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpenny kttppvldsdsfvlvskltvdksrwqqgnvfscsvmhealhnhytqkslsisp	SEQ ID NO: 49
Light chain A	Eivltqspgtlsispgetaiiscrtsqygslawyqqrpqaprlviysgstraagipdrfs gsrwgpdynltisnlesgdfgyycqqyeffgqgtkvqvdikrtvaapsvfifppsd eqlksgtasvvcllnnfyreakvqkwvndalqsgnsqesvteqdsdkdstylsstlt lskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 50
Heavy chain B	qmqlqesgpglvkpsetlsitcsvsgasisdsywswirrspgkglewigyvh ksgdtnyspslksrvnlsldtsknqvsislvaataadsgkyycartlhgrriygi vafnewftyfymdvwngtqvtvssdkthtQvhltsqsgpevrkpgtsvk sckapgnltktydlhwrvsvpgqlqwmgwishegdkkviverfkakvti dwdrstntaylqlsgltsgdavyyacagkskhrlrdyalydddgalnwavdv dylsnlefwgqgtavtvssdkthtastkgpsvfplapsskstsggtaalglvk dyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicn vnhkpsntkvdkkvepkscdkthtcppcpapellggpsvflfppkpkdtlm isrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrsv svsvltvlhqdwlngkeykckvsnkalspapietiskakgqprepqvyltpp crdeltknqvsllwclvkgfypsdiavewesngqpennykttppvldsdsf flyskltvdksrwqqgnvfscsvmhealhnhytqkslsisp	SEQ ID NO: 51
Light chain B	Dfvltqspshlsvtpgesasiscksshlihgdrnnylawyvqkprspqliylasr asgvpdrfsgsgsdktlksrvetdvgttycmqgrespwtfgqgtkvdkdkth tsdisvapgetariscgekslgsravqwyqhragqapsliiynqdrpsgiperfsgs pdpfgttatltitsveagdeadychiwdsrvptkwvfgggtlvtldkthtrtvaaps vfifppsdeqlksgtasvvcllnnfyreakvqkwvndalqsgnsqesvteqdskd stylsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 52
Binding Protein 7 Nucleotide Sequences		
Heavy chain A	caggtgcagctggtgcagtctggcggccagatgaagaacccggcgagagcatcg gatcagctgcagagccagcggctacagttcatcactgcaccctgaactggatcaga ctggcccctggcaagcggcctgagtgatgggatggctgaagcctagaggcggagc cgtgaactacgccagacctctgcagggcagagtaccatgaccgggacgtgtacag cgataccgccttctggaactcgggagcctgaccgtgatgataccgccgtgtacttct gcacccggggcaagaactgcgactacaactgggacttcgagcactggggcgagggc	SEQ ID NO: 53

	<p> accctgtgatcgtgtcaagcgcgtcgaccaagggccccagcgtgttccctctggccc ctagcagcaagagcacatctggcggaacagccgcctgggctgcctcgtgaaggact actttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtgca cacctttccagctgtgtgcagtcagcggcctgtacagcctgagcagcgtcgtgaca gtgcccagcagctctctgggcacccagacctacatctgcaacgtgaaccacaagccca gcaacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccacac ctgtccccctgtctctgccccgaactgctgggaggcccttccgtgttctgttcccc aaagcccaaggacacctgatgatcagccggacccccgaagtacctgcgtggtggt ggatgtgtcccacgaggacctgaagtgaagttcaattggtacgtggacggcgtggaa gtgcacaacgccaaagaccaagccaagagaggaaacagtacaacagcacctaccgggt gggtgtccgtgtgaccgtgtgtcaccaggactggctgaacggcaaaagagtacaagt caaggtgtccaacaagggccctgctgccccatcgagaaaaccatcagcaaggccaa gggccagccccgcgaacccaggtgtgcacactgccccaaagcaggacgagctg accaagaaccaggtgtccctgagctgtgcccgtgaaaggcttctaccctccgatatgc cgtggaatgggagagcaacggccagcccagaaacaactacaagaccacccccctg tgctggacagcgacggctcatttctctggtgtccaagctgacagtggacaagtcggg tggcagcagggcaacgtgttcagctgctcctgatgcacgaggccctgcacaacct acaccagaagtccttgagcctgagccccggc </p>	
Light chain A	<p> gagatcgtgtgacacagagccctggcacctgagcctgtctccaggcgagacagcc atcatcagctgccggacaagccagtagcggcagcctggcctggtatcagcagaggcct ggacaggccccagactcgtgatctacagcggcagcacaagagccgccggaatccc cgatagattcagcggctccagatggggccctgactacaacctgacctcagcaacctg gaaagcggcgacttcggcgtgtactactgccagcagtagagttcttcggccagggca ccaaggtgcaggtggacatcaagcgtacggtggccgctcccagcgtgttcatctccc acctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaac ttctacccccgcgaggccaaagtgcagtggaaggtggacaacgccctgcagagcgg caacagccaggaagcgtgaccgagcaggacagcaaggactccacctacagcctga gcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgc gaagtgaccaccaggccctgtctagccccgtgaccaagagcttcaaccggggcgga gtgt </p>	SEQ ID NO: 54
Heavy chain B	<p> cagatgcagctgcaggagagcggccctggactcgtgaagcccagcgagacctgag cctgacatgcagcgtgagcggcgccagcagcagcagctactggagctggatcag gaggagccctggcaaggccctggagtggatcggtacgtgcacaagagcggcgac accaactacagcccctccctgaagtccagggtgaacctgtccctggacaccagcaaga accaggtgagcctgtccctgggtggctgccacagctgctgacagcggcaagtactactg tgccaggacctgcacggcaggaggtatctacggcatcgtggccttcaacagtggttc acctacttctacatggagctgtggggcaacggcaccaggtgacctgagctccgaca aaaccataccaggtgcacctgacacagagcggacccgaagtgcggaagcctggc acctctgtgaaggtgtcctgcaaggccctggcaacacctgaaaacctagacctgc actgggtgcgcagcgtgccaggacagggactgcagtggatgggctggatcagccac gaggggcgacaagaaaagtgtcgtggaacggttcaaggccaaagtgacctcagctgg gacagaagcaccaacaccgcctacctgcagctgagcggcctgacctctggcgatacc gccgtgtactactgcgccaaggcgagcaagcaccggctgagagactacgcctgtac gacgatgacggcgccctgaactgggctggatgtggactacctgagcaacctggaa ttctggggccaggcgacagccgtgaccgtgtcatctgataagaccacaccgcttcca ccaaggggccatcggtcttccccctggcacctctctccaagagcacctctgggggcac agcggccctgggctgctgtcaaggactactccccgaaccggtgacggtgtcgtgg aactcaggcgcctgaccagcggcgtgcacacctccccggctgtctacagtctcag gactctactccctcagcagcgtggtgacctgcccctccagcagcttgggcacccagac ctacatctgcaacgtgaatcacaagcccagcaacaccaaggtggacaagaaagtga gccccaatctgtgacaaaactcacatgccaccgtgcccagcacctgaactcctgg ggggaccgtcagttctcttccccccaaaacccaaggacacctcatgatctccggg </p>	SEQ ID NO: 55

	<p>accctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaag tcaactggtatgttgacggcgtggaggtgcataatgccaagacaagccgcgggagg agcagtacaacagcacgtaccgtgtgtgcagcgtcctaccgtcctgcaccaggactg gctgaatggcaaggagtacaagtgaaggtctccaacaaagccctcccagccccat cgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacacc tgcccccatgccgggatgagctgaccaagaatcaagtcagcctgtggtgcctggtaaa aggcttctatcccagcgacatcgccgtggagtgggagagcaatggcgagccggaga acaactacaagaccacgcctcccgtgctggactccgacggctccttcttctactcaa aactcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgat gcatgaggctctgcacaaccactacacgcagaagagcctctccctgtctccgggt</p>	
Light chain B	<p>Gacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgaga gcgccagcatcagctgcaagagcagccactccctgatccacggcgaccggaa caactacctggcttggtagctgcagaagcccggcagatccccccagctgctga tctacctggccagcagcagagccagcggcgtgcccgatagatttctggcagc ggcagcgacaaggacttcaccctgaagatcagccgggtggaaaccgaggac gtgggcacctactactgtatgcagggcagagagagccctggaccttggcca gggcaccaaggtggacatcaaggacaaaaccatacctccgacatcagcgtg gccccggagagacagccaggatctcctcgggcgagaagagcctgggaag cagggctgtgcagtggtaccaacacagggccggacaggtcccagcctgatc atctacaacaaccaggacagggccagcggcatccctgagaggttcagcggaa gccccgacagccccttcggaaccacagccaccctgaccatcacaagcgtgga agccggcgacgaggccgactactactgccacatctgggacagcaggggtgcc caccaagtgggtgttggcggcggcaccaccctgaccgtgctggataagacc atacccgtagcgtggcgcctccagcgtgtcatcttccacctagcgacgagc agctgaagtcggcacagcctctgtcgtgtgcctgctgaacaacttctacccc gcgaggccaaagtgcagtggaaggtggacaacgcctgcagagcggcaac agccaggaaagcgtgaccgagcaggacagcaaggactccacctacagcctg agcagcaccctgacactgagcaaggccgactacgagaagcacaaggtgtac gcctgcgaagtgaccaccaggccctgtctagccccgtgaccaagagctcaa ccggggcgagtg</p>	SEQ ID NO: 56
Binding Protein 8 Amino Acid Sequences		
Heavy chain A	<p>Rahlvqsgtamkkpgasvrvcqtsgytftahilfwrqapgrglewvgnwikpqy gavnfgggfrdrvltlrdvyreiaymdirglkpddtavyyccardrsygdsswalda wgqgttvvsaastkgpsvflapsskstsggtaalglvkdyfpepvtvswngal tsghvhtfpavqlssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscd kthtccppcpapellggpsvflfpkpkdtlmsirtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeyckvsnkalpapi ektiskakgqprepqvctlpssrdeltknqvsclavkgfypsdiavewesngqpe nnykttppvldsdgsflvskltvdksrwqqgnvfscsvlhealhshytqkslspsg</p>	SEQ ID NO: 57
Light chain A	<p>Yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedg vpsrfsgsfhtsfnltsldlqaddiatyycvqlqffgrgsrlhikrtvaapsvfifppsd eqlkshtasvvcclnnfyreakvqwkvdnalqsgnsqesvteqdskdstyslsstlt lskadyekkhvyacevthqglsspvtksfnrgec</p>	SEQ ID NO: 58
Heavy chain B	<p>Evrivesggglvkpggslrlscsasgfdndawmtwvrqppgkglewvgr itgpgegwsvdyaesvkgrftisrdntkntlylemnnvrtedtggyfcartgk yydfwwgyppgeeyfqdwgqgtlvivssdkthtqvqlvesgggvvqpgt srlscaasqfrfdgygmhwvrqapgkglewvasishdgikkyhaekvwg rftisrdnsntlylqmnsrlpedtalyycaakdlredeceewwsdydfgkq lpcaksrvgglvgiadnwgggtmvtvssdkthtastkgpsvflapsskstsg gtaalglvkdyfpepvtvswngaltsgvhtfpavqlssglyslssvvtvpss slgtqtyicnvnhkpsntkvdkkvepkscdkthtccppcpapellggpsvflf</p>	SEQ ID NO: 59

	ppkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpr eeqynstyrvvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqpr epqvytlppcrdeltnqvsllwclvkgfypsdiavewesngqpennykttp pvldsdgsfflyskltvdksrwqqgnvfscsvmhealhnhytqkslspsg	
Light chain B	Qsvltqppsvsaaaggkvtiscsgntsniggnfvswyqrrpgrapqlliyetdkrps gipdrfsasksgtsgtlaitglqtgdeadyycatwaaslsarvfgtkvivldkthtas eltqdpavsvalkqvtitcrgdslrshyaswyqkkpgqapvllfygknnrpsgipdr fsgsasgnrasltitgaqaedeaddyessrdksgsrsvfgggkltvldkthtrtvaap svfifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsd dstyslsstltlskadyekkhvyaevthqglsspvtksfnrgec	SEQ ID NO: 60
Binding Protein 8 Nucleotide Sequences		
Heavy chain A	agagcccacgtggtgcagtctggcaccgccatgaagaaccaggcgcctctgtgcgg gtgtcctgtcagacaagcggtacaccttcaccgcccacatcctgttctggttccggca ggccccggcagaggactggaatgggtggatggatcaagccccagtatggcgccg tgaacttcggcggaggcttcgggatagagtaccctgaccgggacgtgtaccgcg agatgcctacatggacatccgggcctgaagcccgatgacaccggcgtgtactactg cgccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagg gcacaaccgtgggtgtgtctgccgcctctacaaggggccccagcgtgtccctctggc ccctagcagcaagagcacatctggcggaacagccgcctgggctgcctctgaagg actacttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtg cacacctttccagctgtgtcgtcagtcacggcctgtacagcctgagcagcgtcgtga cagtggccagcagctctctgggcacccagacctacatctgaacgtgaaccacaagc ccagcaacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccca cacctgtccccctgtcctgccccgaactgtgggaggcccttccgtgtcctgttccc cccaaagcccaagacacccctgatgatcagccggacccccgaagtacactgcgtgtg gggtgatgtgtccacgaggaccctgaagtgaagtcaattggtacgtggacggcgtg gaagtgcacaagcccaagaccaagccaagagaggaacagtacaacagcacctacc gggtgtgtgtccgtgtgaccgtgtgcaccaggactgggtgaacggcaagagtaca agtgaaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaagg ccaagggccagccccgcgaacccaggtgtgcacactgcccccaagcaggggacga gctgaccaagaaccaggtgtccctgagctgtgccgtgaaaggcttaccctccgat atcgccgtggaatgggagagcaacggccagcccagaaactacaagaccaccc cccctgtgtggacagcgacggctattcttctggtgtccaagctgacagtggacaag tcccggtggcagcagggcaacgtgttcagctgtccgtgatgcagaggccctgcac aaccactacaccagaagtcctgagcctgagccccggcaag	SEQ ID NO: 61
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	gtccgtggactacgcggaatctgttaaagggcggtttacaatctcaagggacaatacca agaataccttgatttggagatgaacaacgtgagaactgaagacaccggatattacttct gtgccagaacaggcaatactacgacttctgtgtgggctatccccctggcgaggaaata tttcaagactggggtcagggaaccctgttatcgtgtcctccgacaaaaccataccca gggtgcagttggaggagctgtggggaggcgtgggtccagcctgggacgtccctgagact ctctgtgcagccttcaattcaggtttgatggttatggcatgactgggtccgccaggc cccaggcaaggggctggagtggtggcatctatatcacatgatggaattaaaaagtat cacgcagaaaaagtggtggggcgcttcacatctccagagacaattccaagaacaca ctgtatctacaatgaacagcctgcgacctgaggacacggctctctactactgtgcgaa agatttgcgagaagacgaatgtgaagagtgggtgctggattattacgatttgggaaac aactcccttgcgcaaagtcacgcggcggtgtgttggaattgctgataactggggcca agggacaatgtgcaccgtctcttcagataagaccacaccgtccaccaaggggcca tcggtcttccccctggcacctctccaagagcacctctgggggcacagcggcctgg gctgcctggtaaggactacttccccgaaccgggtgacgggtgctggtggaactcaggcgc cctgaccagcggcgtgcacacctccccggctgtcctacagtcctcaggactctactccc tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaa cgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccaaatctgt gacaaaactcacacatgcccaccgtgccagcacctgaactcctggggggaccgtca gtcttctcttccccccaaaaccaaggacacctcatgatctccggacctctgaggt cacatgcgtgggtgggtgacgtgagccacgaagacctgaggtcaagttcaactggtat gttgacggcgtggaggtgcataatgccaagacaaagccgcgggaggagcagtacaa cagcacgtaccgtgtgtgcagcgtcctcaccgtcctgcaccaggactggctgaatggc aaggagtacaagtgaagggtcacaacaaagccctccagccccatcgagaaaacc atctccaaagccaaagggcagccccgagaaccacaggtgtacacctgccccatgc cgggatgagctgaccaagaatcaagtcagcctgtgtgctggtgtaaaaggcttctatcc cagcgacatcgccgtggagtgaggagcaatgggcagccggagaaactacaag accacgcctccgtgctggactccgacggctccttctctactcaaaactcaccgtg gacaagagcaggtggcagcagggaacgtcttctcatgctccgtgatgcatgaggct ctgcacaaccactacacgcagaagagcctctccctgtctccgggt	
Light chain B	Cagtctgtgtgacgcagccgccctcagtgtctgcggccccaggacagaagg tcaccatctcctgctctggaaacacctccaacattggcaataattttgtcctggt atcaacagcgcggcgagagcccccaactcctcattatgaaactgacaag cgacctcagggattcctgaccgattctctgttccaagtctgtgtacgtcaggca ccctggccatcaccgggtgcagactggggacgaggccgattattactgcgc cacatggggtgccagcctgagttccgcgctgtcttcggaactgggaccaagg tcacgtcctggacaaaaccataaccgcatccgaactgactcaggacctgcc gtctctgtggcactgaagcagactgtgactattacttgcggaggcgactcactgc ggagccactacgcttctggtatcagaagaaacccggccaggcacctgtgtg ctgtttacggaaagaacaataggccatctggcatccccgaccgttttctggca gtgcatcagggaaccgagccagtctgaccattaccggcgccaggctgagga cgaagccgattactattgcagctcccgggataagagcggctccagactgagcg tgttcggaggaggaactaaactgaccgtcctcgataagaccatacccgtagc gtggccgctcccagcgtgttcattctccacctagcgcagcagcgtgaagtcc ggcacagcctctgtcgtgtgctgtgaacaacttctacccccgcgaggccaa agtgcagtggaaaggtggacaacgccctgcagagcggcaacagccaggaaa gcgtgaccgagcaggacagcaaggactccacctacagcctgagcagcaccc tgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagt gaccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcga gtgt	SEQ ID NO: 64
Binding Protein 9 Amino Acid Sequences		
Heavy chain A	Qvqlvqsggqmkkpgesmriscrasgyefidctlnwirlapgkrpewmgwlkpr ggavnyarplqgrvtmtrdvysdaflelrsltvddtavfyfctrknkdynwdfewh	SEQ ID NO: 65

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Light chain A	Eivltqspgtlslspgetaiisrctsqygslawyqqrpqgqaprlviysgstraagipdrfs gsrwgpdynltisnlesgdfgvyyccqyeffgqgtkvqvdikrtvaapsvfifppsd eqlksgtasvvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslstlt lskadyekkhkyacevthqglsspvtksfnrgec	SEQ ID NO: 66
Heavy chain B	Evrlvesggglvkpggslrlscsasgfdfdnawmtwvrppgkglewvgr itgpgegswvdyaesvkgfritsrdntkntlylemnnvrtdetgyyfcartgk yydfwwgyppgeeyfqdwgqgtlvivssdkthtqvqlvesgggvqpqt slrlscaasqfrfdgygmhwwrqapgkglewvasishdgikkyhaekvwg rftisrdnsknltlylqmnslrpedtalyycaakdlredeceewwsdydfgkq lpcaksgglvgiadnwgggtmvtvssdkthtastkgpsvfplapsskstsg gtaalgclvkdyfpepvtvswngaltsgvhtfpavlqssgylsslsvtvpss slgtqtyicnvnhkpsntkvdkkvepkscdkthtcppcpapellggpsvflf ppkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkp reeqynstyrvsvltvlhqdwlngkeykckvsnkalpapietiskakgqpr epqvylppcrdeltknqvsclvkgfypsdiavewesngqpennykttp pvldsdgsfflyskltvdksrwqqgnvfscsvmhealhnhytqkslspsg	SEQ ID NO: 67
Light chain B	qsvltqppsvsaaaggkvitiscsgntsnignnfsvwyqqrpgrapqliyetdkrps gipdrfsasksgtsgtlaitglqtgdeadycatwaaslsarvfgtgkvioldkhtas eltqdpavsvalkqvtitcrdgsrlshyaswyqkkpgqapvllfygknnrpsgipdr fsgsasgnrasltitgaqaeadyccsrldksgrlsvfgggtklvldkthtrtvaap svfifppsdeqlksgtasvvcllnnfypreakvqwkvdnalqsgnsqesvteqds dstyslstltlskadyekkhkyacevthqglsspvtksfnrgec	SEQ ID NO: 68
Binding Protein 9 Nucleotide Sequences		
Heavy chain A	caggctgcagctggtgcagctctggcggccagatgaagaaccggcgagagcatgcg gatcagctgcagagccagcggctacagttcatcgactgcacctgaactggatcaga ctggccctggcaagcggcctgagtgatgggatggctgaagcctagaggcggagc cgtgaactacgccagacctctgcaggcagagtgaccatgaccgggacgtgtacag cgataccgccttctggaactcggagcctgaccgtggatgataccgccgtgtacttct gcacccggggcaagaactcgactacaactgggacttcgagcactggggcagaggc accctgtgatcgtgtcaagcgcgtcgaccaaggccccagcgtgtccctctggccc ctagcagcaagagcacatctggcggaacagccgccctgggctgcctctgaaggact actttccgagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtgca cacctttccagctgtgctgcagtcagcggcctgtacagcctgagcagcgtcgtgaca gtgccagcagctctctgggcaccagacctacatctgcaacgtgaaccacaagccca gcaaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccacac ctgtccccctgtcctgccccgaactgctgggagggcccttccgtgttctgttcccc aaagcccaaggacacctgatgatcagccggacccccgaagtacgtcggtgtggt ggatgtgtccacaggacctgaagtgaagttaattgtacgtggacggcgtggaa gtgcacaacgccaagaccaagccaagagaggaacagtacaacagcacctaccgggt ggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaagagtacaagt caaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaaggccaa gggccagccccggaacccaggtgtgcacactgccccaaagcagggacgagctg accaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccctccgatacgc cgtggaatgggagagcaacggccagcccagagaacaactacaagaccacccccctg	SEQ ID NO: 69

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Light chain A	gagatcgtgctgacacagagccctggcaccctgagcctgtctccaggcgagacagcc atcatcagctgccggacaagccagctacggcagcctggcctggtatcagcagaggcct ggacagggccccagactcgtgatctacagcggcagcacaagagccgccggaatccc cgatagattcagcggctccagatggggccctgactacaacctgacctcagcaacctg gaaagcggcgacttcggcgtgtactactgccagcagctaggtcttcggccagggca ccaaggtgcaggtggacatcaagcgtacggtggcctcccagcgtgttcatttccc acctagcgacgagcagctgaagtccggcacagcctctgtcgtgtcctgctgaacaac ttctacccccgcgagggcaagtgcagtggaaaggtggacaacgccctgcagagcgg caacagccaggaaagcgtgaccgagcaggacagcaaggactccacctacagcctga gcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgc gaagtgaccaccaggggcctgtctagccccgtgaccaagagcttcaaccggggcga gtgt	SEQ ID NO: 70
Heavy chain B	gaggtagactggtggagtcaggagggggcctgtgaagcccgggtgggtctctccgc ctgagctgttctgcctccggttatttcgataacgcctggatgacctgggtcaggcag cctccaggtaaaggactggagtggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgggaatctgttaaaggcggtttacaatctcaaggacaatacca agaatacctgtatttggagatgaacaacgtgagaactgaagacaccggatattacttct gtgccagaacaggcaatactacgacttctgggtgggctatccccctggcgagggaata tttcaagactgggtcagggaaacctgttatcgtgtcctccgacaaaacctataccca gggtgcagttggtggagctctgggggagggcgtggtccagcctgggacgtccctgagact ctcctgtgcagcctctcaattcaggtttagttatggcatgactgggtccgccaggc cccaggcaaggggcgtggagtggtggcgtatctatcacatgatggaattaaaagtatc acgcagaaaaagtgtggggcgttcaccatctccagagacaattccaagaacacact gtatctacaaatgaacagcctgcgacctgaggacacggctctctactactgtcgaaag atttgcgagaagacgaatgtgaagagtgggtgcgattattacgattttgggaaacaac tccttgcgcaaaagtcacgcggcggttgggtgaattgctgataactggggccaagg gacaatggtcacctgtctctcagataagacccacaccgtccaccaaggggcccatcg gtcttccccctggcacctcctccaagagcacctctggggggcacagcggccctgggt gcctggtcaaggactacttcccgaaccgggtgacggtgtcgtggaactcaggcgcct gaccagcggcgtgcacacftcccggctgtcctacagtcctcaggactctactcctca gcagcgtggtgacctgcccctccagcagcttgggacccagacctacatctgcaacgt gaatcacaagcccagcaacaccaaggtggacaagaaagttgagccaaattctgtga caaaactcacacatgccaccgtgccagcacctgaactcctggggggaccgtcagt cttctcttcccccaaaacccaaggacacctcatgatctccggacccctgaggtca catgcgtggtggtggagctgagccacgaagacctgaggtcaagttcaactggtatgtt gacggcgtggaggtgcataatgccaagacaaaagccggggaggagcagtacaaca gcaggtaccgtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaa ggagtacaagtgaaggttccaacaaagccctcccagccccatcgagaaaacat ctccaaagccaaagggcagccccgagaaccacaggtgtacacctgcccccatgcc gggatgagctgaccaagaatcaagtcagcctgtggtgcctggtaaaaggctctatccc agcgacatcgccgtggagtgaggagcaatgggcagccggagaaactacaaga ccacgcctccgtgctggactccgacggctccttcttctactcaaaactaccgtgg acaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggtct gcacaaccactacacgcaagaagcctctccctgtctccgggt	SEQ ID NO: 71
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Binding Protein 10 Amino Acid Sequences		
Heavy chain A	Qvqlvqsggqmkkpgesmriscrasgyefidctlnwirlapgrpewmgwlkpr ggavnyarplqgrvtmtrdvsdtaflelrsltdtavfctrgkncdynwdfehw grgtpvivssastkgpsvfplapsskstsggtaalgclvkdyfpepvtvswngalts gvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscdk htcppcpapellggpsvflfpkpkdtlmisrtpevtcvvvdvshedpevkfnwyv dgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapiet iskakgqprepvctlpssrdeltknqvsclavkfypsdiavewesngqpenny kttpvldsdgsfflvskltvdksrwqqgnvfscsvmhealhnhytqkslsisp	SEQ ID NO: 73
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Heavy chain B	qvqlvesgggvvqpgtslrlscaasqfrfdgygmhwvrqapgkglewvas ishdgikkyhaekvwgrftisrdnsntlylqmnslrpedtalyycaakdlred eceewwsdydfgkqlpcaksrgglvgiadnwgggtmvtvssdkthtevr lvesggglvkpggsrlscsasgfdndawmtwvrqppgkglewvgritgp gegwsvdyaesvkgrftisrdntkntlylemnnvrtedtggyfcartgkyd fwwgyppgeeyfdwgqgtlvivssdkthtastkgpsvfplapsskstsgg taalglvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpsss lgtqtyicnvnhkpsntkvdkkvepkscdkthtcppcpapellggpsvflfp pkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpree qynstyrvsvltvlhqdwlngkeykckvsnkalpapietiskakgqpre pqvytlppcrdeltnqvsclvkgfypsdiavewesngqpennykttp vldsdgsfflvskltvdksrwqqgnvfscsvmhealhnhytqkslsisp	SEQ ID NO: 75
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Light chain A	yihvtqspsslsvsigdrvtincqtsqvgdsdlhwyqhkpgrapkllihhtssvedgv psrfsgsgfhtsfnltsldlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsde qlksgtasvvcllnnfybreakvqwkvdnalqsgnsqesvteqdsksdystylstlts kadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 82
Heavy chain B	evrlvesggglvkpggsrlrlscsasgfdfdnawmtwvrqppgkglewvgri tgpgegswsvdyaesvkgftrtsrdntkntlylemnrvrtedtggyfcartgk yydfwwgyppgeeyfqdwgqgtlvivssdkthtqvhltsqgpevrkpgts	SEQ ID NO: 83

	vkvsckapgnltktydlhwvsvpgqqlqwmgwishegdkkviverfka kvtidwdrstntaylqlsgltsgdtavyycakgskhrlrlydydddgalnwa vdvdylsnlefwwgqgtavtvssdkthtastkgpsvflapsskstsggtaal clvkdyfpepvtvswngaltsgvhtfpavlqssgylssvvtvpssslgtqt yicvnvhkpsntkvdkkvepkscdkthtccppcpapellggpsvflfppkpk dtlmsirtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqyns tyrvsvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepvyt lppcrdeltnqvslwclvkgfypsdiavewesngqpennyktpvldsd gsfflyskltvdksrwqqgnvfscsvmhealnhnhytqkslsisp	
Light chain B	dfvltqspshsvtpgesasiscksshlihgdrnnylawvyvqkprspqliylasr asgvpdprfsgsgsdlkdfstkisrvetedvgtyycmqgrespwtfqggtkvldikdkth taseltqdpavsvalkqtvtitrgdslrshyaswyqkpgqapvllfygknnrpsgi pdrfsgsasgnrasltitgaqaeadyycssrdksgrlsvfgggtklvtldkthtrtv aapsvfifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteq dskdstylsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 84
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	cgcctgcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttca accggggcgagtgt	
Binding Protein 12 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvcqtsgyftahilfwfrqapgrglewv gwikpqy gavnfgggfrdrvltldvryeiaymdirglkpddtavyyccardrsygdsswalda wgqgttvvvsaaatkgpsvfplapsskstsggtaalgclvkdyfpepvtvswngal tsgvhtfpavqlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscd kthtcppcpapellggpsvflfppkpkdtlmsrtpevtcvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeyckkvsnkalspapi ektiskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpe nnyktpvldsdgsfflvskltvdksrwqqgnvfscsvmhleahnhytqkslsisp g	SEQ ID NO: 89
Light chain A	yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapklhihtssvedgv psrfsgsgfhtsfnltsidlqaddiatyycqlqffgrgsrlhikrtvaapsvfifppsde qlkshtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdskdstyslstlts kadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO:90
Heavy chain B	evrlvesggglvlpkpgslrlscsasgfdfdnawmtwvrqppgkglewvgri tgpgegswsvdyaesvkgftrtsrdntkntlylemnnvrtedtggyfcartgk yydfwwgyppgeeyfqdwgqgtlvivssdkthtqmqlqesgpglvkpse tlsltcsvsgasisdsywswirrspgkglewigyvhksgdtnyspslksrvnl sldtsknqvslslvaataadsgkyycartlhgrriygivafnewftyfymdvw gngtqvtvssdkthtastkgpsvfplapsskstsggtaalgclvkdyfpepvtv swngaltsgvhtfpavqlqssglyslssvvtvpssslgtqtyicnvnhkpsntk vdkkvepkscdkthtcppcpapellggpsvflfppkpkdtlmsrtpevtcv vvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqd wlngkeyckkvsnkalspapiektiskakgqprepqvylppcrdeltknqv slwclvkgfypsdiavewesngqpennyktpvldsdgsfflyskltvdks rwqqgnvfscsvmhleahnhytqkslsisp	SEQ ID NO: 91
Light chain B	sdisvapgetariscgekslgravqwyqhragqapsliiynndrpsgiperfsgsp dspfgttatltsveagdeadyychiwdsrvtkwvfgggtltvldkthtaseltqdp avsvalkqtvtitcrdslrshyaswyqkpgqapvllfygknnrpsgipdrfsgsas gnrasltitgaqaedeaddyccsrksgsrlsvfgggtklvldkthtrtaapsvfifp psdeqlkshtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdskdstysls stltskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 92
Binding Protein 12 Nucleotide Sequences		
Heavy chain A	agagcccacctggtgcagtctggcaccgccatgaagaaaccaggcgcctctgtgcgg gtgtcctgtcagacaagcggtacaccttcaccgccacatcctgttctggtccggcag gcccctggcagaggactggaatgggtgggatgatcaagccccagtatggcgccgtg aacttcggcgaggctccgggatagagtaccctgaccgggacgtgtaccgcgag atcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtggtggtgtctgccgcctctacaaaggccccagcgtgtccctctggcccc tagcagcaagagcacatctggcggaacagccgcctgggctgcctctgtaaggacta ctttcccgagcccgtagcctgtcctggaattctggcgccctgaccagcggcgtgcac accttccagctgtgctgcagtccagcggcctgtacagcctgagcagcgtcgtgacagt gcccagcagctctctgggcacccagacctacatctgcaacgtgaaccacaagcccag caacaccaaggtggacaagaaggtgaaccaagagctgcgacaagaccacacct gtccccctgtcctgccccgaactgctgggaggcccttcctgttctgttcccccaa agcccaaggacacctgatgatcagccggacccccgaagtacctgcgtggtggtgg atgtgtccacgaggacctgaagtgaattcaattggtacgtggacggcgtggaagt gcacaacgccaagaccaaggaaggaacagtacaacagcacctaccgggtg	SEQ ID NO: 93

	gtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaagagtacaagtgc aaggtgtccaacaaggccctgctgccccatcgagaaaaccatcagcaaggccaag ggccagccccgcgaacccaggtgtgcacactgccccaaagcaggagcagctga ccaagaaccaggtgtccctgagctgtccgtgaaaggcttctacccctccgatatcgcc gtggaatgggagagcaacggccagcccagagaacaactacaagaccacccccctgt gctggacagcgacggctcatttctctggtgtccaagctgacagtggacaagtccgggt ggcagcagggaacgtgttcagctgtccgtgatgcagaggccctgcacaaccact acaccagaagtccctgagcctgagccccggcaag	
Light chain A	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacag agtgaccatcaactgccagacctctcagggcgtgggcagcgacctgcaactggt atcagcacaagcctggcagagccccaaagctgctgatccaccacacaagcag cgtggaagatggcgtgcccagcagattttccggcagcgggttccacaccagct tcaacctgaccatcagcgatctgcaggccgacgacattgccacctactattgtca ggtgctgcagttcttcggcagaggcagcagactgcacatcaagcgtacgggtgg ccgctcccagcgtgttcattcttcccactagcgacgagcagctgaagtccggc acagcctctgtcgtgtgcctgtgaacaacttctacccccgcgaggccaaagt cagtggaaggtggacaacgcctgcagagcggcaacagccaggaaagcgt gaccgagcaggacagcaaggactccacctacagcctgagcagcaccctgac actgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgacc caccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 94
Heavy chain B	gaggttagactggtggagtcaggaggggggctgtgaagccccggtgggtctctccgc ctgagctgttctgcctccggcttatttcgataacgcctggatgacctgggtcaggcag cctccaggtgaaggactggagtggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaatctgttaaaggcggtttacaatctcaagggacaatacca agaataccttgtatttgagatgaacaacgtgagaactgaagacaccggatattacttct gtgccagaacaggcaatactacgacttctggtggggctatccccctggcgagggaata tttcaagactggggtcagggaaccctgttatcgtgtcctccgacaaaaccatacca gatgcagctgcaggagagcggccctggactcgtgaagcccagcgagaccctgagcc tgacatgcagcgtgagcggcgccagcatcagcgacagctactggagctggatcagga ggagccctggcaagggcctggagtggatcggtctacgtgcacaagagcggcgacacc aactacagccccctctgaagtccagggtgaacctgtccctggacaccagcaagaacc aggtgagcctgtccctggtggctgccacagctgctgacagcggcaagtactactgtgc caggacctgcacggcaggaggtctacggcatcgtggccttaacgagtgttacc tacttctacatggacgtgtggggcaacggcaccaggtgacctgtgagctccgataaga cccacaccgttccaccaaggggccatcggttctccccctggcaccctctccaagag cacctctgggggcacagcggccctgggtgctgtcaaggactacttccccgaacc ggtgacggtgtcgtggaactcaggcgcctgaccagcggcgtgcacacctccccggc tgtctacagtctcaggacttactccctcagcagcgtggtgacctgtccctccagca gcttgggcaccagacctacatctgcaacgtgaatcacaagcccagcaacaccaaggt ggacaagaaagttgagcccaaatctgtgacaaaactcacacatgccaccgtgccc gcacctgaactcctggggggaccgtcagttcttcttcccccaaaaaccaaggaca ccctcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagccacga agacctgaggtcaagttcaactggtatgttgacggcgtggaggtgcataatgccaaga caaagccgcgggagggagcagtaaacagcacgtaccgtgtggtcagcgtcctcacc gtcctgcaccaggactggctgaatggcaaggagtacaagtgaaggtctccaacaaa gcccctccagccccatcgagaaaaccatctccaaagccaaagggcagccccgaga accacaggtgtacacctgccccatgccgggatgagctgaccaagaatcaagtcag cctgtgtgctggtgtaaaaggcttctatcccagcgacatcgccgtggagtgaggagc aatgggcagccggagacaactacaagaccacgcctccgtgctggactccgacgg ctcttcttctctactcaaaactcaccgtggacaagagcaggtggcagcaggggaac gtcttctcatgtccgtgatgcatagagctgtgcacaaccactacgcagaagagcct ctcctgtctccgggt	SEQ ID NO: 95

Light chain B	tccgacatcagcgtggccccggagagacagccaggatctcctgcggcgag aagagcctgggaagcagggtgtgcagtgtaccaacacagggccggacag gctcccagcctgatcatctacaacaaccaggacagggccagcggcatccctga gaggttcagcgggaagccccgacagccccttcggaaccacagccaccctgacc atcacaagcgtggaagccggcgacgagggcgactactactgccacatctggg acagcagggtgcccaccaagtgggtgtttggcgggcaccaccctgaccgt gctggacaaaaccataccgcatccgaactgactcaggaccctgccgtctctgt ggcactgaagcagactgtgactattacttgcggagggcactactgcggagcc actacgcttctgtatcagaagaaaccggccaggcacctgtgctgtgttcta cggaagaacaataggccatctggcatccccgaccgctttctggcagtgcac aggggaaccgagccagtctgaccattaccggcgcccaggctgaggacgaagc cgattactattgcagctcccgggataagagcggctccagactgagcgtgttcgg aggaggaactaaactgaccgtcctcgataagaccataccgtacggtggccg ctcccagcgtgttcattctcccacctagcgacgagcagctgaagtcgggcaca gcctctgtcgtgtcctgtgaacaacttctacccccgcgaggccaaagtgcag tggaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtgacc gagcaggacagcaaggactccacctacagcctgagcagcacctgacactga gcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccacc agggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 96
Binding Protein 13 Amino Acid Sequences		
Heavy chain A	qvhltqsgpevrkpgtsvkvsckapgnltktydlhwrvsvpgqlqwmgwishe gdkkviverfkakvtidwdrstntaylqlsgltsgdavyycaakgskhrlrdyalydd dgalnwavdvdylnlefwgqgtavtvssastk gpsvflp apsskstsggtaalgcl vkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgtqtyicnvn hkpsntkvdkkvepkscdktht cppepapellggpsvflfppkpkdtlmisrtpevt cvvvdvshedpevkfnwyvdg vevhnaktkpreeqynstyrvvsvltvlhqdwl ngkeyckvsnkalpapiektiskakg qprepqvctlppsrdeitknqvslscavkg fypsdiavewesngqpennyk ttppvldsdgsfflvskltvdksrwqqgnvfscsv mhealhnhytqkslslspg	SEQ ID NO: 97
Light chain A	dfvltqspshslsvtpgesasiscksshlihgdrnnylawyvqkprspqlliylasr asgvprdfsgsgsdktlktisrvetdvgttycmqgrespwtfgqgtkvdikrtva apsvfifppsdeqlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqd skdstylsstltlskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 98
Heavy chain B	evrlvesggglvkpggslrlscsasgfdfdnawmtwvrqppgkglewvgr itgpgegwsvdyaesvkgrftisrdntkntlylemnnvrtdtgyyfcartgk yydfwwgyppgeeyfqdwgqgtlvivssdkthtqmqlqesgpglvkpse tlltcsvsgasisdsywswirrspgkglewigyvhskdtnyspslksrvnl sldtsknqvslslvaataadsgkyycartlhgrriygivafnewftyfymdv wngtqvvtvssdkthtastk gpsvflp apsskstsggtaalgclvkdyfpepv tvswngaltsgvhtfpav lqssglyslssvvtvpssslgtqtyicnvn hkpsn tkvdkkvepkscdkthtcppepapellggpsvflfppkpkdtlmisrtpevt cvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlh qdwlngkeyckvsnkalpapiektiskakgqprepqvylppcrdeitkn qvslwclvkgyfypsdiavewesngqpennykttppvldsdgsfflvskltv dksrwqqgnvfscsvmhealhnhytqkslslspg	SEQ ID NO: 99
Light chain B	sdisvapgetariscgekslgsravqwyqhragqapsliiynndrpsgiperfsgsp dspfgttatlitsveagdeadyychiwdsrvtkwvfgggtltvldkthtaseltqd pavsvalkqtvtitcrdgsrlshyaswyqkkpgqapvllfygknnrpsgipdrfsgs asgnrasltitgaqaeadyycssrdksgrlsvfgggtklvldkthtrtvaapsvfif ppsdeqlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdsdkdstys	SEQ ID NO: 100

	lsstltlskadyekhkvyacevthqglsspvtksfnrgec	
Binding Protein 13 Nucleotide Sequences		
Heavy chain A	caggtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaa ggtgtcctgcaagggccctggcaacacctgaaaacctacgacctgcactgggtgcg cagcgtgccaggacagggactgcagtggatgggctggatcagccacgagggcgac aagaaagtgatcgtggaacgggtcaaggccaaagtgaccatcgactgggacagaagc accaacaccgcctacctgcagctgagcggcctgacctctggcgataccggcgtgtact actgcgccaaagggcagcaagcaccggctgagagactacgccctgtacgacgatgac ggcgccctgaactgggccgtggatgtggactacctgagcaacctggaattctggggc cagggcacagccgtgaccgtgtcatctgcttcgaccaagggccccagcgtgttcctc tggcccctagcagcaagagcacatctggcggaacagccgccctgggctgcctcgtga aggactactttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagcgg cgtgcacacettccagctgtgctgcagtccagcggcctgtacagcctgagcagcgtc gtgacagtggccagcagctctctgggcacccagacctacatctgcaactgaaccaca agcccagcaacaccaaggtggacaagaaggtggaaccaagagctgcgacaagac ccacacctgtccccctgtcctgccccgaactgctgggaggccctccgtgttcctgtt cccccaaagcccaaggacacctgatgatcagccggacccccgaagtgacctgcg tggtggtggatgtgtcccacgaggacctgaagtgaagtcaattggtacgtggacgg cgtggaagtgcacaacccaagaccaagccaagagaggaacagtacaacagcacct accgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaaaggt acaagtgaaggtgtccaacaaggccctgcctgccccatcgagaaaacctacagca aggccaagggccagccccgcgaacccaggtgtgcacactgcccccaagcaggga cgagctgaccaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccctcc gatacgcctggaatgggagagcaacggccagcccagaaactacaagaccac ccccctgtgctggacagcgacggctcattcttctggtgtccaagctgacagtggaca agtcccggtggcagcagggaacgtgttcagctgtccgtgatgcagaggccctgc acaaccactacaccagaagtcctgagcctgagccccggcaag	SEQ ID NO: 101
Light chain A	gacttcgtgctgacctagagccctcacagcctgagcgtgacacctggcgagagcgcc agcatcagctgcaagagcagccactccctgatccacggcgaccggaacaactacctg gcttggtacgtgcagaagcccggcagatccccccagctgctgatctacctggccagca gcagagccagcggcgtgcccatagattttctggcagcggcagcgacaaggacttca ccctgaagatcagccgggtggaaccgaggacgtgggcacctactactgtatgcagg gcagagagagccctggacctttggccagggcaccgaaggtggacatcaagcgtacg gtggccgctccagcgtgttcattctccacctagcgacgagcagctgaagtccggca cagcctctgtcgtgtgctgtgaacaacttctacccccgcgaggccaaagtgcagtg gaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtgaccgagca ggacagcaaggactccactacagcctgagcagcaccctgacactgagcaaggccg actacgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcctgtctagcc ccgtgaccaagagcttcaaccggggcgagtg	SEQ ID NO: 102
Heavy chain B	gaggttagactggtggagtcaggagggggcctgtgaaagccgggtgggtctctccgc ctgagctgttctgcctccggcctttgatttcgataacgcctggatgacctgggtcaggcag cctccaggtaaaggactggagtggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaatctgttaaaggcggtttacaatctcaagggacaatacca agaataccttgatttggagatgaacaacgtgagaactgaagacaccggatatttct gtgccagaacaggcaatactacgacttctggtggggctatccccctggcgaggaata ttttcaagactggggtcagggaaccctgttatcgtgtcctccgacaaaaccataacca gatgcagctgcaggagagcggccctgactcgtgaagcccagcgagacctgagcc tgacatgcagcgtgagcggcgccagcatcagcgacagctactggagctggatcagg aggagccctggcaagggcctggagtggatcggctacgtgcacaagagcggcgaca ccaactacagccccctccctgaagtccagggtgaacctgtccctggacaccagcaaga accaggtgagcctgtccctgggtggctgccacagctgctgacagcggcaagtactactg tgccaggacctgcacggcaggagatctacggcatcgtggccttcaacagtggttc	SEQ ID NO: 103

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Light chain B	tccgacatcagcgtggccccggagagacagccaggatctcctgcggcgag aagagcctgggaagcagggctgtgcagtggtaccaacacagggccggacag gtccccagcctgatcatctacaacaaccaggacagggccagcggcatcctg agagggtcagcgggaagccccgacagcccttcggaaccacagccaccctga ccatcacaagcgtggaagccggcgacgaggccgactactactgccacatctg ggacagcaggggtgcccaccaagtgggtgtttggcggcgccaccacctgac cgtgctggacaaaaccataaccgcatccgaactgactcaggacctgccgtct ctgtggcactgaagcagactgtgactattacttgcggagcgcactactgcgga gccactacgcttctgtatcagaagaaccggccaggcacctgtgctgctgt tctacggaaagaacaataggccatctggcatccccgaccgctttctggcagt catcaggggaaccgagccagtctgaccattaccggcgcccaggctgaggacg aagccgattactattcgactcccgggataagagcggctccagactgagcgtg ttcggaggaggaactaaactgaccgtcctcgataagaccatacccgtagcgt ggcgcctcccagcgtgtcatcttcccacctagcgacgagcagctgaagtccg gcacagcctctgtcgtgtgctgctgaacaacttctacccccgcaggccaaa gtgcagtgggaaggtggacaacgcctgcagagcggcaacagccaggaaag cgtgaccgagcaggacagcaaggactccacctacagcctgagcagcacct gacactgagcaaggccgactacgagaagcacaaggtgtacgctgcgaagt gaccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcgga gtgt	SEQ ID NO: 104
Binding Protein 14 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvcqtsgytftahilfwfrqapgrglewvgnwikipqy gavnfgggfrdrvlttrdvreiaymdirglkpddtavvyccardsygdsswalda wgqgtvvvsaastkgpsvflapsskstsggtaalglvkdypcpvvtvswngal tsghvthpavlqssglyslssvvtvpssslgtqyicvnhkpsntkvdkkvepkscd kthtccppapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalpapi ektiskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpe nnyktpvldsdgsfflvskltvdksrwqqgnvfscsvmhealnhhtqkslsisp g	SEQ ID NO: 105
Light chain A	yihvtqspsslsvisgdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedg vpsrfsgsfhtsfnltsldlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsd	SEQ ID NO: 106

	eqlksqtasvvcclnnfyreakvqwkvdnalqsgnsqesvteqdsksdstylsstlt lskadyekkhkyacevthqglsspvtksfnrgec	
Heavy chain B	Qvhltqsgpevrkpgtsvkvsckapgnltktydlhwvrsvpqgqlqwmg wishegdkkviverfkakvtidwdrstntaylqlsgltsgdavyycakgsk hrlrdyalydddgalnwavdvdylnlefwgggtavtvssdkthtevrives ggglvkpggslrlscsasgfdndawmtwvrpppgklewvgritgpgeg wsvdyaesvkgrftisrdntkntlylemnnvrtdetgyyfcartgkyydfw wgyppeggeyfwdwgqgtlvivssdkthtastkgpsvfplapsskstsggtaa lgclvkdyfpepvtvswngaltsgvhtfpavllqssglyslssvvtvpssslgt qtyicvnkhpsntkvdkkvepkscdkthtppcpapellggpsvflfppk pkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeq ynstyrvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprep qvytlppcrdeltnqvslwclvkgyfypsdiavewesngqpennyktppv ldsdgsfflyskltvdksrwqqgnvfscsvmhleahnhytqkslsisp	SEQ ID NO: 107
Light chain B	aseltqdpavsvalkqtvtitcrsdlrshyaswyqkkpgqapvllfygknrpsgi pdrfsgsasgnrasltitgaqaeadyycssrdksgrlsvfgggtklvldkthtdfv ltqspshlsvtptgesasisckssshlihgdrnnylawyvqkprspqliylassarag vpdrfsgsgskdftlkisrvetedvgytymqgrespwtfgggtkvdkdkthtrt vaapsvfifppsdeqlksqtasvvcclnnfyreakvqwkvdnalqsgnsqesvte qdsksdstylsstltlskadyekkhkyacevthqglsspvtksfnrgec	SEQ ID NO: 108
Binding Protein 14 Nucleotide Sequences		
Heavy chain A	agagcccacctgggtgcagtctggcaccgccatgaagaaccaggcgcctctgtgcgg gtgtcctgtcagacaagcggtacacctcaccgccacatcctgttctggtccggca ggccccctggcagaggactggaatgggtggatggatcaagccccagtatggcgccg tgaactcggcggaggcttccgggatagatgacctgaccgggacgtgtaccgcg agatcgctacatggacatccggggcctgaagcccgatgacaccgcccgtgtactactg cgccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagg gcacaaccgtgggtgtctgcccgcctctacaaggccccagcgtgttccctctggc ccctagcagcaagagcacatctggcggaacagccgccctgggctgcctcgtgaagg actacttcccagccccgtgaccgtgtcctggaattctggcgccctgaccagcgccgtg cacacattccagctgtgctgcagtccagcggcctgtacagcctgagcagcgtcgtga cagtgcacagcagctctctgggcaccagacctacatctgcaacgtgaaccacaagc ccagcaacaccaaggtggacaagaaggtggaaccaagagctgcgacaagacca cacctgtccccctgtcctgccccgaactgctgggaggcccttccgtgttctgttccc cccaaagcccaagacacctgatgatcagccggacccccgaagtgacctgcgtgtg gggtgatgtgtccacgaggacctgaagtgaagttcaattgtacgtggacggcgtg gaagtgcacaagccaagaccaaggaagaggaacagtacaacagcacctacc gggtgtgtcctgctgaccgtgtgcaccaggactggctgaacggcacaagagtaca agtgaaggtgtccaacaaggccctgcctgccccatcgagaaaacctacagcaagg ccaagggccagccccgcgaacccaggtgtgcacactgcccccaagcaggagcga gctgaccaagaaccaggtgtccctgagctgtgccgtgaaaggtcttaccctccgat atcgccgtggaatgggagagcaacggccagcccagagaacaactacaagaccacc ccccgtgtgacagcgacggctcattcttctggtgtccaagctgacagtggacaag tcccggtggcagcagggaacgtgttcagctgtccgtgatgcacgaggccctgcac aaccactacaccagaagtccctgagcctgagccccggcaag	SEQ ID NO: 109
Light chain A	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcgggcgacag agtgacctcaactgccagacctctcaggcggtgggcagcgacctgcactggt atcagcacaagcctggcagagcccccaagctgctgatccaccacacaagcag cgtggaagatggcgtgcccagcagattttcggcagcggcttccacaccagct tcaacctgacctacagcgtctgcaggccgacgacattgccacctactattgtc aggtgctgcagttcttcggcagaggcagcagactgcacatcaagcgtacggtg	SEQ ID NO: 110

	<p>gccgctcccagcgtgttcattctccacctagcgcagcagcagctgaagtcgg cacagcctctgtcgtgtgctgctgaacaacttctacccccgcgaggccaaagt gcagtggaaaggtggacaacgccctgcagagcggcaacagccaggaaagcg tgaccgagcaggacagcaaggactccacctacagcctgagcagcacctga cactgagcaaggccgactacgagaagcacaaggtgtacgctgcgaagtga cccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagt t</p>	
Heavy chain B	<p>caggtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaa ggtgtcctgcaagggccctggcaacacctgaaaacctacgactgcactgggtgcg cagcgtgccaggacagggactgcagtggatgggctggatcagccacgaggcgac aagaaagtgtcgtggaacggtcaaggccaaagtaccatcgactgggacagaagc accaacaccgcctacctgcagctgagcggcctgacctctggcgataccgccgtgtact actgcgccaagggcagcaagcaccgctgagagactacgccctgtacgacgatgac ggcgccctgaactgggcccgtggatgtggactacctgagcaacctggaattctggggc cagggcacagccgtgaccgtgtcatctgacaaaaccataccagggttagactgggtg gagtcaggaggggggcctgtgaagcccgggtgggtctctccgctgagctgttctgcct ccggcttgatttcgataacgcctggatgacctgggtcagcagcctccaggttaaggg actggagtgggtgggaagaatcacaggtccaggcgagggtggtccgtggactacg cggaatctgttaaaggcggtttacaatctcaagggacaataccaagaatacctgtattt ggagatgaacaacgtgagaactgaagacaccggaattacttctgtccagaacaggc aaatactacgacttctgggtgggctatccccctggcgaggaaatatttcaagactgggt cagggaacccttgtatcgtgtcctccgataagaccacaccgcttcaccaagggcc catcggtcttccccctggcacctctccaagagcacctctgggggcacagcggccct gggctgcctggtaaggactacttccccgaaccgggtgacgggtgctgtggaactcagg cgccctgaccagcggcgtgcacacctccccgctgtcctacgtcctcaggactctact ccctcagcagcgtgtgacgtgacctccagcagcttgggcacccagacctacatctg caacgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagcccaaatc ttgtgacaaaactcacacatgccaccgtgccagcacctgaactcctggggggacc gtcagtcttctcttccccccaaaaccaaggacacctcatgatctccggaccctg aggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaact ggtatgttgacggcgtggaggtgcataatgccaagacaaagccgcgggaggagcag tacaacagcagctaccgtgtggtcagcgtcctcaccgtcctgcaccaggactggctga atggcaaggagtacaagtgcagggtctccaacaaagccctccagccccatcgaga aaaccatctccaaagccaaaggcgagccccgagaaccacaggtgtacacctgccc ccatgccgggatgagctgaccaagaatcaagtcagcctgtggtgcctggtaaaaggct tctatcccagcgacatcgccgtggagtgggagagcaatgggcagccggagaacaac tacaagaccacgctcccgtgctggactccgacggctccttcttctactcaaaactc accgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgc gaggtctgcacaaccactacacgcagaagagcctctccctgtctccgggt</p>	SEQ ID NO: 111
Light chain B	<p>gcataccgaactgactcaggacctgcccgtctctgtggcactgaagcagactgt gactattacttgccgaggcgactactgcggagccactacgcttctgtgtatca gaagaaacccggccaggcacctgtgctgctgttctacggaaagaacaatagg ccatctggcatccccgaccgcttttctggcagtgcatcagggaaccgagccagt ctgaccattaccggcgcccaggctgaggacgaagccgattactattgcagctc ccgggataagagcggctccagactgagcgtgttcggaggaggaaactaaactg accgtcctcgacaaaaccataccgacttcgtgctgacctagagccctcacag cctgagcgtgacacctggcgagagcggcagcatcagctgcaagagcagcca ctccctgatccacggcgaccggaacaactacctggcttggtacgtgcagaagc ccggcagatccccccagctgctgatctacctggccagcagcagagccagcgg cgtgcccgatagattttctggcagcggcagcgacaaggacttcacctgaaga tcagccgggtggaaaccgaggacgtgggcacctactactgtatgcagggcag agagagccccctggaccttggccagggcaccaaggtggacatcaaggataag</p>	SEQ ID NO: 112

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Binding Protein 15 Amino Acid Sequences		
Heavy chain A	<p>qvhltqsgpevrkpgtsvkvsckapngntlktydlhwrvsvpgqlqwmgwishe gdkkviverfkakvtidwdrstntaylqlsgltsdgtavyycakgskhrlrdyalydd dgalnwavdvdylnlefwggtavtvssastkgpsvflapsskstsggtaalgcl vkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicnvn hkpsntkvdkkvepkscdkthtppcpapellggpsvflfppkpkdtlmisrtpevt cvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlhqdlw ngkeyckvsnkalpapiektiskakgpprepqvctlppsrdeltknqvslescavkg fypsdiawesngqpennyktpvldsdgsfflvskltvdksrwqqgnvfscsv mhealhnhytqkslsisp</p>	SEQ ID NO: 113
Light chain A	<p>dfvltqspshslsvtpgesasiscksshlihgdrnnylawyvqkprspqliylasr asgvprdfsgsgsdktlktisrvetedvgttycmqgrespwtfqggtkvdikrtva apsvfifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqds kdstyslstltlskadyekhkvyacevthqglsspvtksfnrgec</p>	SEQ ID NO: 114
Heavy chain B	<p>Evrlvesggglvkpggslrlscasgfdnawmtwvrqppgkglewvgr itgpgegwsvdyaesvkgrftisrdntkntlylemnnvrtedtgyyfcartgk yydfwsgyppgeeyfqdwgqgtlvivssdkthtqmqlqesgpglvkpsel lsltcsvsgasisdsywswirrspgkglewigyvhksgdtnyspslksrvnls ldtsknqvslslvaataadsgkyycartlhgrriygiavfnewftyfymdvw gngtqvvtssdkthtastkgpsvflapsskstsggtaalgclvkdyfpepvtv swngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntk vdkkvepkscdkthtppcpapellggpsvflfppkpkdtlmisrtpevtcv vvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlhqdlw wlngkeyckvsnkalpapiektiskakgpprepqvytlppcrdeltnqv slwclvkgyfypsdiawesngqpennyktpvldsdgsfflvskltvdks rwqqgnvfscsvmhealhnhytqkslsisp</p>	SEQ ID NO: 115
Light chain B	<p>sdisvapgetariscgekslgsravqwyqhragqapsliiynndrpsgiperfsgsp dspfgttatlitsveagdeadyychiwdsrvtkwvfgggttlvldkthtaseltqdp avsvalkqtvtitcrghslrshyaswyqkpgqapvllfygknnrpsgipdrfsgsas gnrasltitgaqaedeaddyccsrksgsrlsvfgggtklvldkthtrtvaapsvfifp psdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsdstysls stltlskadyekhkvyacevthqglsspvtksfnrgec</p>	SEQ ID NO: 116
Binding Protein 15 Nucleotide Sequences		
Heavy chain A	<p>caggtgcacctgacacagagcggaccggaagtgcggaagcctggcacctctgtgaa ggtgtcctgcaaggccctggcaacacctgaaaacctacgacctgcactgggtgcg cagcgtgccaggacaggactgcagtggatgggctggatcagccacgaggcgac aagaaagtgatcgtggaacggtcaaggccaaagtgaccatcgactgggacagaagc accaacaccgcctacctgcagctgagcggcctgacctctggcgataccgccgtgtact actgcgccaaggcagcaagcaccggctgagagactacgcctgtacgacgatgac ggcgccctgaactgggccgtggatgtggactacctgagcaacctggaattctggggcc agggcacagccgtgaccgtgtcatctgcttcaccaaggccccagcgtgttcctct ggccctagcagcaagagcacatctggcggaacagccgcctgggctgcctcgtga aggactactttcccagcccgtagcgtgtcctggaattctggcgccctgaccagcgg cgtgcacacctttcagctgtgctgcagtcacggcctgtacagcctgagcagcgtc</p>	SEQ ID NO: 117

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Binding Protein 16 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvcqtsgyftahilfwfrqapgrglewv gwipqy gavnfgggfrdrvltlrdvyreiaymdirglkpdtdavyycardrsygdsswalda wgqgttvvsaastkgpsvfplapsskstsggtaalglvkdyfpepvtvswngal tsghvtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscd kthtccppapellggpsvflfppkpkdtlmsrtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapi ektiskakgqprepqvctlppsrdeitknqvsiscavkgfypsdiavewesngqpe nnyktppldsdgsfflvskltvdksrwqqgnvfscsvmhealnhhytqkslslsp g	SEQ ID NO: 121
Light chain A	yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedgv psrfsfgsfhtsfnlitidldiadiatycqvlqffgrgsrlhikrtvaapsvfifppsde qlksqtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslsltlsl kadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 122
Heavy chain B	Evrlvesggglvkpggsrlscsasgfdnawmtwvrqppgkglewvgr itgpgegwsvdyaesvkgrftisrdntkntlylemnnvrtdtgyyfcartgk yydfwsgyppeeyfqdwgqgtlvivssdkthtqmqlqesgpglvkpset lsltcsvsgasidsywswirrspgkglewigyvhksgdtnyspslksrvnls ldtsknqvsllvaataadsgkyycartlhgrriygivafnewftyfymdvw ngtqtvtvssdkthtastkgpsvfplapsskstsggtaalglvkdyfpepvtv swngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntk vdkkvepkscdkthtccppapellggpsvflfppkpkdtlmsrtpevtcv vvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdw wlngkeykckvsnkalpapiektiskakgqprepqvylppcrdeitknqv slwclvkgyfypsdiavewesngqpennyktppldsdgsfflvskltvdks	SEQ ID NO: 123

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Heavy chain A	agagcccacctgggtgcagtctggcaccgccatgaagaaccaggcgctctgtgcgg gtgtcctgtcagacaagcggtacaccttcaccgcccacatcctgttctggtccggcag gcccctggcagaggactggaatgggtgggatgatcaagccccagtatggcgccgtg aacttcggcggaggcttcgggatagagtaccctgacccgggacgtgtaccgcgag atcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtggtgtgtctgccgcctctacaaggggccccagcgtgtccctctggcccc tagcagcaagagcacatctggcggaacagccgcccctgggctgcctcgtgaaggacta cttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtgcac accttccagctgtgtgcagtccagcggcctgtacagcctgagcagcgtcgtgacagt gcccagcagctctctgggcaccagacctacatctgcaacgtgaaccacaagcccag caacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccacacct gtccccctgtcctgccccgaactgctgggaggcccttcggttctgttcccccaa agccccagacacctgatgatcagccggacccccgaagtgcctgctggtggtgg atgtgtccacgaggaccctgaagtgaagttcaattggtacgtggacggcgtggaagt gcacaacgccaaagaccaagccaagaggaacagtacaacagcacctaccgggtg gtgtccgtgctgaccgtgtgcaccaggactggctgaacggcgaagagtacaagtgc aaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaaggccaag ggccagccccgcgaaccccaggtgtgcacactgccccaaagcagggacgagctga ccaagaaccaggtgtccctgagctgtgccgtgaaaggcttctacccctccgatatgcc gtggaatgggagagcaacggccagccgagaacaactacaagaccacccccctgt gctggacagcgacggctatttctcgtgtccaagctgacagtggacaagtcccgtg ggcagcagggcaacgtgttcagctgtccctgatgcacgagggccctgcacaaccact acaccagaagtcctgagcctgagccccggcaag	SEQ ID NO: 125
Light chain A	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcgggcgacag agtgacctcaactgccagacctctcagggcgtgggcagcgacctgcactggt atcagcacaagcctggcagagccccaaagctgctgatccaccacacaagcag cgtggaagatggcgtgcccagcagattttccggcagcggcttccacaccagct tcaacctgacctcagcgatctgcaggccgacgacattgccacctactattgtca ggtgctgcagttcttcggcagaggcagcagactgcacatcaagcgtacgggtgg ccgctcccagcgtgttcatttcccacctagcgcagcagcagctgaagtccggc acagcctctgtcgtgtgctgctgaacaacttctacccccgcgaggccaaagtg cagtggaaggtggacaacgccctgcagagcggcaacagccaggaaagcgt gaccgagcaggacagcaaggactccacctacagcctgagcagcaccctgac actgagcaagggcgactacgagaagcacaaggtgtacgcctgcgaagtgacc caccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtggt	SEQ ID NO: 126
Heavy chain B	gaggttagactggtggagtcaggaggggggctgtgaagcccgggtgggtctctccgc ctgagctgttctgcctccggcttgatttcgataacgcctggatgacctgggtcaggcag cctccaggttaagggactggagtggtgggaagaatcacaggctccaggcgagggtg gtccgtggactacgcgaatctgttaaggggcgggttacaatctcaagggaacaatcca agaataccttgatttgagatgaacaacgtgagaactgaagacaccggatattactct gtgccagaacaggcaatactacgacttctggtccggctatccccctggcgaggaatat tttaagactggggtcagggaaccctgttatcgtgtcctccgacaaaaccataccag atgcagctgcaggagagcggccctggactcgtgaagcccagcgagacctgagcct	SEQ ID NO: 127

	gacatgcagcgtgagcggcgccagcatcagcgacagctactggagctggatcagga ggagccctggcaagggcctggagtggatcggctacgtgcacaagagcggcgacacc aactacagccctccctgaagtcagggtgaacctgtccctggacaccagcaagaacc aggtgagcctgtccctgtggctgccacagctgtgacagcggcaagtactactgtgc caggacctgcacggcaggaggtatcggcatcgtggccttaacgagtgggtcacc tactttacatggacgtgtggggcaacggcacccaggtgacctgagctccgataaga cccacaccgctccaccaaggggcccatcggctctccctggcacccctcctccaagag cacctctggggcacagcggcctgggctgctggtcaaggactacttccccgaacc ggtgacggtgtcgtggaactcaggcgcctgaccagcggcgtgcacacctcccggc tgtctacagtctcaggactctactccctcagcagcgtggtgacctgacctccagca gcttgggcaccagacctacatctgaacgtgaatcacaaagcccagcaacaccaaggt ggacaagaaagttgagccaaatctgtgacaaaactcacacatgccaccgtgccc gcacctgaactcctggggggaccgtcagtcttcttcccccaaaaaccaaggaca ccctcatgatctccggaccctgaggtcacatgcgtggtggtggacgtgagccagga agacctgaggtcaagttcaactggtatgttgacggcgtggaggtgcataatgcaaga caaagccgaggaggagcagtagacaacagcagtagctgtgtgagcgtcctcacc gtctgcaccaggactggctgaatggcaaggagtacaagtgaagggtcctcaaaaa gcccctccagccccatcgagaaaaccatctccaaagccaaagggcagccccgaga accacaggtgtacacctgccccatgccgggatgagctgaccaagaatcaagtcag cctgtggtgctgtgtaaaggcttctatcccagcgacatgccgtggagtgggagagc aatgggcagccggagaacaactacaagaccacgcctccctgctggtgactccgacgg ctccttctctactcaaaactaccgtggacaagagcaggtggcagcaggggaac gtcttctcatgctcgtgatgcatgaggtctgcacaaccactacagcagaagagcct ctcctgtctccgggt	
Light chain B	tccgacatcagcgtggccccggagagacagccaggatctcctgcggcgag aagagcctgggaagcagggtgtgcagtgtgtaccaacacagggccggacag gtccccagcctgatcatctacaacaaccaggacaggcccagcggcatccctga gaggttcagcgggaagccccgacagcccttcggaaccacagccacctgacc atcacaagcgtggaagccggcgacgagggcgactactactgccacatctggg acagcagggtgcccaccaagtgggtgtttggcggcgaccacctgacctg gctggacaaaaccataccgcatccgaactgactcaggacctgcccgtctgt ggcactgaagcagactgtgactattacttgcggaggcgactactgcggagcc actacgcttctgtatcagaagaaccggccaggcacctgtgctgtgttcta cggaaagaacaataggccatctggcatccccgaccgctttctggcagtgcac aggggaaccgagccagctgtgaccattaccggcgcccaggtgaggacgaagc cgattactattgcagctccccgggataagagcggctccagactgagcgtgtcgg aggaggaactaaactgaccgtcctcgataagaccataccgtacggtggccg ctcccagcgtgttcattctccacctagcagcagcagctgaagtccggcaca gcctctgtcgtgtgcctgctgaacaactctacccccgcgaggccaaagtgcag tggaaggtggacaacgcctgcagagcggcaacagccaggaaagcgtgacc gagcaggacagcaaggactccacctacagcctgagcagcaccctgacactga gcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccacc agggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 128
Binding Protein 17 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvcstqsgyftahilfwfrqapgrglewvfwikpqy gavnfgggfrdrvltlrdvyreiaymdirglkpddtavyyccardrsygdsswalda wgqgttvvsaastkgpsvflapsskstsggtaalglvkdyfpepvtvswngal tsghvhtpavlqssglyslsvvtpssslgtqyicvnvhkpsntkvdkkvepkscd kthtccppcapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapi ektiskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpe nnyktpvldsdgsfflvskltdksrwqqgnvfscsvmhcalnhnhytqkslsfsp	SEQ ID NO: 129

	g	
Light chain A	yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedgv psrfsgsgfhtsfnltsidlqaddiatyycqlqffgrgsrlhikrtvaapsvfifppsde qlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslstlts kadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 130
Heavy chain B	qvhltsqgpevrkpgtsvkvsckapgnltktydlhwvrvpqqglqwmw wishegdkkviverfkakvtidwdrstntaylqlsgltsgdavyyacagksg hrlrdyalydddgalnwavdvdylnlefwggtavtvssdkthtqmqlqe sgpglvkpsetlsitcsvsgasisdsywswirrspgkglewigyvhksgdtn yspslksrvnlsltdsknqvsllvaataadsgkyycartlhgrriygivafne wftyfyndvwgngtqvtvssdkthtastkgpsvflapsskstsggtaalgc lvkdyfpepvtvswngaltsghvhtfpavllqssgylssvvtvpssslgtqty icnvnhkpsntkvdkkvepkscdkthtccppcapellggpsvflfppkpkd tlmistrpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynst yrvvsvltvlhqdwlngkeyckvsnkalpapiektiskakgpprepqvytl ppcrdeltknqvsllwclvkgyfypsdiavewesngqpennyktpvpvldsdg sfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspg	SEQ ID NO: 131
Light chain B	sdisvapgetariscgekslgsravqwyqhragqapsliiynndrpsgiperfsgsp dspfgttatltsveagdeadyychiwdsvptkwvfgggtlvtldkthtdfvltsqsp hslsvtpgesasiscksshlihgdrnnylawyvkpgrspqliylasrasgvprdf sgsgskdkdftlkisrvetedvgytymqgrespwftggqtkvdikdkthtrvaaps vfifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskd styslstltskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 132
Binding Protein 17 Nucleotide Sequences		
Heavy chain A	agagcccacctggtgcagtctggcaccgccatgaagaaccaggcgctctgtgcgg gtgtcctgtcagacaagcggtacaccttaccgcccacatcctgttctggtccggcag gcccctggcagaggactggaatgggtgggatgatcaagccccagtatggcgccgtg aacttcggcggaggcttccgggatagagtaccctgacccgggacgtgtaccgcgag atcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtggtggtgtctgccgcctctacaaaggccccagcgtgtccctctggcccc tagcagcaagagcacatctggcggaacagccgcccctgggctgcctcgtgaaggacta cttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtgcac accttccagctgtgtgcagtccagcgccctgtacagcctgagcagcgtcgtgacagt gcccagcagctctctgggcacccagacctacatctgcaacgtgaaccacaagcccag caacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccacacct gtccccctgtcctgccccgaactgctgggaggcccttccgtgttctgttcccccaa agccccagacacctgatgatcagccggacccccgaagtgacctgcgtggtggtgg atgtgtccacagaggacctgaagtgaagttcaattggtacgtggacggcgtggaagt gcacaacgccaagaccaagccaagagaggaacagtacaacagcacctaccgggtg gtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaagagtacaagtgc aaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaaggccaag ggccagccccgcgaaccccaggtgtgcacactgccccaaagcaggacgagctga ccaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccttccgatatgcc gtggaatgggagagcaacggccagcccgagaacaactacaagaccacccccctgt gctggacagcgacggctcattctctggtgtccaagctgacagtggacaagtcccgtg ggcagcagggcaacgtgttcagctgtccgtgatgcacgagggccctgcacaaccact acaccagaagtcctgagcctgagccccggcaag	SEQ ID NO: 133
Light chain A	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacag agtgacctcaactgccagacctctcaggcggtgggcagcgacctgcactggt	SEQ ID NO: 134

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Heavy chain B	cagggtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaa ggtgtcctgcaaggcccctggcaacacctgaaaacctagacctgactgggtgcg cagcgtgccaggacagggactgcagtggatgggtggtatcagccacgagggcgac aagaaagtgtcgtggaacggtcaaggccaaagtaccatcgactgggacagaagc accaacaccgctacctgcagctgagcggcctgacctctggcgataccgccgtgtact actgcgccaaggcagcaagcaccggctgagagactacgccctgtacgacgatgac ggcgccctgaactgggcccgtggatgtggactacctgagcaacctggaattctggggc agggcacagccgtgacctgtcatctgacaaaaccataccagatgcagctgcagg agagcggccctggactcgtgaagcccagcagacctgagcctgacatgcagcgtg agcggcgccagcatcagcagcagctactggagctggatcaggaggagccctggcaa gggctggagtggatcggctacgtgcacaagagcggcgacaccaactacagcccct ccctgaagtccagggtgaacctgtccctggacaccagcaagaaccagggtgagcctgt ccctgggtggctgccacagctgctgacagcggcaagtactactgtgccaggacctgca cggcaggaggatctacggcatcgtggccttcaacgagtgggtcacctacttctacatgg acgtgtggggcaacggcaccaggtgacctgagctccgataagaccacaccgctt ccaccaaggggcccatcggtcttccccctggcacctctccaagagcacctctggggg cacagcggccctggggtgcctgtcaaggactactccccgaaccgggtgacggtgtc gtggaactcaggcgccctgaccagcggcgtgcacacctccccggtgtcctacagtcc tcaggacttactccctcagcagcgtggtgacctgacctccagcagcttgggcacc agacctacatctgaacgtgaatcacaagcccagcaaccaaggtggacaagaaag ttgagcccaaatctgtgacaaaactcacatgccaccgtgcccagcacctgaactc ctggggggaccgtcagttctcttccccccaaaaccaaggacacctcatgatctc ccggacccctgaggtcacatgcgtggtggtggacgtgagccacgaagacctgaggt caagttcaactggtatgttgacggcgtggaggtgcataatgccaagacaaagccggg gaggagcagtacaacagcacgtacctgtgtgcagcgtctcaccgtctgcaccag gactggctgaatggcaaggagtacaagtgaaggtctccaacaaagccctcccagcc ccatcgagaaaacctatccaaaagccaaaggcagccccgagaaccacaggtgta caccctgcccccatgccgggatgagctgaccaagaatcaagtcagcctgtggtgctg gtaaaaggcttctatcccagcgacatcgccgtggagtgggagagcaatgggcagccg gagaacaactacaagaccacgcctcccgtgctggactccgacgctcttctctcta ctcaaaactcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatgtcc gtgatgcatgaggctctgcacaaccactacgcagaagagcctctccctgtctccgg gt	SEQ ID NO: 135
Light chain B	tccgacatcagcgtggccccggagagacagccaggatctctcgggcgag aagagcctgggaagcagggtgtgcagtgtgtaccaacacaggggccggacag gtcccagcctgatcatctacaacaaccaggacaggcccagcggcatccctga gaggttcagcgggaagccccgacagcccccttggaaccacagccacctgacc atcacaagcgtggaagccggcgacgaggccgactactactgccacatctggg acagcagggtgcccaccaagtgggtgtttggcggcgccaccacctgaccgt gctggacaaaaccataccgacttctgtgctgacctagagccctcacagcctga gcgtgacacctggcgagagcgccagcatcagctgcaagagcagccactccct gatccacggcgaccgggaacaactacctggcttggtacgtgcagaagccccggc	SEQ ID NO: 136

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Binding Protein 18 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvscqtsgytftahilfwfrqapgrglewv gwipqy gavnfgggfrdrvltlrdvyreiaymdirglkpddtavyyccardrsygdsswalda wgqgttvvsaastkgpsvfplapsskstsggtaalglvkdyfpepvtvswngal tsgvhtfpavllqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscd kthtccppcapellggpsvflfppkpkdtl misrtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapi ektiskakgqprepqvctlp srdeltnqvslscavkgfypsdiavewesngqpe nnyktpvldsdgsfflvskltvdksrwqqgnvfscsvmhealhnhytqkslsisp g	SEQ ID NO: 137
Light chain A	yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedgv psrfsfgfhtsfnltsldlqaddiatyycqlvqffgrgsrlhikrtvaapsvfifppsde qlksgtasvcllnnfypreakvqwkdnlqsgnsqesvteqdskdstyslstl skadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 138
Heavy chain B	qmqldesgpglvkpsetlsltcsvsgasidsywswirrspgkglewigyv ksgdtnyspslksrvnslsdtsknqvsllvaataadsgkyycartlhgrriygi vafnewftyfymdvwngtqvtvssdkthtevrivesggglvkpggslrls csasgfdfdnawmtwvrqppgkglewvgritgpegwsvdyaesvkrf tisrdntkntlylemnnvrtedtgyyfcartgkyydfwsgyppeeyfqdw gqgtlvivssdkthtastkgpsvfplapsskstsggtaalglvkdyfpepvtv swngaltsgvhtfpavllqssglyslssvvtvpssslgtqtyicnvnhkpsntk vdkkvepkscdkthtccppcapellggpsvflfppkpkdtl misrtpevtcv vvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdw wlngkeykckvsnkalpapiektiskakgqprepqvylppcrdeltnqv slwclvkgyfypsdiavewesngqpennyktpvldsdgsfflvskltvdks rwqqgnvfscsvmhealhnhytqkslsisp	SEQ ID NO: 139
Light chain B	aseltqdpavsvalkqtvtitcrdgsrlshyaswyqkkpgqapvllfygknnrpsgip drfsgsasgnrasltitgaqaeadyycssrdksgrslsvfgggkltvldkthtsdis vapgetariscgekslgsravwyqhraqapsliiynqdrpsgiperfsgspdsp fgttatlitsveagdeadyychiwdsrvtkwvfgggtltvldkthtrtvaapsvfif ppsdeqlksgtasvcllnnfypreakvqwkdnlqsgnsqesvteqdskdstys lsstltskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 140
Binding Protein 18 Nucleotide Sequences		
Heavy chain A	agagcccacctggcagctctggcaccgccatgaagaaccaggcgccctctgtgcgg gtgtcctgtcagacaaggcgctacaccttcaccgcccacatcctgttctgggtccggcag gcccctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtg aacttcggcgaggcttcgggatagagtaccctgaccggggacgtgtaccgcgag atcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtggtgtctgccgcctctacaaaggccccagcgtgtccctctggcccc	SEQ ID NO: 141

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Light chain A	tataccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacag agtgacctcaactgccagacctctcaggcgtgggcagcgacctgcactggt atcagcacaagcctggcagagccccaaagctgctgatccaccacacaagcag cgtggaagatggcgtgcccagcagattttccggcagcggcttccacaccagct tcaacctgacctcagcgatctgcaggccgacgacattgccacctactattgtca ggtgctgcagttcttcggcagaggcagcagactgcacatcaagcgtacgggtgg ccgtctccagcgtgttcattctccacctagcgcagcagcagctgaagtccggc acagcctctgtcgtgtgctgctgaacaacttctacccccgcgaggccaaagtg cagtggaaaggtggacaacgccctgcagagcggcaacagccaggaaagcgt gaccgagcaggacagcaaggactccacctacagcctgagcagcacccctgac actgagcaagggcgactacgagaagcacaaggtgtacgcctgcgaagtgacc caccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 142
Heavy chain B	cagatgcagctgcaggagagcggccctggactcgtgaagcccagcgagacctgag cctgacatgcagcgtgagcggcgccagcagcagcagctactggagctggatcag gaggagccctggcaagggcctggagtggatcggtacgtgcacaagagcggcgac accaactacagcccctccctgaagtccagggtgaacctgtccctggacaccagcaaga accaggtgagcctgtccctgggtgctgccacagctgctgacagcggcaagtactactg tgccaggacctgcacggcaggaggtatctacggcatcgtggccttcaacagtggttc acctactctacatggacgtgtggggcaacggcaccaggtgacctgagctccgaca aaaccataccgaggttagactggtggagtcaggaggggggcttgtgaagccgggtg ggtctctccgctgagctgttctgcctccggctttgatttcgataacgctggatgacctg ggtcaggcagcctccaggtgaaggactggagtgggtgggaagaatcacaggtccag gcgagggtgtgctccgtggactacgcggaatctgttaaaggcggtttacaatctcaag ggacaataccaagaatacctgtatttgagatgaacaacgtgagaactgaagacacc ggatattacttctgtgccagaacaggcaataactacgacttctggtccggctatccccct ggcgagggaatattttcaagactggggtcagggaaccctgttatcgtgtcctccgataag accacaccgcttcaccaaggggccatcgggttccccctggcaccctctccaaga gcacctctgggggcacagcggccctgggtgctgtaaggactacttccccgaac cggtgacgggtgtcgtggaactcaggcggcctgaccagcggcgtgcacacctccccg ctgtctacagtctcaggactctactccctcagcagcgtggtgacctgccccccagc agcttgggcacccagacctacatctgcaacgtgaatcacaagcccagcaacaccaag gtggacaagaaagttgagcccaaatcttgtgacaaaactcacacatgccaccgtgcc cagcacctgaactctgtgggggaccgtcagcttctcttcccccaaaaaccaagga caccctcatgatctccggaccctgaggtcacatgcgtggtggtggacgtgagccac gaagacctgaggtcaagttcaactggtatgttgacggcgtggaggtgcataatgccaa	SEQ ID NO: 143

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Light chain B	gcacccgaactgactcaggaccctgccgtctctgtggcactgaagcagactgtg actattacttgcaggcgactcactgcggagccactacgcttctggtatcaga agaaacccggccaggcacctgtgctgctgtttctacggaaagaacaataggcca tctggcatccccgaccgcttttctggcagtgcacaggaaccgagccagtctg accattaccggcgccaggctgaggacgaagccgattactattgcagctcccg ggataagagcggctccagactgagcgtgttcggaggaggaactaaactgacc gtcctcgacaaaaccatactccgacatcagcgtggccccggagagacag ccaggatctctgcggcgagaagagcctgggaagcagggctgtgcagtggta ccaacacagggccggacaggtcccagcctgatcatctacaacaaccaggac aggcccagcggcatccctgagaggttcagcgggaagccccgacagccccttcg gaaccacagccaccctgaccatcacaagcgtggaagccggcgacgaggccg actactactgccacatctgggacagcaggggtcccaccaagtgggtgtttggc ggcggcaccacctgaccgtgctggataagaccataccgtacggtggccg ctcccagcgtgttcatcttcccacctagcgacgagcagctgaagtccggcaca gcctctgtcgtgtgctgctgaacaacttctacccccgcaggccaaagtgcag tggaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtgacc gagcaggacagcaaggactccacctacagcctgagcagcaccctgacctga gcaagggcgactacgagaagcacaaggtgtacgcctgcgaagtgaccacc agggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 144
Binding Protein 19 Amino Acid Sequences		
Heavy chain A	evrlvesggglvkggslrlscsasgfdndawmtwvrrppgkglewvgritpg egwsvdyaesvkgrftisrdntkntlylemnnvrtedtggyfcartgkydfwsy ppgeeyfqdwgqgtlvivssastkgpsvflapsskstsggtaalgclvkdyfpepv <u>tvswngaltsgvhtfpavllqssglyslssvvtvpssslgtqtyicnvnhkpsntkvd</u> <u>kkvepkscdkthtccppcapellggpsvflfppkpkdtlmsirtpevtcvvvdvshe</u> <u>dpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlhqdwlngkeykckv</u> <u>snkalpapietiskakgqprepqvctlppsrdeltknqvsiscavkgfypsdiave</u> <u>wesngqpennyktppvldsdgsfflvskltvdksrwqqgnvfscsvmhealhn</u> <u>ytqkslslspg</u>	SEQ ID NO: 145
Light chain A	aseltqdpavsvalkqvtitcrdgsrlshyaswyqkpgqapvllfygknrrspgip drfsgsasgnrasltitgaqaedeadyycssrdksgrlsfvgggtklvlsqpkaaps vtlfpssseelqankatlvlisdfypgavtvawkadsspvkagvettpskqsnnky aassylstpeqwkshrsyscqvtthegstvektvaptcs	SEQ ID NO: 146
Heavy chain B	qmqlqesgpglvkpsetslstcsvsgasidsywswirrspgkglewigyvh ksgdtnyspslksrvnlsldtsknqvsllvaataadsgkyycartlhgrriygi vafnewftyfyndvwngtqvvtssdkthtQvhltqsgpevrkpgtsvk sckapgnltktydlhwrvspgqglqwmgwishegdkkviverfkavti dwdrstntaylqlsgltsgdtavyycakgskhrlrdyalydddgalnwavdv dylsnlefwggtavtvssdkthtastkgpsvflapsskstsggtaalgclvk dyfpepvtswnsgaltsgvhtfpavllqssglyslssvvtvpssslgtqtyicn	SEQ ID NO: 147

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Light chain B	dfvltqspshsvtpgesasisckssshlihgdrnnylawyvkpgrspqliylasr asgvprdfsgsgsdktfklisrvetdvgttycmqgrespwtfggtkvdikdkth tsdisvapgetariscgekslgsravqwyqhraqapsliiynndrpsgiperfsgs pdsfpgttatltitsveagdeadyychiwdsrvtkwvfgggtltvldkthtrtvaaps vfifppsdeqlkshtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskd styslsstltlskadyekkhvyacevthqglsspvtksfnrgec	SEQ ID NO: 148
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Light chain B	gacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgaga gcgccagcatcagctgcaagagcagccactccctgatccacggcgaccggaa caactacctggcttggtagctgcagaagcccggcagatccccccagctgctga tctacctggccagcagcagagccagcggcgtgcccgatagatttctggcagc ggcagcgacaaggacttcacctgaagatcagccgggtggaaaccgaggac gtgggcacctactactgtatgcagggcagagagagccctggaccttggcca gggcaccaaggtggacatcaaggacaaaaccatactccgacatcagcgtg gcccccgagagacagccaggtatcctcgggcgagaagagcctgggaag cagggtgtgtagtggtagcaaacacagggccggacaggtcccagcctgatc atctacaacaaccagagcagggccagcggcatccctgagaggttcagcggaa gccccgacagccccttcggaaccacagccacctgacctacaaagcgtgga agccggcgacgaggccgactactactgccacatctgggacagcaggggtgcc cacciaagtgggtgtttggcggcggcaccacctgaccgtgctggataagacc ataccgtacggtggccgtcccagcgtgttcattctccacctagcagcagc agctgaagtccggcacagcctctgtcgtgtgctgctgaacaacttctacccc gcgaggccaaagtgcagtggaaaggtggacaacgcctgcagagcggcaac agccaggaaagcgtgaccgagcaggacagcaaggactccacctacagcctg agcagcaccctgacactgagcaaggccgactacgagaagcacaaggtgtac gcctgcgaagtgaccaccaggccctgtctagccccgtgaccaagagcttcaa ccggggcgagtg	SEQ ID NO: 152
Binding Protein 20 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvcqtsgyftahilfwfrqapgrglewvgnwipqy	SEQ ID NO:

	gavnfgggfrdrvltlrdvyreiaymdirglkpddtavyyccardrsygdsswalda wgqgttvvvsastkgpsvfplapsskstsggtaalgclvkdyfpepvtvswngal tsghvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscd kthtccppcapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeyckvsnkalpapi ektiskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngqpe nnyktpvldsdgsfflvskltvdksrwqqgnvfscsvmhealnhhytqkslslsp g	153
Light chain A	yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedgv psrfsgsgfhtsfnltsldlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsde qlkshtasvvcllnnfyprcakvqwkvdnalqsgnsqesvteqdsksdystlsstlts kadyekkhvyacevthqglsspvtksfnrgec	SEQ ID NO: 154
Heavy chain B	qmqlqesgpglvkpsetlsltsvsgasidsywswirrspgkglewigyvh ksgdtnyspksrsvnlsltdsknqvslslvaataadsgkyycartlhgrriygi vafnewftyfymdvwngtqvtvssdkthtQvhltsqsgpevrkpgtskv sckapngtlktydlhwrvsvpggqlqwmgwishegdkkviverfkakvti dwdrstntaylqlsgltsgdavyycakgskhrlrdyalydddgalnwavdv dylsnlefwgqgtavtvssdkthtastkgpsvfplapsskstsggtaalgclvk dyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicn vnhkpsntkvdkkvepkscdkthtccppcapellggpsvflfppkpkdtlm isrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrv svltvlhqdwlngkeyckvsnkalpapiektiskakgqprepqvylpp crdeltnqvslwclvkgfypsdiavewesngqpennyktpvldsdgsf flyskltvdksrwqqgnvfscsvmhealnhhytqkslslspg	SEQ ID NO: 155
Light chain B	dfvltqspshslsvtpgesasiscksshlihgdrnnylawyvqkprspqlliylasr asgvpdrfsgsgsdldfklisrvetdvgttycmqgrespwtfgqgtkvdkdkth tsdisvapgetariscgeklsgravqwyqhraqapsliiynnqdrpsgiperfsgs pdpfgttatltitsveagdeadyychiwsrvptkwvfgggtltvldkthtrtvaaps vfifppsdeqlkshtasvvcllnnfyprcakvqwkvdnalqsgnsqesvteqdskd styslsltslkadyekkhvyacevthqglsspvtksfnrgec	SEQ ID NO: 156
Binding Protein 20 Nucleotide Sequences		
Heavy chain A	agagcccacctggtgcagtctggcaccgccatgaagaaccaggcgccctctgtgcgg gtgtcctgtcagacaaggcggtacaccttcaccgccacatcctgttctggtccggca ggccccctggcagaggactggaatgggtgggatggaacccccagtatggcgccg tgaactcggcggaggtctccggatagagtaccctgaccgggacgtgtaccgcg agatcgctacatggacatccgggcctgaagcccgatgacaccggcgtgtactactg cgccagagacagaagctacggcgacagcagctgggctctggatgctggggccagg gcacaaccgtgggtgtctgcccctctacaaaggccccagcgtgtccctctggc ccctagcagcaagagcacatctggcggaacagccgccctgggctgcctcgtgaagg actactttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagggcgtg cacacatttcagctgtgctgcagtccagcggcctgtacagcctgagcagcgtcgtga cagtggccagcagctctctgggcaccagacctacatctgaacgtgaaccacaagcc cagcaacaccaaggtggacaagaaggtggaaccaagagctgcgacaagaccac acctgtccccctgtcctgccccgaactgctgggagggccttccgtgttctgttccc caaagcccaaggacacctgatgacagccggacccccgaagtacctgcgtgtg gtggatgtgtcccacaggaccctgaagtgaagttaattgtacgtggacggcgtgg aagtgcacaacgccaagaccaagccaagagaggaacagtacaacagcacctaccgg gtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaagagtacaagt gcaaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaaggcca agggccagccccgcgaacccaggtgtgcacactgcccccaagcaggagcagct gaccaagaaccaggtgtccctgagctgtgccgtgaaggtcttaccctccgatatcg ccgtggaatgggagagcaacggccagcccagacaactacaagaccacccccct	SEQ ID NO: 157

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Light chain A	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacag agtgacctcaactgccagacctctcagggcgtgggcagcgacctgcaactggt atcagcacaagcctggcagagcccccaagctgtgatccaccacacaagcag cgtggaagatggcgtgcccagcagattttccggcagcggcttccacaccagct tcaacctgacctcagcgatctgcaggccgacgacattgccacctactattgtca ggtgctgcagttcttcggcagaggcagcagactgcacatcaagcgtacgggtgg ccgctcccagcgtgttcattcttcccacctagcgacgagcagctgaagtccggc acagcctctgtcgtgtgctgctgaacaacttctacccccgcgaggccaaagt cagtggaaagtggaacaacgccctgcagagcggcaacagccaggaaagcgt gaccgagcaggacagcaaggactccacctacagcctgagcagcacctgac actgagcaaggccgactacgagaagcacaaggtgtacgctgcgaagtgacc caccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 158
Heavy chain B	cagatgcagctgcaggagagcggccctggactcgtgaagcccagcgagacctgag cctgacatgcagcgtgagcggcgccagcatcagcgacagctactggagctggatcag gaggagccctggcaaggcctggagtggatcggctacgtgcacaagagcggcgac accaactacagccccctccctgaagtccagggtgaacctgtccctggacaccagcaaga accaggtgagcctgtccctgggtgctgccacagctgctgacagcggcaagtactactg tgccaggacctgcacggcaggaggtatctacggcatcgtggccttcaacgagtgttc acctacttctacatggacgtgtggggcaacggcaccaggtgacctgagctccgaca aaaccataaccaggtgcacctgacacagagcggaccggagtgccgaagcctggc acctctgtgaaggtgtcctgcaaggccctggcaacacctgaaaacctacgacctgc actgggtgcgcagcgtgccaggacagggactgcagtggatgggtggatcagccac gaggggcgacaagaaagtgtcgtggaacggtcaaggccaaagtgacctcgaactg ggacagaagcacaacaccgacctgacgtgagcggcctgacctctggcgatac cgccgtgtactactgcgcaaggcagcaagcaccggctgagagactacgccctgta cgacgatgacggcgccctgaactgggcccgtggatgtggactacctgagcaacctgga attctggggccagggcacagccgtgacctgtcattgataagaccacaccgcttcc accaaggggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggca cagcggccctgggtgtcctggtaaggactacttccccgaaccgggtgacggtgtcgtg gaactcaggcgccctgaccagcggcgtgcacaccttccggctgtcctacagtctca ggactctactccctcagcagcgtggtgacctgtccctccagcagcttgggcaccaga cctacatctgaacgtgaatcacaagcccagcaacaccaaggtggacaagaaagtga gccccaatcttgacaaaactcacatgccaccgtgcccagcacctgaactcctgg ggggaccgtcagttcttcttcccccaaaaccaaggacacctcatgatctccgg accctgaggtcacatgcgtgggtgggtgacgtgagccacgaagacctgaggtcaag ttcaactggtatgttgacggcgtggaggtgcataatgccaagacaagcgcgggag gagcagtacaacagcagctaccgtgtggtcagcgtcctaccgtcctgcaccaggact ggctgaatggcaaggagtacaagtgcaagggtctccaacaaagccctccagcccca tcgagaaaaccttccaagccaaggcagccccgagaaccacaggtgtacacc ctgcccccatgccgggatgagctgaccaagaatcaagtcagcctgtggtgcctggtaa aaggcttctatccagcgacatcgccgtggagtgggagagcaatgggcagccggag aacaactacaagaccacgcctcccgtgctggactccgacggctccttcttctactca aaactaccgtggacaagagcaggtggcagcaggggaacgttcttctcatgtccgtg atgcatgaggtctgcacaaccactacacgcagaagagcctctccctgtctccgggt	SEQ ID NO: 159
Light chain B	gacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgaga gcgccagcatcagctgcaagagcagccactccctgatccacggcgaccgga acaactacctggcttggtagctgcagaagcccggcagatccccccagctgctg atctacctggccagcagcagagccagcggcgtgcccgatagatttttggcag	SEQ ID NO: 160

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Binding Protein 21 Amino Acid Sequences		
Heavy chain A	qvhltsqsgpevrkpgtsvkvsckapgnltktydlhwvrsvpqglqwmgishe gdkkviverfkakvtidwdrstntaylqlsgltsgdavyycakgskhrlrdyalydd dgalnwavdvdylnlefwwggtavtvssastkgpsvfplapsskstsaggtaalgcl vkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicnv hkpsntkvdkkvepkscdkthtccppapellggpsvflfppkpkdtlmisrtpevt cvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdwl ngkeykckvsnkalpapietiskakgqprepqvclppsrdeltknqvsclavkg fypsdiavewesngqpennyktpvldsdgsfflvskltvdkrsrwqqgnvfscsv mhealhnhytqkslsisp	SEQ ID NO: 161
Light chain A	dfvltqspshlsvtpgesasiscksshlihgdrnnylawyvqkprspqlliylasr asgvprdfsgsgsdldfklisrvetedvgtyycmqgrespwtfgqgtkvdkirtva apsvfifppsdeqlkshtasvcllnnfyprvakvqkvdnalqsgnsqesvteqds kdstylsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 162
Heavy chain B	Evrlvesggglvkpgslrlscasgfdndawmtwvrqppgkglewvgr itgppegwsvdyaesvkgrftisrdntkntlylemnnvrtdtgyyfcartgk yydfwsgyppgeeyfqdwgqgtlvivssdktht rahlvqsgtamkkpgasvrvscqtsgytftahilfwfrqapgrglewvgrwik pqygavnfgggfrdrvtlrdvyreiaymdirglkpddtavycardrsygd sswaldawgqgttvvsadkthtastkgpsvfplapsskstsaggtaalgclvk dyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicn vnhkpsntkvdkkvepkscdkthtccppapellggpsvflfppkpkdtlm isrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrv vsvltvlhqdwlngkeykckvsnkalpapietiskakgqprepqvclpps crdeltnqvsclwclvkgfypsdiavewesngqpennyktpvldsdgsf flyskltvdkrsrwqqgnvfscsvmhealhnhytqkslsisp	SEQ ID NO: 163
Light chain B	yihvtqspsslsvsigdrvtincqtsqvgsgdlhwyqhkpgrapkllihhtssvedgv psrfsgsgfhtsfnltsldqaddiatyycqlqffgrgsrlhikdkthtaseltqdpavs valkqvtitcrdgsrlshyaswyqkkpgqapvllfygknnrpsgipdrfsgsasgnr asltitgaqaeadedyessrdksgrlsvfgggtklvldkthtrtaapsvfifppsd eqlkshtasvcllnnfyprvakvqkvdnalqsgnsqesvteqdsdstylsstlt lskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 164
Binding Protein 21 Nucleotide Sequences		

Heavy chain A	caggtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaa ggtgtcctgcaaggccctggcaacacctgaaaacctacgacctgactgggtgcg cagcgtgccaggacagggactgcagtggatgggctggatcagccacgagggcgac aagaaagtatcgtggaacgggtcaaggccaaagtaccatcactgggacagaagc accaacaccgcctacctgcagctgagcggcctgacctctggcgataccgccgtgtact actgcgccaaggcgagcaagcaccggctgagagactacgccctgtacgacgatgac ggcgccctgaactggccgtggatgtggactacctgagcaacctggaattctggggc agggcacagccgtgaccgtgtcatctgctcgaccaaggggccccagcgtgttcctct ggccccctagcagaagagcacatctggcgaacagccgccctgggctgcctcgtga aggactactttccgagcccgtagccgtgtcctggaattctggcgccctgaccagcgg cgtgcacacctttcagctgtgctgcagtcagcggcctgtacagcctgagcagcgtc gtgacagtgcccagcagctctctgggcaccagacctacatctgcaactgaaccaca agcccagcaacaccaaggtggacaagaagtggaaccaagagctgcgacaagac ccacacctgtccccctgtcctgccccgaactgctgggagggcccttccgtgttcctgtt cccccaagcccaaggacacctgatgatcagccggacccccgaagtgcacctgcgt ggtggtggatgtgtccacgaggacctgaagtgaagttcaattggtacgtggacggc gtggaagtgcacaacccaagaccaagccaagagagggaacagtacaacagcaccta ccgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcgaagagta caagtgcgaaggtgtccaacaaggccctgcctgccccatcgagaaaacctcagcaa ggccaaggggccagccccgcgaaccccaggtgtgcacactgcccccaagcagggac gagctgaccaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccttccg atatgccgtggaatgggagagcaacggccagcccgagaacaactacaagaccacc ccccctgtgctggacagcgacggctcattcttctggtgtccaagctgacagtggacaa gtccccgtggcagcagggcaacgtgttcagctgtccgtgatgcagaggccctgca caaccactacaccagaagtcctgagcctgagccccggcaag	SEQ ID NO: 165
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Heavy chain B	gaggttagactggtggagtcaggagggggccttgtgaagcccgggtgggtctctccgc ctgagctgttctgctccggctttagtttcgataacgcctggatgacctgggtcaggcag cctccaggtaaaggactggagtggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaatctgttaaaggcggtttacaatctcaagggaataacca agaataccttgtatttggagatgaacaacgtgagaactgaagacaccggatattactct gtgccagaacaggcaatactacgacttctgtccggctatccccctggcgaggaaat tttaagactggggtcagggaaccctgttatcgtgtcctccgacaaaaccataaccaga gccacctggtgcagctgtgcaccgcatgaagaaaccaggcgctctgtcggggtg tcctgtcagacaagcggtacaccttcaccgcccacatcgttctgttccggcaggc ccctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtgaa cttcggcgaggcttccgggtagagtaccctgaccgggacgtgtaccgcgagat cgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcgc cagagacagaagctacggcgacagcagctgggctctggatgcttggggccaggggca caaccgtggtggtgtgtccgataagaccacaccgcttccaccaaggggcccatcggt cttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctg	SEQ ID NO: 167

	cctggtcaaggactacttccccgaaccggtgacggtgtcgtggaactcaggcgcctg accagcggcgtgcacaccttcccggtgtcctacagtctcaggactctactccctcag cagcgtggtgaccgtgccctccagcagcttgggcaccagacctacatctgcaacgtg aatcacaagcccagcaacaccaaggtggacaagaaagttgagcccaaatcttgtgaca aaactcacatgcccaccgtgcccagcacctgaactctggggggaccgtcagtctt ccttcccccaaaaaccaaggacacctcatgatctccggaccctgaggtcacat gctgtgtgtgtgacgtgagccacgaagaccctgaggtcaagttcaactggtatgtga cggcgtggaggtgcataatgccaagacaagccgcgaggaggagcagtacaacagc acgtaccgtgtgtgcagcgtcctcaccgtcctgcaccaggactggctgaatggcaagg agtacaagtgaaggtctccaacaagccctccagccccatcgagaaaaccatctc caaagccaaagggcagccccgagaaccacaggtgtacacctgccccatgccggg atgagctgaccaagaatcaagtcagcctgtgtgctggttaaaggcttctatccagc gacatcgccgtggagtgaggagcaatgggcagccggagaacaactacaagaccac gcctcccggtgctggactccgacggctcttcttcttactcaaaactaccgtggacaa gagcaggtggcagcaggggaacgtcttctatgctccgtgatgcatgaggtctgcac aaccactacacgcagaagagcctctccctgtctccgggt	
Light chain B	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacagagtga ccatcaactgccagacctctcagggcgtgggcagcgacctgcactggtatcagcaca gcctggcagagccccaaagctgtgatccaccacacaagcagcgtggaagatggcgt gccagcagattttccggcagcggctccacaccagcttcaactgacctcagcagtc tgcagggcgacgacattgccactactattgtcaggtgctgcagttcttcggcagaggc agcagactgcacatcaaggacaaaaccataccgcacatccgaactgactcaggaccct gccgtctctgtggcactgaagcagactgtgactattacttgcggaggcgactcactgcg gagccactacgcttctggtatcagaagaaaccggccaggcacctgtgctgctgttct acggaaagaacaataggccatctggcaccctccgaccgcttttctggcagtgcatcagg gaaccgagccagctctgaccattaccggcgccagggtgaggacgaagccgattacta ttgcagctccccgggataagagcggctccagactgagcgtgttcggaggaggactaa actgaccgtctcgataagaccataccgtacgggtggcgctccagcgtgttcatctt cccacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaac aacttctacccccgcgaggccaaagtgcagtgaaggtggacaacgccctgcagagc ggcaacagccaggaagcgtgaccgagcaggaacgaaggactccacctacagcct gagcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgct gcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaaccggggc gagtg	SEQ ID NO: 168
Binding Protein 22 Amino Acid Sequences		
Heavy chain A	qvhltqsgpevrkpgtsvkvsckapgnltkydlhwrvsvpgqlqwmgwishe gdckviverfkakvtidwdrstntaylqlsgltsgdtavyycakgskhrlrdyalydd dgalnwavdvdylnlefwggtavtvssastkgpsvflapsskstsggtaalgcl vkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtienvn hkpsntkvdkkvepkscdkthtppcpapellggpsvflfppkpkdtlmisrtpvt cvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdwl ngkeykckvsnkalpapiektiskakgqprepqvctlpssrdeltknqvsiscavkg fypsdiavewesngqpennyktpvldsdgsfflvskltvdkrsrqgnvfscsv mhealhnhytqkslspsg	SEQ ID NO: 169
Light chain A	dfvltqspshlsvtpgesasiscksshlihgdrnnylawyvqkprspqlliylasr asgvpdrrfsgsgsdktlksrvetdvgtiycmqgrespwtfggktkdikrtva apsvfifppsdeqlksgtasvcllnfybreakvqwkvdnalqsgnsqesvteqds kdstylsstltlskadyekhkvyacevthqglssptksfnrgec	SEQ ID NO: 170
Heavy chain B	rahlvqsgtamkkpgasvrvscqtsgytftahilfwfrqapgrglewvlgwik pqygavnfgggfrdrvtlrdvyreiaymdirglkpdtdavyycardrsygd sswaldawgqgttvvvsadkthtevrivesggglvkpggsrlrscsasgfdfd	SEQ ID NO: 171

	nawmtwvrpppgkglewvgritgpegwsvdyaesvkgrftisrdntknt lylemnnvrtdtgyyfcartgkydfwsgyppgeeyfqdwgqgtlvivss dkthtastkgpsvflapsskstsggtaalglvkdypvptvswnsgalts gvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepk scdkthtccppcpapellggpsvflfppkpkdtlmisrtpevtcvvvdvshed pevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkey kckvsnkalpapiektiskakgqprepqvylppcrdeltnqvslwclvkg fypsdiavewesngqpennyktppvldsdgsf	
Light chain B	aseltqdpavsvalkqtvtitcrdlsrshyaswyqkkgpqapvllfygknrpsgip drfsgsasgnrasltitgaqaedeaddyccsrdrksgrlsvfgggtklvtl dktht Yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkgprapklhihtssvedg vpsrfsqsgfhtsfnlitidlqaddiatyycqlqffgrgsrlhik dkthtrtvaapsvfifppsdeqlksqstasvcllnnfypreakvqwkdnalqsgns qesvteqdskdstyslstltskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 172
Binding Protein 22 Nucleotide Sequences		
Heavy chain A	cagggtcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaa gggtgctcctgcaaggccctggcaacacctgaaaacctacgacctgactgggtgcg cagcgtgccaggacagggactgcagtggatgggctggatcagccacgagggcgac aagaaagtgatcgtggaacggtcaaggccaaagtaccatcgactgggacagaagc accaacaccgcctacctgcagctgagcggcctgacctctggcgataccgccgtgtact actgcgccaaagggcagcaagcaccggctgagagactacgccctgtacgacgatgac ggcgccctgaactgggctggatgtggactacctgagcaacctggaattctggggcc agggcacagccgtgacctgtcatctgcttcgaccaagggccccagcgtgtccctct ggccccctagcagaagagcacatctggcggaacagccgccctgggctgcctctga aggactactttcccgagccgtgacctgtcctggaattctggcgccctgaccagcgg cgtgcacacctttccagctgtgctgcagtccagcggcctgtacagcctgagcagcgtc gtgacagtgcccagcagctctctgggcaccagacctacatctgcaacgtgaaccaca agcccagcaacaccaaggtggacaagaagtggaaccaagagctgcgacaagac ccacacctgtccccctgtcctgccccgaactgctgggagggcccttccgtgttctgtt cccccaagcccaaggacaccctgatgatcagccggacccccgaagtgacctgcgt gggtgtggtatgtgtccacgaggaccctgaagtgaagttcaattgttacgtggacggc gtggaagtgcacaacgccaagaccaagccaagagaggaaacagtacaacagcaccta ccgggtgtgtccgtgctgacctgtgctgcaccaggaactggtgaacggcaaagagta caagtgaaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaa ggccaaggggcagccccgcgaacccaggtgtgcacactgccccaaagcaggggac gagctgaccaagaaccaggtgtccctgagctgtccgtgaaaggcttctaccctccg atatgccctgggaatgggagagcaacggccagcccagagaaactacaagaccacc ccccctgtgctggacagcgacggctcattcttctggtgtccaagctgacagtggacaa gtcccgtgtggcagcagggcaacgtgttcagctgtcctgtatgcacgaggccctgca caaccactacaccagaagtcctgagcctgagccccggcaag	SEQ ID NO: 173
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	tgaccaagagcttcaaccggggcgagtgt	
Heavy chain B	agagcccacctgggtgcagtctggcaccgccatgaagaaccaggcgccctgtgctgg gtgtcctgtcagacaagcggtacaccttcaccgcccacatcctgttctggttccggcag gcccctggcagaggactggaatgggtgggatgatcaagccccagtatggcgccgtg aacttcggcgaggcttccgggatagagtgacctgacctgggacgtgtaccgcgag atcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtgggtgtctgccacaaaaccataccaggttagactgggtgagtcag gaggggggcttgaagcccgtgggtcttccgctgagctgttctgcctccggcttt gatttcgataacgctggatgacctgggtcaggcagcctccaggttaagggtgaggt gggtgggaagaatcacaggtccaggcgagggtggtcctggactacgcggaatct gttaaggggcggtttacaatctcaagggacaataccaagaatacctgtatttggagatg aacaacgtgagaactgaagacaccggatattacttctgtccagaacaggcaatacta cgacttctgggtccggctatccccctggcgagggaatatttcaagactgggggtcaggga ccctgttatcgtgtcctccgataagaccacaccgcttcaccaaggggcccatcggctt tccccctggcaccctcctccaagagcacctctgggggcacagcgccctgggtgctc tggtcaaggactacttccccgaaccggtgacggtgtcgtggaactcaggcgccctgac cagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccctagca gcgtggtgacctgcccctccagcagcttgggcaccagacctacatctgcaacgtgaa tcacaagcccagcaacaccaaggtggacaagaaagttgagcccaatctgtgacaaa actcacacatgcccaccgtgccagcacctgaactctggggggaccgtcagtcttct cttcccccaaaaacccaaggacacctcatgatctcccggaccctgaggtcacatgc gtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtatgttgacg gcgtggaggtgcataatgccaaagacaagccgcgggaggagcagtacaacagcac gtaccgtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaaggag tacaagtgaaggtctccaacaaagccctcccagccccatcgagaaaaccatctcca aagccaaggggcagccccgagaaccacaggtgtacacctgcccccatgccgggat gagctgaccaagaatcaagtcagcctgtgtgctggtgtaaaaggcttctatcccagcga catcgccgtggagtgggagagcaatgggcagccggagaacaactacaagaccacgc ctcccgtgtgactccgacggctccttcttctactcaaaactaccgtggacaaga gcaggtggcagcaggggaacgttctctcatgctcgtgatgcatgaggctctgcacaa ccactacacgcagaagagcctctcctgtctccgggt	SEQ ID NO: 175
Light chain B	gcatccgaactgactcaggacctgcccgtctctgtggcactgaagcagactgtg actattacttggcaggcgactcactgcggagccactacgcttctggtatcaga agaaacccggccaggcacctgtgtgtgttctacggaaagaacaataggcca tctggcatccccgaccgcttttctggcagtgcacaggaaccgagccagtctg accattaccggcgcccaggctgaggacgaagccgattactattgcagctccc ggataagagcggctccagactgagcgtgttcggaggaggaactaaactgacc gtcctcgacaaaaccatacctacatccacgtgaccagagccccagcagcct gtccgtgtccatcgggcgacagagtgacctcaactgccagacctctcaggggc tgggcagcgacctgcactggtatcagcacaagcctggcagagcccccaagct gctgatccaccacacaagcagcgtggaagatggcgtgccagcagattttccg gcagcgggttccacaccagcttcaacctgacctcagcgatctgcaggccgac gacattgccacctactattgtcaggtgtgcagttcttcggcagaggcagcaga ctgcacatcaaggataagaccataccgtacgggtggccgctcccagcgtgtt catcttcccacctagcgacgagcagctgaagtcgggcacagcctctgtcgtgtg cctgctgaacaacttctacccccgcaggccaaagtgcagtggaaaggtggac aacgccctgcagagcggcaacagccaggaaagcgtgaccgagcaggacag caaggactccacctacagcctgagcagcacctgacactgagcaaggccgac tacgagaagcacaaggtgtacgcctgcgaagtgaccaccaggggcctgtcta gccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 176

Binding Protein 23 Amino Acid Sequences		
Heavy chain A	evrlvesggglvkpggsrlrlscasgfdndawmtwvrqppgkglewvgritpgp egwsvdyaesvkgrftisrdntkntlylemnnvrtedtggyfcartgkydfwsgy ppgeeyfqdwgqgtlvivssastkgpsvflapsskstsggtaalgclvkdyfpepv tvswngaltsgvhtfpavqlssgylssvvtvpssslgtqtyicnvnhkpsntkvd kkvepkscdkthtcppcpapellggpsvflfppkpkdtlmisrtpevtcvvvdvshe dpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeyckv snkalpapiektiskakgqprepqvctlppsrdeltknqvsiscavkgfypsdiave wesngqpennyktpvldsdgsfflvskltvdksrwqqgnvfscsvmhealnhh ytqkslsisp	SEQ ID NO: 177
Light chain A	Aseltqdpavsvalkqtvtitcrdslrshyaswyqkkpgqapvllfygknnrpsgi pdrfsgsasgnrasltitgaqaeadyyccssrdksgsrlsvfgggtklvtlsqkaap svtlfppsseelqankatlvelisdfypgavtvawkadsspvkagvettpskqsnnk yaassylstpeqwkshrsyscqvtthegstvektvaptecs	SEQ ID NO: 178
Heavy chain B	rahlvqsgtamkkpgasvrvscqtsgytftahilfwfrqapgrglewvgrwik pqygavnfgggfrdrvtlrdvyreiaymdirglkpdtdavyycardrsygd sswaldawgqgttvvvsadkthtQvhltqsgpevrkpgtsvkvsckapgn lktydlhwrvsvpgqlqwmngwishegdkkviiverfkakvtidwdrstnt aylqlsgltsgdtavyycakgskhrlrdyalydddgalnwavdvdylnlef wgqgtavtvssdkthtastkgpsvflapsskstsggtaalgclvkdyfpepv tvswngaltsgvhtfpavqlssgylssvvtvpssslgtqtyicnvnhkpsn tkvdkkvepkscdkthtcppcpapellggpsvflfppkpkdtlmisrtpevt cvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvsvltvlh qdwlngkeyckvsnkalpapiektiskakgqprepvytlppcrdeltn qvsllwclvkgyfypsdiavewesngqpennyktpvldsdgsfflyskltvd ksrwqqgnvfscsvmhealnhytqkslsisp	SEQ ID NO: 179
Light chain B	dfvltsphslsvtpgesasiscksshlihgdrnnylawyvkpgrspqliylasr asgvprdfsgsgsdkdftlkisrvetedvgtyycmqgrespwtfqggtkvdkdkth t yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedgv psrfsfgsfhtsfnltsdlqaddiatyycqlqffgrgsrlhikdkthtrvaapsvfifp psdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsdstysls stltlskadyekkhvyacevthqglsspvtksfnrgec	SEQ ID NO: 180
Binding Protein 23 Nucleotide Sequences		
Heavy chain A	gaggttagactggtgagtcaggagggggccttggaagcccggtgggtctctccgc ctgagctgttctgcctccggccttgattcgataacgcctggatgacctgggtcaggcag cctccaggaaggactggagtggtgggaagaatcacaggctcaggcgagggtg gtccgtggactacgcggaatctgttaaggcggtttacaatctcaagggacaatacca agaataccttgatttgagatgaacaacgtgagaactgaagacaccggatattactct gtgccagaacaggcaatactacgacttctggtccggctatccccctggcgaggaaat ttcaagactggggtcagggaaccctgttatcgtgtcctccgcgtcgaccaagggcc cagcgtgtccctctggccctagcagcaagagcacatctggcggaacagccgcct gggctgcctcgtgaaggactacttcccagcccgtgaccgtgtcctggaattctggcg ccctgaccagcggcgtgcacaccttccagctgtgctgcagtcagcggcctgtacag cctgagcagcgtgacagtgcccagcagctctctgggacccagacctacatctgc aacgtgaaccacaagcccagcaacaccaaggtggacaagaaggtggaaccaaga gctgcgacaagaccacacctgtccccctgtcctgccccgaactgctgggaggccc ttcgtgttctgttcccccaagcccaaggacaccctgatgatcagccggacccccg aagtgcctgcgtggtggtgatgtgtccacaggaccctgaagtgaagttcaattgg tacgtggacggcgtggaagtgcacaacccaagaccaagcaagagaggaacagta caacagacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaac	SEQ ID NO: 181

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Light chain A	gcatccgaactgactcaggaccctgccgtctctgtggcactgaagcagactgtg actattacttgcgaggcgactcactgcggagccactacgcttctggtatcaga agaaacccggccaggcacctgtgtgtgtttctacgaaagaacaataggcca tctggcatccccgaccgcttttctggcagtgcatcaggaaccgagccagctctg accattaccggcgcccaggtgaggacgaagccgattactattgcagctcccg ggataagagcggctccagactgagcgtgttcggaggaggaactaaactgacc gtcctcagtcagcccaaggctgccccctcggtcactctgttcccgccctcagtg gaggagcttcaagccaacaaggccacactggtgtgtctcataagtgcattctac ccgggagccgtgacagtgccctggaaggcagatagcagccccgtcaaggcg ggagtggagaccaccacacctccaaacaaagcaacaacaagtacgcgcc agcagctacctgagcctgacgcctgagcagtggaagtccacagaagctaca gctgccaggtcacgcatgaaggagcaccgtggagaagacagtgggcccta cagaatgtca	SEQ ID NO: 182
Heavy chain B	agagccacactggtgcagctgtggcaccgccatgaagaaccaggcgccctgtgcgg gtgtcctgtcagacaagcggtacacctaccgcccacatcctgttctggtccggcag gccccgtggcagaggactggaatgggtgggatggaatgaagccccagtatggcgccgtg aacttcggcgaggcttccgggatagagtaccctgacccgggacgtgtaccgcgag atcgctacatggacatccgggacctgaagcccgatgacaccgccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtggtggtgtctgccgacaaaaccataccaggtgcacctgacacagagc ggaccggaagtgcggaagcctggcacctctgtgaaggtgtcctgcaaggccccctggc aacacctgaaaacctacgacctgcactgggtgcgcagcgtgccaggacagggactg cagtggtatgggctggtacagccacgagggcgacaagaagtgtcgtggaacggttc aaggccaaagtgacctcgactgggacagaagcacaacaccgcctacctgcagctg agcggcctgacctctggcgataccgccgtgtactactgcgcaagggcagcaagcac cggctgagagactacgcctgtacgacgatgacggcgccctgaactgggcccgtggtat gtggactacctgagcaacctggaattctggggccagggcacagccgtgacctgtcat ctgataagaccacaccgcttccaccaagggcccatcggttccccctggcacctcc tccaagagcacctctgggggacagcggccctgggctgctgtaaggactacttcc ccgaaccgggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtgcacacct tcccggtgtcctacagtcctcaggactctactccctcagcagcgtggtgacctgacct ccagcagcttggggcaccagacctacatctgcaactgtaatcacaagcccagcaaca ccaaggtggacaagaaagttgagcccaatctgtgacaaaactcacacatgccacc gtgcccagcactgaactcctggggggaccgtcagcttcttcttcccccaaaacca aggacacctcatgatctcccggaccttgaggtcacatgcgtggtggtggactgag ccacgaagacctgaggtcaagtcaactggtatgttgacggcgtggaggtgcataatg ccaagacaaagccgaggagagcagtagacaacagcacgtaccgtgtgtcagcgtc ctaccgtcctgcaccaggactggctgaatggcaaggagtacaagtgaaggttcca acaaagccctcccagccccatcgagaaaaccatctccaaagccaaagggcagccc cgagaaccacaggtgtacacctgccccatgccgggatgagctgaccaagaatcaa gtcagcctgtggtgacctgtaaaaggcttctatcccagcgacatcgccgtggagtggg agagcaatgggcagccggagaacaactacaagaccacgcctcccgtgtggtgactcc gacggctccttcttcttactcaaaactaccgtggacaagagcaggtggcagcagg ggaacgtcttctcatgctcgtgatgcatgaggctctgcacaaccactacacgagaag agcctctcctgtctccgggt	SEQ ID NO: 183

Light chain B	gacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgaga gcgccagcatcagctgcaagagcagccactccctgatccacggcgaccggaa caactacctggcttggtacgtgcagaagcccggcagatccccccagctgctga tctacctggccagcagcagagccagcggcgtgcccgatagatttctggcagc ggcagcgacaaggacttcaccctgaagatcagccgggtggaaaccgaggac gtgggcacctactactgtatgcagggcagagagagcccctggacctttggcca gggaccaaggtggacatcaaggacaaaaccatactacatccacgtgacc cagagccccagcagcctgtccgtgtccatcggcgacagagtaccatcaactg ccagacctctcagggcgtgggcagcgacctgcactggtatcagcacaagcct ggcagagcccccaagctgctgatccaccacacaagcagcgtggaagatggc gtgccagcagattttccggcagcggcttcacaccagcttcaacctgaccatc agcgatctgcagggcgacgacattgccacctactattgtcaggtgctgcagttct tcggcagaggcagcagactgcacatcaaggataagaccatacccgtagcgt ggccgctcccagcgtgttcattctcccacctagcgacgagcagctgaagtcg gcacagcctctgtcgtgtgctgctgaacaacttctacccccgcgaggccaaa gtgcagtggaaaggtggacaacgccctgcagagcggcaacagccaggaaag cgtgaccgagcaggacagcaaggactccacctacagcctgagcagcacctg acactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtga cccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtg t	SEQ ID NO: 184
Binding Protein 24 Amino Acid Sequences		
Heavy chain A	evrlvesggglvkpggsrlrscsasgfdnawmtwvrqppgkglewvgritgpe gwsvdyaesvkgrftisrdntkntlylemnnvrtedtgyyfcartgkyydfwsgypp geeyfqdwgqgtlvivssastkgpsvflapsskstsggtaalglvkdyppepvtvs wnsgaltsgvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkve pkscdkthtcppcpapellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpev kfnwyvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkal papiektiskakgqprepqvctlpssrdeltknqvsiscavkgfypsdiavewesngq pennyktpvldsdgsfflvskltvdksrwqqgnvfscsvmhealnhhtqksls pg	SEQ ID NO: 185
Light chain A	aseltqdpavsvalkqvtvitergdsrlrshyaswyqkkpgqapvllfygknnrpsgip drfsgsasgnrasltitgaqadeadyccsrksgsrlsvfgggkltvlsqkaapsv tlfppsseelqankatlvcldsfypgavtvawkadsspvkagvettptskqsnkya assylsltpewkshrsyscqytheqstvektvaptecs	SEQ ID NO: 186
Heavy chain B	Qvhltqsgpevrkpgtsvkvsckapgentlkttydlhwvrsvpqgqlqwmg wishgedkkviverfkakvtidwdrstntaylqlsgltsgdavyycakgskh rlrlyalydddgalnwavdvdylnlefwgqgtavtvss dkthtrahlvqsgtamkkpgasvrvcqtsgytftahilfwfrqapgrglewv gwikipqygavnfgggfrdrvlttrdvyreiaymdirglkpdtdavyycardrs ygdsswaldawgqgttvvsadkthtastkgpsvflapsskstsggtaalgc lvkdyfpepvtvswnsgaltsgvhtfpavlqssglyslssvvtvpssslgtqtyi cnvnhkpsntkvdkkvepkscdkthtcppcpapellggpsvflfppkpkdtl misrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyr vsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepqvyltp crdeltknqvsllwclvkgfypsdiavewesngqpennyktpvldsdgsffl yskltvdksrwqqgnvfscsvmhealnhhtqksls spg	SEQ ID NO: 187
Light chain B	yihvtqspsslsvsigdrvtincqtsqvggsdlhwyqhkpgrapkllihhtssvedgv psrfsqsgfhtsfnltsldlqaddiatyycqvlqffgrgsrlhikdkthtdfvtqsp hslsvtpgesasiscksshlihgdrnnylawyvqkpgrspqlliylasrasgvpd rfsqsgsdkdftlkisrvetedvgtyycmqgrespwtfqggtkvdkdkthtrtva apsvfifpp sdeqlksqtasvvcllnnfyreakvqkwvdnalqsgnsqesvteqdskdstyslsst	SEQ ID NO: 188

	ltlskadyekhhkvyacevthqglsspvtksfnrgec	
Binding Protein 24 Nucleotide Sequences		
Heavy chain A	gaggttagactggtggagtcaggagggggcgttgtaagcccgtgggtctctccgcc tgagctgttctccctccggtttgatttcgataacgcctggatgacctgggtcaggcagcc tccaggttaagggactggagtggtgggaagaatcacagggtccaggcgagggtggtc cgtggactacgcggaatctgttaagggcggtttacaatctcaagggaataaccaaga ataccttgatttggagatgaacaacgtgagaactgaagacaccggatattacttctgtgc cagaacaggcaataactacgacttctgtccggctatccccctggcgagggaatatttca agactggggtcagggaacccttgtatcgtgtcctccgcgtcgaccaagggccccagcg tgttccctctggccctagcagcaagagcacatctggcggaacagccgctctgggtg cctcgtgaaggactacttcccagcccgtgaccgtgtcctggaattctggcgccctgac cagcggcgtgcacaccttccagctgtgctgcagtcacggcctgtacagcctgagca gcgtcgtgacagtgccagcagctctctgggcacccagacctacatctgcaacgtgaac cacaagcccagcaacaccaaggtggacaagaaggtggaaccaagagctcgacaa gaccacacctgtccccctgtcctgccccgaactgctgggaggcccttccgtgttct gttcccccaagcccaaggacacctgatgatcagccggacccccgaagtgacctgc gtggtggtggtgtgtccacgaggacctgaagtgaagttcaattggtactggacgg cgtggaagtgcacaacgccaagaccaagccaagagaggaacagtacaacagcaccta ccgggtgtgtcctgctgaccgtgtgcaccaggactggctgaacggcaagagtag aagtgaaggtgtccaacaaggccctgctgccccatcgagaaaaccatcagcaagg ccaagggccagccccgcaaccccaggtgtgcacactgcccccaagcaggagcag ctgaccaagaaccaggtgtcctgagctgtgccgtgaaaggcttctaccctccgatatc ggcgtggaatgggagagcaacggccagcccagaaactacaagaccaccccccc tgtgtggacagcgacggctcatttctcgtgtccaagctgacagtggacaagtcgg gtggcagcagggcaacgtgttcagctgtccgtgatgcacaggccctgcacaaccac tacaccagaagtcctgagcctgagccccggcaag	SEQ ID NO: 189
Light chain A	gcatccgaactgactcaggacctgccgtctctgtggcactgaagcagactgtg actattacttggcgaggcgactcactgcggagccactacgttctctggtatcaga agaaacccggccaggcacctgtgctgtgttctacggaaagaacaatagccat ctggcatccccgaccgcttttctggcagtgcacagggaaccgagccagtctga ccattaccggcgccaggtgaggacgaagccgattactattgcagctccgg gataagagcggctccagactgagcgtgttcggaggaggaactaaactgacct cctcagtcagcccaaggctgccccctggctactctgttcccgcctcagtgag gagcttcaagccaacaaggccacactgggtgtgtctcataagtacttctaccgg gagccgtgacagtggcctggaaggcagatagcagccccgtcaaggcgggagt ggagaccaccacacctccaacaaagcaacaacaagtacgcggccagcagc tacctgagcctgacgcctgagcagtgaagtcccacagaagctacagctgcca ggtcacgcatgaaggagcaccgtggagaagacagtggccctacagaatgtt ca	SEQ ID NO: 190
Heavy chain B	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacagagtga ccatcaactgccagacctctcagggcgtgggcagcgacctgcactggtatcagcaca gcctggcagagcccccaagctgtgatccaccacacaagcagcgtggaagatggcgt ggccagcagatttccggcagcggcttccacaccagcttcaacctgacctcagcgatct gcaggccgacgacattggcacctactattgtcaggtgtcagttcttcggcagaggca gcagactgcacatcaaggacaaaaccataccgacttctgtgctgacctagagccctca cagcctgagcgtgacacctggcgagagcgccagcatcagctgcaagagcagccactc cctgatccacggcgaccggaacaactacctggcttggtacgtgcagaagccccggcaga tccccccagctgctgatctacctggccagcagcagagccagcggcgtgccgatagatt ttctggcagcggcagcgacaaggacttcacctgaagatcagccgggtggaaaccga ggacgtgggcacctactactgtatgcagggcagagagagccctggaccttggccag ggcaccaaggtggacatcaaggataagaccataccgtacgggtggcgctccagc gtgttcatttccacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgc	SEQ ID NO: 191

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Light chain B	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacag agtgaccatcaactgccagacctctcagggcgtgggcagcgacctgcactggt atcagcacaagcctggcagagccccaagctgctgatccaccacacaagcagc gtggaagatggcgtgcccagcagattttccggcagcggcttcacaccagcttc aacctgaccatcagcgatctgcaggccgacgacattgccactactattgtcagg tgctgcagttcttcggcagaggcagcagactgcacatcaaggacaaaaccata ccgacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgag agcgccagcatcagctgcaagagcagccactccctgatccacggcgaccgga acaactacctggcttggtacgtgcagaagcccgagatccccccagctgctga tctacctggccagcagagccagcggcgtgcccgatagattttctggcagcg gcagcgacaaggacttcacctgaagatcagccgggtggaaccgaggacgt gggcacctactactgtatgcagggcagagagagccccctggacctttggccagg gcaccaaggtggacatcaaggataagaccatacccgtagcgtggccgctccc agcgtgttcattctccacctagcgacgagcagctgaagtccggcacagcctct gtcgtgtgcctgctgaacaacttctacccccgcgaggccaaagtgcagtgaag gtggacaacgcctgcagagcggcaacagccaggaaagcgtgaccgagcag gacagcaaggactccacctacagcctgagcagcaccctgacactgagcaagg ccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcct gtctagccccgtgaccaagagcttcaaccggggcgagtg	SEQ ID NO: 192
Binding Protein 25 Amino Acid Sequences		
Heavy chain A	qvqlvqsggqmkkpgesmriscrasgyefidctlnwirlapgkrpewmgwlkprg gavnyarplqgrvtmtrdvysdtaflelrslvddtavvfctrkncdynwdfehwgr gtpvivssastkgpsvflapsskstsggtaalgclvkdyfpepvtvswngaltsgvh tfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscdkthtcp pcpapellggpsvflfppkpkdtlmsirtpevtcvvvdvshedpevkfnwyvdgve vhnaktkpreeqynstyrvsvltvlhqdwlngkeyckvsnkalpapiektiskak gqprepqvctlppsrdeltknqvsiscavkgfypsdiavewesngqpennyktpppv ldsdgsfflvskltvdksrwqqgnvfscsvlhealhshytqkslslspg	SEQ ID NO:193
Light chain A	eivltqspgtlslspgetaiiscrtsqygslawyqqrpgqaprlviysgstraagipdrfs gsrwgpdynltisnlesgdfvyycqqyeffggqtkvqvdiqrtvaapsvfifppsde qlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsdstyslstlts kadyekhkvacevthqglsspvtksfnrgec	SEQ ID NO: 194
Heavy chain B	evrlvesggglvkpggslrlscsasgfdfdnawmtwvrqppgkglewvgrit gpgegwsvdyaesvkgrftisrdntkntlylemnnvrtdtggyfcartgkyy dfwsgyppgeeyfqdwgqgtlvivssdkthtqvqlvesgggvvqpgtslrls caasqfrfdgygmhwvrqapgkglewvasishdgikkyhaekvwgrftisr dnskntlylqmnsrlpedtalyycakdlredeceewwsdydfgkqlpcaks rgglvgiadnwgggtmvtvssdkthtastkgpsvflapsskstsggtaalgcl vkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyic nvnhkpsntkvdkkvepkscdkthtppcpapellggpsvflfppkpkdtl msirtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyr vsvltvlhqdwlngkeyckvsnkalpapiektiskakgqprepqvylpp crdeltknqvsllwclvkgfypsdiavewesngqpennyktpppvldsdgsffl yskltdksrwqqgnvfscsvlhealhshytqkslslspg	SEQ ID NO: 195
Light chain B	qsvltqppsvisaapgkvvtiscsgntsnignnfsvwyqqrpgrapqlliyetdkrpsgi pdrfsasksgtsgltaitglqtgdeadyycatwaaslsarvfgtgtkvivldkthtaselt	SEQ ID NO: 196

	qdpavsvalkqvtitcrdsrlrshyaswyqkkpgqapvllfygknnrpsgipdrfsg sasgnrasltitgaqaeadyycssrdksgrlsvfgggtklvldkthtrtvaapsvfif ppsdeqlksgrtasvcllnnfypreakvqwkvdnlqsgnsqesvteqdskdstysl sstltlskadyekkhkyacevthqglsspvtksfnrgec	
Binding Protein 25 Nucleotide Sequences		
Heavy chain A	cagggtgcagctggtgcagctctggcggccagatgaagaacccggcgagagcatgcgg atcagctgcagagccagcgggtacagagttcatcagctgcacccctgaactggatcagact ggcccctggcaagcggcctgagtgatgggatggctgaagcctagaggcggagccgt gaactacgccagacctctgcagggcagagtaccatgacccgggacgtgtacagcgat accgccttcctggaactgcggagcctgaccgtggatgataccgccgtgtactttgcacc cggggcaagaactcgactacaactgggacttcgagcactggggcagaggcacccct gtgatcgtgtcaagcgcgtcgaccaaggggcccagcgtgtccctctggcccctagcag caagagcacatctggcgaacagccgccctgggctgcctcgtgaaggactactttccc agcccgtgaccgtgtcctggaattctggcggcctgaccagcggcgtgcacaccttcca gctgtgctgcagtcacagcggcctgtacagcctgagcagcgtcgtgacagtgcacagca gctctctgggcacccagacctacatctgcaacgtgaaccacaagcccagcaaacacaa gggtggacaagaagggtggaaccaagagctgcgacaagaccacacctgtcccccctgt cctgccccgaactgctgggagggccttccgtgttctgttcccccaagcccaagga cacctgatgatcagccggacccccgaagtacgtgcgtggtggtggtgatgtgtccacg aggacctgaagtgaagtcaattggtacgtggacggcgtggaagtgcacaacgccaa gaccaagccaagagaggaacagtacaacagcacctaccgggtggtgtccgtgctgac cgtgctgcaccaggactggctgaacggcaaagagtacaagtgaaggtgtccaacaag ggcctgcctgccccatcgagaaaaccatcagcaaggccaaggggccagccccgcgaa ccccaggtgtgcacactgcccccaagcaggagcagctgaccaagaaccaggtgtcc ctgagctgtgccgtgaaaggcttctacccctccgatatcgccgtggaatgggagagcaa cgccagcccagacaactacaagaccacccccctgtgctggacagcgacggctc attcttctggtgtccaagctgacagtggacaagtcccggtggcagcagggcaacgtgtt cagctgctccgtgctgcatgaggctctgcacagccactacacgcagaagagcctctccc tgtctccgggt	SEQ ID NO: 197
Light chain A	Gagatcgtgctgacacagagccctggcaccctgagcctgtctccaggcgagacagcc atcatcagctgccggacaagccagtagcggcagcctggcctggtatcagcagaggcctg gacaggccccagactcgtgatctacagcggcagcacaagagccggcgaatccccg atagattcagcggctccagatggggccctgactacaacctgacctacagcaacctggaa agcggcgacttcggcgtgtactactgccagcagtagagttcttcggccagggcaccaa gggtgcaggtggacatcaagcgtacgggtggcgcctcccagcgtgtcatcttccacctag cgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgtgaacaacttctacc ccgcgagggcaaaagtgcagtggaggtggacaacgcctgcagagcgggcaacagcc aggaaagcgtgaccgagcaggacagcaaggactccactacagcctgagcagcacc ctgacactgagcaaggccgactacgagaagcacaagggtgtacgcctgcgaagtgacc caccaggcctgtctagccccgtgaccaagagcttcaaccggggcgaggtgt	SEQ ID NO: 198
Heavy chain B	gaggttagactggtggagtcaggaggggggcttgtgaagccgggtgggtctctccgct gagctgttctgcctccggcttgaatttcgataacgcctggatgacctgggtcaggcagcct ccaggtaaaggactggagtggtgggaagaatcacaggtccaggcgagggtggtcc gtggactacgcggaatctgttaaggcgggttacaatctcaagggacaataccaagaat acctgtatttgagatgaacaacgtgagaactgaagacaccggatattacttctgtgcca gaacaggcaatactacgacttctggcggctatccccctggcgagggaatattttcaag actggggtcagggaaccttgttatcgtgtcctccgacaaaaccataccaggtgcagt tggtggagctctgggggaggcgtggtccagcctgggacgtccctgagactctcctgtgca gcctctcaattcaggtttgatggttatggcatgcactgggtccgccaggccccaggaag gggctggagtggtggcatctatatcacatgatggaattaaaaagtatcacgcagaaaaa gtgtggggccgcttaccatctccagagacaattccaagaacacactgtatctacaaatg aacagcctgcgacctgaggacacggctcttactactgtgcgaagatttgcgagaaga cgaatgtgaagagtggtggtcggtattattacgatttgggaacaactcccttgcgcaag	SEQ ID NO: 199

	tcacgcggcggttggttgaattgctgataactggggccaagggacaatggtcaccgt ctcttcagataagaccacaccgcttccaccaagggcccatcggtcttccccctggcacc ctctccaagagcacctctgggggcacagcggccctgggctgctgtgtaaggactac tccccgaaccggtgacggtgctgtggaactcaggcgcctgaccagcggcgtgcaca cctccccggctgtcctacagtcctcaggactctactccctcagcagcgtggtgaccgtgc cctccagcagcttgggcacccagacctacatctgcaacgtgaatcacagcccagcaac accaaggtggacaagaaagttagcccaaatcttgacaaaactcacacatgccacc gtgccagcacctgaactcctggggggaccgtcagttctcttcccccaaaacccaa ggacaccctcatgatctcccgaccctgaggtcacatgcgtggtggtgacgtgagcc acgaagaccctgaggtcaagtcaactggtatgttgacggcgtggaggtgcataatgcc aagacaaaagccgcgggagggagcagtacaacagcacgtaccgtgtggtcagcgtcctc accgtcctgcaccagactggctgaatggcaaggagtacaagtgaaggtctcaaca aagccctcccagccccatcgagaaaaccatctccaagccaaagggcagccccgag aaccacaggtgtacaccctgccccatgccgggatgagtgaccaagaatcaagtcag cctgtggtgctgtgtaaaaggcttctatcccagcgacatcgccgtggagtgggagagca atgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctc cttcttcttactcaaaactcacctgggacaagagcaggtggcagcaggggaacgtctt ctcatgtccgtgctgcatgaggtctgcacagccactacacgcagaagagcctctccct gtctccgggt	
Light chain B	cagtctgtgctgacgcagccgcctcagtgctgcggccccaggacagaaggt caccatctctgctctgaaacacctccaacattggcaataattttgtctctggtat caacagcggccccggcagagcccccaactcctcatttatgaaactgacaagcga ccctcagggaattcctgaccgattctctgcttcaagtctgtacgtcaggcacct ggccatcacccgggtgcagactggggacgaggccgattattactgcgccacat gggctgccagcctgagttccgcgctgtcttcggaactgggaccaaggtcatcg tcttgacaaaaccataaccgcatccgaactgactcaggaccctgccgtctctgt ggcactgaagcagactgtgactattacttgcggaggcactactgcggagcca ctacgcttctggtatcagaagaaccggccaggcacctgtgctgctgttctac ggaaagaacaataggccatctggcatccccgaccgctttctggcagtgcacag ggaaccgagccagtctgaccattaccggcgccaggctgaggacgaagccga ttactattgcagctcccgataagagcggctccagactgagcgtgttcggagg aggaaactaaactgaccgtcctcgataagaccatacccgtagcgtggccgctcc cagcgtgttcattctcccacctagcgacgagcagctgaagtccggcacagcctct gtcgtgtgctgctgaacaacttctacccccgcgaggccaaagtgcagtggag gtggacaacgccctgcagagcggcaacagccaggaaagcgtgaccgagcag gacagcaaggactccacctacagcctgagcagcaccctgacactgagcaagg ccgactacgagaagcacaaaggtgtacgcctgcgaagtgaccaccagggcct gtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 200
Binding Protein 26 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvcqstg gyftahil fwfrqapgrglewv gwikpqyg avn fggfrdrvltldvryeiaymdirglkpddtavvycard rsygdsswaldawg qgttvvsaastkgpsvfplapsskstsggtaalglvkdyfpepvtvswngaltsgv htfpavllqssglyslssvtpssslgtqtyicnvnhkpsntkvdkkvepkscdkthtc ppcpapellggpsvflfppkpkdtlmisrtpvctcvvdvshedpevkfnwyvdgv evhnaktkpreeqynstyrvsvltvlhqdwlngkeyckvsnkalpapiektiska kgqprepqvctlppsrdeltknqvsiscavkgfypsdiavewesngqpennykttpp vldsdgsfflvskltvdksrwqqgnvfscsvlhealhshytqkslsisp	SEQ ID NO: 201
Light chain A	yihvtqspsslsvsigdrvincqst qgvgsdl hwyqhkgpgrapkllihhtssvedgvp srfsgsg fh tsfnltisdlqaddiatyyc qvlqff grsrlhikrtvaapsvfifppsdeql ksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdskdstyslsstltska dyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 202

Heavy chain B	<p>evrlvesggglvkpggslrlscsasgfdndawmtwvrppgkglewvgrit gpgegswdyaesvkgrftisrdntkntlylemnnvrtdtggyfcartgkyy dfwsgyppgeeyfqdwgqgtlvivssdkthtqvqlvesgggvvpqgtslrls <u>caasqfrfdgygmhwvrqapgkglewvasishdgikkyhaekvwgrftisr</u> <u>dnskntlylqmnsrlrpedtalyycahdlredeceewwsdydfgkqlpcaks</u> <u>rgglvgiadnwgggtmvtvssdkthtastkgpsvfplapsskstsggtaalgcl</u> <u>vkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyic</u> <u>nvnhkpsntkvdkkvepkscdkthtppcpapellggsvglfpkpkdltl</u> <u>misrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyr</u> <u>vsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepvytlpp</u> <u>crdeltnqvslwclvkgyfypsdiavewesngqpennyktpvldsdgsffl</u> <u>yskltdksrwqqgnvfscsvlhealhshytqkslsisp</u></p>	SEQ ID NO: 203
Light chain B	<p>qsvltqppsvsaaaggkvtiscsgntsnignnfsvwyqqrprapqlliyetdkrpsgi pdrfsasksgtsgtlaitglqtgdeadyycatwaaslssarvfgtgtkvi vldkthtaselt qdpavsvalkqtvtitcrgdsrlrshyaswyqkpgqapvllfygknnrpsgipdrfsg sasgnrasltitgaadeadyycssrdksgrlsvfgggkltvldkthtrtvaapsvfif ppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstysl sstltlskadyekkhvyacevthqglsspvtksfnrgec</p>	SEQ ID NO: 204
Binding Protein 26 Nucleotide Sequences		
Heavy chain A	<p>agagccacctggcagctctggcaccgccatgaagaaaccaggcgctctgtgcggg tgtcctgtcagacaagcggtacacctcaccgccacatcctgttctggtccggcagg cccctggcagaggactggaatgggtgggatggaatgaagccccagtaggcgccgtgaa cttcggcggaggcttccgggatagagtaccctgacccgggacgtgtaccgcgagatc gcctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcgcca gagacagaagctacggcgacagcagctgggctctggatgcttggggccagggcacaa ccgtggtggtgtctgccgctctacaaaggccccagcgtgtccctctggccccctagca gcaagagcacatctggcggaacagccgccctgggctgcctctgtaaggactacttccc gagcccgtagcctgtcctggaattctggcgccctgaccagcggtgcacaccttcc agctgtgctgcagtcagcgccctgtacagcctgagcagcgtcgtgacagtgcaccagc agctctctgggcacccagacctacatctgcaacgtgaaccacaagcccagcaacacca aggtggacaagaaggtggaacccaagagctgcgacaagaccacacctgtcccccttg tcctgccccgaactgctgggaggcccttccgtgttctgttcccccaagcccaagga caccctgatgatcagccggacccccgaagtacctgcgtggtggtggtgatgtgtccacg aggacctgaagtgaagtcaattggtacgtggacggcgtggaagtgcacaacgccaa gaccaagccaagagaggaacagtacaacagcacctaccgggtggtgtccgtgctgac cgtgctgcaccaggactggctgaacggcaaagagtacaagtgaaggtgtccaacaag gccctgctgccccatcgagaaaaccatcagcaaggccaaggccagccccgcgaa ccccaggtgtgcacctgcccccaagcaggacgagctgaccaagaaccaggtgtcc ctgagctgtgccgtgaaaggcttctacccctccgatatcggcgtggaatgggagagcaa cggccagcccagagaacaactacaagaccacccccctgtgctggacagcgacggctc attcttctggtgtccaagctgacagtggacaagtccgggtggcagcagggaacgtgtt cagctgctccgtgctgcatgaggctctgcacagccactacacgcagaagagcctctccc tgtctccgggt</p>	SEQ ID NO: 205
Light chain A	<p>tacatccacgtgacccagagccccagcagcctgtccgtgtccatcggcgacagagtga ccatcaactgccagacctctcaggcggtgggcagcgacctgcactggtatcagcaca gcctggcagagcccccaagctgctgatccaccacacaagcagcgtggaagatggcgt gcccagcagatttccggcagcggttccacaccagcttcaacctgacctcagcgatct gcaggccgacgacattgccacctactattgtcaggtgctgcagttcttcggcagaggcag cagactgcacatcaagcgtacgggtggccgtcccagcgtgttcatcttcccacctagcga cgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaacttctacccccg cgaggccaaagtgcagtgaaggtggacaacgccctgcagagcggcaacagccagg aaagcgtgaccgagcaggacagcaaggactccacctacagcctgagcagcacctga cactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccacc</p>	SEQ ID NO: 206

Heavy chain B	agggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt gagggttagactggtggagtcaggagggggccttgtgaagcccgtgggtctctccgcct gagctgttctgcctccggccttgatttcgataacgcctggatgacctgggtcaggcagcct ccaggtaaaggactggagtgggtgggaagaatcacaggtccaggcgagggtgtcc gtggactacgcggaatctgttaaaggcggtttacaatctcaagggacaataccaagaat acctgtatttggagatgaacaacgtgagaactgaagacaccggatattacttctgtgcc gaacaggcaataactacgacttctgggtccggctatccccctggcgagggaatatttcaag actggggtcagggaacccttgtatctgtcctccgacaaaaccataaccagggtgcagt tggtggagcttgggggagggcgtgggtccagcctgggacgtccctgagacttctctgtgca gccttcaattcaggtttgatggtatggcatgactgggtccgacggccccagggaag gggtgtgagtggtggcatctatacatgatggaattaaaaagtatcacgcagaaaaa gtgtggggccgcttaccatctccagagacaattccaagaacacactgtatcacaatg aacagcctgcgacctgaggacacggctcttactactgtgcgaaagatttgcgagaaga cgaatgtgaagagtgggtggcggattattacgatttgggaaacaactcccttgcgaaag tcacgcggcggttgggtggaattgctgataactggggccaagggaacaatgtgcaccgt ctcttcagataagaccacaccgcttccaccaaggggcccatcggttctccccctggcacc ctctccaagagcacctctgggggacagcggccctgggtgcctggtaaggactac tccccgaaccgggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtgcaca ccttccccgggtgtcctacagtcctcaggacttactcctcagcagcgtggtgaccgtgc cctccagcagcttgggacaccagacctacatctgcaacgtgaatcacaagcccagcaac accaaggtggacaagaaagttgagcccaaatcttgacaaaactcacacatgccacc gtgcccagcacctgaactcctgggggacggcagtcagtcttcttcccccaaaaaccaa ggacacccctcatgtctccggacccctgaggtcacatgcgtggtggtggagtgagcc acgaagaccctgaggtcaagttcaactggtatgttgacggcgtggaggtgcataatgcc aagacaaagccgaggagagcagtagacaacagcacgtaccgtgtggtcagcgtctc accgtcctgcaccaggactgggtgaatggcaaggagtagaagtgcaaggtctccaaca aagccctcccagccccatcgagaaaaccatctccaaagccaaaggcgagccccgag aaccacaggtgtacacacctgccccatgccgggatgagctgaccaagaatcaagtcag cctgtgtgctgctgtaaaaggcttctatccagcgacatcgccgtggagtgggagagca atgggcagccggagaacaactacaagaccacgctccctgctggtgactccgacggctc cttctcttactcaaaactcaccgtggacaagagcaggtggcagcaggggaacgtctt ctatgtcctgtgctgcatgaggtctgcacagccactacacgcagaagagcctctccct gtctccgggt	SEQ ID NO: 207
Light chain B	cagtctgtgctgacgcagccgccctcagtgctgtgcccaggacagaaggtcacat ctctgtcttgaaacacctccaacattggcaataatttgtgtcctggtatcaacagcgcc ccggcagagcccccaactcctcattatgaaactgacaagcgaccctcagggtattctg accgattctctgctccaagtctggtacgtcaggcaccctggccatcaccgggctgcaga ctggggacgagggcgattattactgcgccacatgggtgcccagcctgagttccgcgct gtcttcggaactgggaccaaggtcatcgtcctggacaaaaccataaccgcatccgaact gactcaggaccctgccgtctgtggtcactgaagcagactgtgactattacttgcgagg cgactcactcggagccactacgttctggtatcagaagaaaccggccagggcacct gtgtgtgttctacggaaagaacaataggccatctggcatccccgaccgcttttctggca gtgcatcagggaaccgagccagctgtgaccattaccggcgcccaggctgaggacgaag ccgattactattgcagctcccggtgataagagcggctccagactgagcgtgttcggagga ggaactaaactgaccgtctcgtatagaccataaccgtacggtggccgctccagcgt gttcatcttcccacttagcgacgagcagctgaagtccggcacagcctctgtcgtgtgct gtgaacaacttctacccccgcgaggccaaagtgcagtggaaaggtggacaacgcctg cagagcggcaacagccaggaaagcgtgaccgagcagagacagcaaggactccacta cagcctgagcagaccctgacactgagcaaggccgactacgagaagcacaaggtgta cgctgcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaaccgg ggcgagtgt	SEQ ID NO: 208
Binding Protein 27 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkgpvasrvscqts <i>gyftah</i> ilfwfrqapgrglewv <i>gwikipqyg</i> <i>avn</i> fgggfrdrvlttrdvyreiaymdirglkpddtavvyycard <i>rsygdsswaldawg</i>	SEQ ID NO: 209

	qgttvvsaastkgpsvfplapssksts ggtaalglvkdypvptvswngaltsgv htfpavlqssgylssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscdkthtc ppcpapellggpsvflfppkpkdtlmsrtpevtcvvvdvshedpevkfnwyvdgv evhnaktkpreeqynstyrvvsvltvlhqdwlngkeyckvsnkalpapiektiska kgqprepqvctlpssrdeltnqvs lscavkgfypsdiavewesngqpennykttpp vldsdsfflvskltvdksrwqqgnvfscsvlhealthshytqkslslspg	
Light chain A	yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapklihtssvedgv psrfs gsgfhtsfqltisdlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsdeq lks gtasvvc lnnfybreakvqwkvdnalqsgnsqesvteqdskdstyslssltsk adyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 210
Heavy chain B	Evrivesggglvkpggsrlscsasgfdfnawmtwvrpppgkglewvgri tgpggegwsvdyaesvkgrftisrdntkntlylemnnvrtedtggyfcartgky ydfwsgyppeeyfqdwgqgtlvivssdkthtqhvtlqsgpevrkpgtsvk vsc kapgntlktydlhwvrvpgqglqwm gwishegdkkviverfkakvti dwdrstntaylqlsgltsgdtavyycakgskhrlrdyalydddgalnwavdvd ylsnlefwgqgtavtvssdkthtastkgpsvfplapssksts ggtaalglvkdyp fpeptvswngaltsgvhtfpavlqssgylssvvtvpssslgtqtyicnvnh kpsntkvdkkvepkscdkthtcppcpapellggpsvflfppkpkdtlmsrt evtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltv lhqdwlngkeyckvsnkalpapiektiskakgqprepqvylppcrdeltn nqvs lwclvkgfypsdiavewesngqpennykttppvldsdsfflvskltv dksrwqqgnvfscsvlhealthshytqkslslspg	SEQ ID NO: 211
Light chain B	dfvltqspshlsvtpgesasiscksshlihgdrnnylawyvqkprspqliylasra sgvpdrfsgsgsdkdftlkisrvetedvgtyymqgrespwtfqggtkvdkdkthta seltqdpavsvalkqtvtitergdsrlrshyaswyqkkpgqapvllfygknrpsgipdr fsgsasgnrasltitgaqaeadyycssrdksgrlsvfgggtklvldkthtrtvaaps vfifppsdeqlks gtasvvc lnnfybreakvqwkvdnalqsgnsqesvteqdskdst yslssltskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 212
Binding Protein 27 Nucleotide Sequences		
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Heavy chain B	gaggttagactggtgagtcaggaggggggcttgtgaagcccgggtgctctccgc ctgagctgttctgcctccggcttggatttcgataacgcctggatgacctgggtcaggcag cctccaggtgaaggactggagtggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaatctgttaaaggcggtttacaatctcaagggacaatacca agaataccttgtatttgagatgaacaacgtgagaactgaagacaccggatattactct gtgccagaacaggcaatactacgacttctgttccggctatccccctggcgaggaatat tttaagactggggtcagggaaccttgttatcgtgtcctccgacaaaaccataccag gtgcacctgacacagagcggaccggaagtgcggaagcctggcacctctgtgaaggtg tctgcaagggccctggcaacacctgaaaacctacgacctgactgggtgcgcagc gtgccaggacagggactgcagtggtggctggatcagccacgaggcgacagaaga aagtgatcgtggaacgggtcaaggccaaagtaccatcactgggacagaagcacca acaccgcctacctgcagctgagcggcctgacctctggcgataccgccgtgtactactg cgccaaaggcgacgaagcaccggctgagagactacgcctgtacgacgatgacggcg ccctgaactggggcgtggatgtggactacctgacaacctggaattctggggccagg gcacagccgtgaccgtgtcatctgataagaccacaccgctccaccaaggggcccatc ggctttccccctggcacctcctccaagagcacctctggggggcacagcggccctggg ctgcctgtcaaggactacttccccgaaccgggtgacggtgtcgtggaactcaggcgcc ctgaccagcggcgtgcacaccttcccggctgtcctacagtctcaggaacttactccct cagcagcgtggtgacctgcccctccagcagcttgggcacccagacctacatctgcaac gtgaatcacaagcccagcaacaccaaggtggacaagaaagttagcccaaatctgtg acaaaactcacacatgccaccgtgcccagcacctgaactcctggggggaccgtcag tcttctcttcccccaaaaccaaggacacctcatgatctccggacctctgaggtca catgcgtggtggtggacgtgagccacgaagacctgaggtcaagttaactggtatgtt gacggcgtggaggtgcataatgccaagacaaagccgcgggagggagcagtacaaca gcacgtaccgtgtgtcagcgtcctcaccgtctgcaccaggactggctgaatggcaa ggagtacaagtgaaggttccaacaaagccctcccagccccatcgagaaaacctat ctccaaagccaaaggcgagccccgagaaccacaggtgtacacctgccccatgcc gggatgagctgaccaagaatcaagtcagcctgtggtgcctggtaaaaggcttctatccc agcgacatcgccgtggagtgaggagcaatgggcagccggagaaactacaaga ccacgcctcccgtgtgactccgacggctccttctctactcaaaactaccgtgg acaagagcaggtggcagcaggggaacgtcttctcatgctccgtgctgcatgaggtct gcacagccactacacgcagaagagcctctcctgtctccgggt	SEQ ID NO: 215
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Binding Protein 28 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvscqts <i>gyftahil</i> fwfrqapgrglewv <i>gwikipqy</i> <i>gavn</i> fgggfrdrvlttrdvireiaymdirklpddtavyy <i>cardrsygdsswalda</i> wgqgtvvvsaastkgpsvflapsskstsggtaalgclvkdyfepvvtvswngal tsgvhtfpavlqssglyslssvvtvpssslgtqtyicnvnhkpsntkvdkkvepkscd kthtcppcpapellggpsvflfppkpkdtlmsirtpevtcvvvdvshedpevkfnw yvdgvevhnaktkpreeqynstyrvsvltvlhqdwlngkeykckvsnkalpapi ektiskakgqprepqvctlpssrdeltknqvsclavkfypsdiavewesngqpe nnykttppvldsdsfflvskltvdksrwqqgnvfscsvlhealthshytqkslsisp	SEQ ID NO: 217
Light chain A	yihvtqspsslsvisgdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssveegv psrfsgsgfhtsfnltsldlqaddiatyycqlqffgrgsrlhikrtvaapsvfifppsde qlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsdstylsstltl skadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 218
Heavy chain B	Evrlvesggglvkpggsrlscsasgfdfdnawmtwvrpppgkglewvgr itpggegwsvdyaesvkgrftisrdntkntlylemnnvrtdtgyyfcartgk yydfwsgyppgeeyfqdwgqgtlvivssdkthtqvhltqsgpevrkpgtsv kvscapgnltktydlhwvrsvpqglqwmngwishegdkkviiverfkak vtidwdrstntaylqlsgltsgdtavyycaagkskhrlrdyalydddgalnwav dvdylsnlefwgqgtavtvssdkthtastkgpsvflapsskstsggtaalgcl vkdyfepvvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtqtyi cnvnhkpsntkvdkkvepkscdkthtcppcpapellggpsvflfppkpkdt lmsirtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynsty rvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepqvylp pcrdeltknqvsclwclvkfypsdiavewesngqpennykttppvldsds fflyskltvdksrwqqgnvfscsvlhealthshytqkslsisp	SEQ ID NO: 219
Light chain B	dfvltqsphslsvtpgesasiscksshslihgdrnnylawyvqkprspqlliylasr asgvpdrfsgsgsdkdfklisrvetedvgttycmqgrespwtfqggtkvdkdkth taseltqdpavvalkqvtitcrdslrshyaswyqkkgqapvllfygknnrpsgi pdrfsgsasgnrasltitgaqaedeaddyssrdksgrlsvfgggtklvldkthtrtv aapsvfifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteq dsdstylsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 220
Binding Protein 28 Nucleotide Sequences		
Heavy chain A	agagcccacctggtgcagtctggcaccgccatgaagaaaccaggcgctctgtgcgg gtgtcctgtcagacaagcggctacacctcaccgccacatctgttctggtccggca ggccccctggcagaggactggaatgggtgggatggaagccccagtatggcgccg tgaacttcggcgaggctccgggatagagtaccctgaccgggacgtgtaccgcg agatcgctacatggacatccggggcctgaagccgatgacaccgccgtgtactactg cgccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagg gcacaaccgtggtgtgtctgccgctctacaaaggccccagcgtgtccctctggc ccctagcagcaagagcacatctggcggaacagccgccctgggctgcctctgaagg actactttcccagcccgtgaccgtgtcctggaattctggcgccctgaccagcggcgtg	SEQ ID NO: 221

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Light chain A	<p>tacatccacgtgaccagagccccagcagcctgtccgtgtccatcgggcagacagtg accatcaactgccagacctctcaggcgtgggcagcgacctgcactggtatcagcac aagcctggcagagccccaaagctgtgatccaccacacaagcagcgtggaagaagg cgtgccagcagattttccggcagcggcttccaccagcttaacctgacctcagc gatctgcaggccgacgacattgccacctactattgtcaggtgtcagttcttcggcaga ggcagcagactgcacatcaagcgtacgggtggcgtcccagcgtgtcatcttccac ctagcagcagcagctgaagtccggcacagcctctgtcgtgtgctgtgaacaactt ctacccccgcgagggccaaagtgcagtggaaaggtggacaacgccctgcagagcggc aacagccaggaagcgtgaccgagcaggacagcaaggactccacctacagcctga gcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgc gaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcga gtgt</p>	SEQ ID NO: 222
Heavy chain B	<p>gaggttagactggtggagtcaggagggggcgttgaagcccggtgggtctctccgc ctgagctgttctgcctccggcttggatttcgataacgcctggatgacctgggtcaggcag cctccaggtaaaggactggagtgggtgggaagaatcacaggtccaggcagggcgtg gtccgtggactacgcggaatctgttaaaggcggtttacaatcgaaggacaatacca agaatacctgtatttgagatgaacaacgtgagaactgaagacaccggatattactct gtgccagaacaggcaatactacgacttctgtccggctatccccctggcgaggaatat tttaagactggggctagggaaccttgtatcgtgtcctccgacaaaaccataaccag gtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaaggt gtcctgcaaggccccctggcaacacctgaaaacctacgacctgactgggtgcgcag cgtgccaggacaggactgcagtggatgggtggtgatcagccacgagggcgacaag aaagtgtatcgtggaacggttcaaggccaaagtaccatcactgggacagaagcacc aacaccgcctactgcagctgagcggcctgacctctggcgataccgccgtgtactact gcgccaaggcagcaagcaccggctgagagactacgccctgtacgacgatgacgg cgccctgaactgggcccgtgatgtggactacctgagcaacctggaattctggggccag ggcacagccgtgaccgtgtcatctgataagaccacaccgttccaccaaggggcccat cggcttccccctggcacctctccaagagcacctctgggggcacagcggccctgg gctgctgtgtaaggactacttccccgaaccggtgacggtgtcgtggaactcaggcgc cctgaccagcggcgtgcacaccttccggctgtcctacagtctcaggactctactccc tcagcagcgtgggtgacctgtccctccagcagcttgggcacccagacctacatctgcaa cgtgaatcacaaagcccagcaacaccaaggtggacaagaagttgagcccaaatctgt gacaaaaactcacatgcccaccgtgcccagcactgaactcctggggggaccgtca gtcttctcttcccccaaaacccaaggacacctcatgatctccggaccctgaggt cacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttaactggtat gttgacggcgtggaggtgcataatgccaagacaaagccgaggaggagcagtacaa cagcacgtacctgtgtgacgtcctcaccgtcctgcaccaggactggctgaatggc aaggagtacaagtgaaggtgtccaacaaagccctccagccccatcgagaaaacc atctcaaagccaaaggcagccccgagaaccacaggtgtacacctgccccatgc</p>	SEQ ID NO: 223

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Heavy chain A	agagcccacctgggtgcagtctggcaccgcatgaagaaaccaggcgcctctgtgcgg gtgtcctgtcagacaagcggctacaccttcaccgcccacatcctgttctgggtccggcag gcccctggcagaggactgggaatgggtgggatggatcaagccccagtatggcgccgtg aacttcggcggaggcttcgggataagtgacctgacccgggacgtgtaccgcgag atcgctacatggacatccggggcctgaagcccgatgacaccgcccgtgtactactgcg ccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagggc acaaccgtgggtgtgtctgccgcctctacaaagggccccagcgtgttccctctggcccc tagcagaagagcacatctggcggaacagccgcccctgggctgcctcgtgaaggacta ctttcccagcccgtgacctgtcctggaattctggcgcccctgaccagcggcgtgcac acctttccagctgtgctgcagtcacggcctgtacagcctgagcagcgtcgtgacagt gcccagcagctctctgggcaccagacctacatctgcaacgtgaaccacaagcccag caacaccaaggtggacaagaaggtggaacccaagagctgcgacaagaccacacct gtccccctgtctcgtccccgaactgctgggaggcccttcctgttctctgttcccccaa agcccaaggacaccctgatgatcagccggacccccgaagtacctgcgtgggtgtgg atgtgtcccacgaggacctgaagtgaagttaattgtacgtggacggcgtggaagt gcacaacgccaagaccaagccaagagagggaacagtacaacagcacctaccgggtg gtgtccgtgtgacctgtctgcaccaggactggctgaacggcaaagagtacaagtgc aaggtgtccaacaaggccctgcctgccccatcgagaaaaccatcagcaaggccaag ggccagcccccggaaccccagggtgtgcacactgcccccaagcaggagcagctga ccaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccctccgatatgcc gtggaatgggagagcaacggccagcccagagaacaactacaagaccacccccctgt gctggacagcgacggctcattctcctggtgtccaagctgacagtggacaagtcccggt ggcagcagggaacgtgttcagctgtccgtgtgcacgaggccctgcacagccact acaccagaagtccctgagcctgagccccggc	SEQ ID NO: 229
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Heavy chain B	gaggttagactgggtgagtcaggaggggggcttgtgaagcccggtgggtctctccgc ctgagctgttctgcctccggctttgatttcgataacgcctggatgacctgggtcaggcag cctccaggttaagggactggagtgggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaatctgttaaggggcgtttacaattctcaaggacaatacca agaataccttgatttgagatgaacaacgtgagaactgaagacaccggatattactct gtgccagaacaggcaatactacgacttctgtccggctatccccctggcgagggaatat tttcaagactggggtcagggaaccttgttatcgtgtcctccgacaaaaccataccag gtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaaggtg tcttgaaggccccctggcaacacctgaaaacctacgacctgactgggtgcgcagc gtgccaggacagggactgcagtggatgggctggatcagccacgaggggcgacaaga aagtgatcgtggaacggttaaggccaaagtgacctcactgggacagaagcacca acaccgctacctgcagctgagcggcctgacctctggcgataccgccgtgtactactg cgccaaggcgagcaagcaccggctgagagactacgcctgtacgacgatgacggcg ccctgaactgggctggtgactgtgactacgtgagcaacctggaattctggggccaggg	SEQ ID NO: 231

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Light chain B	gacttcgtgtgaccagagccctcacagcctgagcgtgacacctggcgagagcgcc agcatcagctgaagagcagccactcctgatccacggcgaccggaacaactacctg gcttggtacgtgcagaagcccggcagatccccccagctgctgatctacctggccagca gcagagccagcggcgtgcccgatagatttctggcagcggcagcgacaaggacttca ccctgaagatcagccgggtggaaaccgaggacgtgggcacctactactgtatgcagg gcagagagagccccggaccttggccagggcaccaaggtggacatcaaggacaaa accataccgcacccgaactgactcaggaccctgccgtctctgtggcactgaagcaga ctgtgactattacttggcaggcgactactcgggagccactacgcttctggtatcaga agaaaccggccagcgacctgtgtgctgttctacggaaagaacaataggccatctgg catccccgaccgcttcttggcagtgcatcaggggaaccgagccagtctgaccattaccg gcgccagcgtgaggacgaagccgattactattgcagctccgggataagagcggct ccagactgagcgtgttcggaggaggaactaaactgacctctcgataagaccatac ccgtacgggtggccgctcccagcgtgttcatttcccacctagcgacgagcagctgaagt ccggcacagcctctgtcgtgtgcctgctgaacaactctacccccgcaggccaaagt gcagtgggaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtgacc gagcaggacagcaaggactccacctacagcctgagcagcacctgacctgagcaa ggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcctgt ctagccccgtgaccaagagcttcaaccggggcgaggtgt	SEQ ID NO: 301
Binding Protein 30 Amino Acid Sequences		
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Light chain A	yihvtqspsslsvisgdrvtincqtsqvgsgdlhwyqhkpgrapkllihhtssveegv psrfsgsgfhtsfqltisdlqaddiatyycqlqffgrgsrlhikrtvaapsvfifppsde qlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdskdstyslstltl skadyekkhkvacevthqglsspvtksfnrgec	SEQ ID NO: 233
Heavy chain B	Evrlvesggglvkpggsrlrscsasgfdfdnawmtwvrqppgkglewvgr itgpggegwsvdyaesvkgrftisrdntkntlylemnrvrtedtggyfcartgk yydfwsgyppgeeyfqdwgqgtlvivssdkthtqvhltsqgpevrkpgtsv	SEQ ID NO: 234

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Light chain A	<p> tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacagagtga ccatcaactgccagacctctcagggcgtgggcagcgacctgcactggtatcagcacaa gcctggcagagcccccaagctgctgatccaccacacaagcagcgtggaagaaggcg tgccagcagattttccggcagcggcttccacaccagcttccagctgacctcagcgat ctgcaggccgacgacattgccacctactattgtcaggtgctgcagttcttcggcagagg cagcagactgcacatcaagcgtacggtggcgctcccagcgtgttcatttccaccta gcgacgagcagctgaagtcggcacagcctctgtcgtgtgcctgtgaacaacttctac ccccgcgaggccaaagtgcagtgaaggtggacaacgccctgcagagcggcaaca ggcaggaaaagcgtgaccgagcaggacagcaaggactccacctacagcctgagcag caccctgacctgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagt gaccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtg </p>	SEQ ID NO: 237
Heavy chain B	<p> gaggttagactgggtgagtcaggaggggggctgtgaagcccggtgggtctctccgc </p>	SEQ ID NO:

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Light chain B	Gactctgtgtgaccagagccctcacagcctgagcgtgacacctggcgagagcgc cagcatcagctgcaagagcagccactccctgatccacggcgaccggaacaactacct ggcttggtacgtgcagaagccccgcagatccccccagctgctgatctacctggccagc agcagagccagcggcgtgcccgatagattttctggcagcggcagcgacaaggacttc accctgaagatcagccgggtggaaccgaggacgtgggcacctactactgtatgcag ggcagagagagccccctggaccttggccagggcaccaaggtggacatcaaggacaa aaccataaccgatccgaactgactcaggaccctgccgtctctgtggcactgaagcag actgtgactattacttggcaggcactcactgcggagccactacgttctctgtatcag aagaaacccggccaggcacctgtgctgtgttctacggaaagaacaataggccatctg gcatccccgaccgcttttctggcagtgatcagggaaccgagccagtctgaccattacc ggcgcccaggctgaggacgaagccgattactattgcagctccgggataagagcggc tccagactgagcgtgttcggaggaggaactaaactgaccgtcctcgataagaccata cccgtagcgtggccgtcccagcgtgttcatcttccacctagcgacgagcagctgaa gtccggcacagcctctgtcgtgtgcctgctgaacaacttctacccccgcaggccaaa gtgcagtgggaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtga ccgagcaggacagcaaggactccacctacagcctgagcagcaccctgacactgagc aagccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcct gtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 239
Binding Protein 31 Amino Acid Sequences		
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Light chain A	<p> Yihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssveda vpsrfsqsgfhtsfqltisdlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsd eqlksqgasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsdstyslsstlt lskadyekkhvyacevthqglsspvtksfnrgec </p>	SEQ ID NO: 241
Heavy chain B	<p> Evrivesggglvkpggsrlscsasgfdfnawmtwvrpppgkglewvgr itgpggegwsvdyaesvkgfritsrdntkntlylemnrvtedtgyyfcartgk yydfwsgyppeggyfwdwgqgtlvivssdkthtqvhltqsgpevrkpgtsv kvscapngntlktydlhwrvsvpgqglqwmngwishegdkkviverfkak vtidwdrstntaylqlsgltsgdtavyycakgskhrlrdyalydddgalnwav dvdylsnlefwgqgtavtvssdkthtastkgpsvflapsskstsggtaalgl vkdyfpepvtvswngaltsgvhtfpavqlssglyslssvvtvpssslgtqyti cnvnhkpsntkvdkkvepkscdkthtccppcapellggpsvflfppkpkdt lmisrtpevtcvvvdvshedpevkfnwyvdgvevhnaktkpreeqynsty rvsvltvlhqdwlngkeyckvsnkalpapiektiskakgqprepqvyltp pcrdeltknqvsclvkgfypsdiavewesngqpennnyktpvldsdgs fflyskltvdksrwqqgnvfscsvlhealthshytqkslslspg </p>	SEQ ID NO: 242
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Binding Protein 31 Nucleotide Sequences		
Heavy chain A	<p> agagccacactgggtgcagctctggcaccgccatgaagaaaccaggcgctctgtgcgg gtgtcctgtcagacaagcggctacacctaccgccacatcctgttctgttccggca ggccctggcagaggactggaatgggtgggatggaagccccagatggcgccg tgaactcggcgaggcttccgggatagagtaccctgacccgggacgtgtaccgag agatgcctacatggacatccgggacctgaagcccgatgacaccgctgtactactg cgccagagacagaagctacggcgacagcagctgggctctggatgcttggggccagg gcacaaccgtggtgtgtctgccgctctacaaagggccccagcgtgtccctctggc ccctagcagcaagagcacatctggcggaacagccgacctgggctgctctgtgaagg actacttccccgagcccgtagcctgtcctggaattctggcgccctgaccagcgcggtg cacaccttccagctgtgctgcagtcagcggcctgtacagcctgagcagcgtcgtga cagtgccagcagctctctgggcaccagacctacatctgcaacgtgaaccacaagc ccagcaacaccaaggtggacaagaaggtggaaccaagagctgcgacaagacca cacctgtccccctgtcctgccccgaactgctgggaggcccttccgtgttctgttccc cccaaagcccaaggacacctgatgatcagccggacccccgaagtacgtgcgtggt ggtggatgtgtccacaggaccctgaagtgaagtcaattgtgtgacgtggacggcgtg gaagtgcacaacgccaagaccaagccaagagaggaaacagtacaacagcacctacc gggtggtgtcctgtgctgaccgtgctgcaccaggactggctgaacggcaaagagtaca agtgcgaaggttccaacaaggccctgcctgcccccatcgagaaaaccatcagcaagg ccaagggccagccccgcgaacccaggtgtgcacactgcccccaagcaggagcga gctgaccaagaaccaggtgtccctgagctgtgccgtgaaaggcttctaccctccgata tcgcccgtggaatgggagagcaacggccagcccagagaacaactacaagaccacccc cctgtgctggacagcagcgctcattcttctgtgtccaagctgacagtggacaagtc ccggtggcagcagggaacgtgttcagctgctcgtgctgcagaggccctgcacag ccactacaccagaagtcctgagcctgagccccggc </p>	SEQ ID NO: 244

Light chain A	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacagagtg accatcaactgccagacctctcagggcgtgggcagcgacctgactggatcagcac aagcctggcagagccccaaagctgctgatccaccacacaagcagcgtggaagatgc cgtgcccagcagattttccggcagcggctccacaccagcttccagctgaccatcagc gatctgcaggccgacgacattgccactactattgtcaggtgctgcagttcttcggcaga ggcagcagactgcacatcaagcgtacgggtggcgcctccagcgtgtcatcttccac ctagcgcagcagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaactt ctacccccgcgaggccaaaagtgcagtggaaggtggacaacgccctgcagagcggc aacagccaggaagcgtgaccgagcagcagcagcaaggactccactacagcctga gcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgc gaagtgacccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcga gtgt	SEQ ID NO: 245
Heavy chain B	gaggttagactggtggagtcaggaggggggcttgaagcccggtgggtctctccgc ctgagctgttctgctccggcttggatttcgataacgcctggatgacctgggtcaggcag cctccaggtgaagggactggagtggggtgggaagaatcacaggtccaggcgagggtg gtccgtggactacgcggaaatctgttaaaggcggtttacaatctcaagggaataacca agaatacctgtatttgagatgaacaacgtgagaactgaagacaccggatattactct gtgccagaacaggcacaatactacgacttctgtccggctatccccctggcgaggaatat tttcaagactggggtcagggaaccttgttatctgtctccgacaaaaccataaccag gtgcacctgacacagagcggaccggaagtgcggaagcctggcacctctgtgaaggt gtcctgcaaggcccctggcaacacctgaaaacctacgacctgactgggtgcgcag cgtgccaggacagggactgcagtgatgggtggtgacccacgaggcgacaaag aaagtatcgtggaacggttcaaggccaaagtaccatcactgggacagaagcacc aacaccgcctacctgcagctgagcggcctgaccttggcgataaccgcctgtactact gcgccaaggcgagcaagcaccggctgagagactacgcctgtacgacgatgacgg cgccctgaactgggcccgtggatgtggactacctgagcaacctggaattctggggccag ggcacagccgtgaccgtgtcatctgataagaccacaccgcttccaccaagggcccat cggcttccccctggcaccttctccaagagcacctctgggggcacagcggccctgg gctgcctgggtcaaggactacttccccgaaccgggtgacggtgtcgtggaactcaggcgc cctgaccagcggcgtgcacaccttcccggctgtctacagtctcaggactctactccc tcagcagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaa cgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagcccaaatctgt gacaaaactcacatgcccaccgtgccagcacctgaactcctggggggaccgtca gttctctcttcccccaaaacccaaggacacctcatgatctcccggaccctgaggt cacatgcgtggtggtggacgtgagccacgaagacctgaggtcaagttaactggtat gttgacggcgtggaggtgcataatgccaaagacaaagccgcgaggagcagtagaa cagcacgtaccgtgtggtcagcgtctcaccgtctgcaccaggactggctgaatggc aaggagtacaagtgcaaggtctccaacaaagcctccagcccccatcgagaaaacc atctccaaagccaaaggcgagccccgagaaccacaggtgtacacctgccccatgc cgggatgagctgaccaagaatcaagtcagcctgtggtgcctggtaaaaggcttctatcc cagcgacatcggcgtggagtgggagagcaatgggcagccggagaaactacaag accacgcctcccgtgtgactccgacggctccttcttctactcaaaactaccgtg gacaagagcaggtggcagcaggggaacgtcttctcatgtccgtgctgcatgaggctc tgacagccactacacgcagaagagcctctcctgtctccgggt	SEQ ID NO: 246
Light chain B	Gacttcgtgtgacccagagccctcacagcctgagcgtgacacctggcgagagcgc cagcatcagctgcaagagcagccactcctgatccacggcgaccggaacaactacct ggcttggtacgtgcagaagcccgagatccccccagctgctgatctacctggccagc agcagagccagcggcgtgcccgatagatttctggcagcggcagcgacaaggacttc acctgaagatcagccgggtggaaccgaggacgtgggcacctactactgtatgcag ggcagagagagcccctggaccttggccagggcaccaggtggacatcaaggacaa aaccataaccgatccgaactgactcaggaccctgccgtctctgtggcactgaagcag actgtgactattacttcccaggcgactactgcggagccactacgcttctggtatcag aagaaacccggccaggcacctgtgctgctgttctacggaaagaacaataggccatctg gcatccccgaccgcttcttggcagtgcatcagggaaccgagccagctgtgaccattacc	SEQ ID NO: 247

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Binding Protein 32 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvscqtsgyftfahilfwfrqapgrglewvgwikpqyg avnfgggrdrvtltdrvyreiaymdirglkpdtdavyycardrsygdsswaldawg qgtvvvsaastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgv htfpavlqssglyslssvvtvpssslgtktytcenvdhkpsntkvdrveskygppcp cpapeflggpsvflfppkpkdtlmsirtpevtcvvvdvsqedpevqfnwyvdgvev hnaktkpreeqfnstyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakg qprepqvylppcqeemtknqvslwclvkgyfypsdiavewesngqpennykttpp vldsdgsfflyskltvdksrwqegnfvscsvmhhealhnhytqkslsislglk	SEQ ID NO: 302
Light chain A	Yihvtqspsslsvsigdrvtincqtsqvgdhlwyqhkgprapklhihtssvedgv psrfsgsgfhtsnltisdlqaddiatyycqvlqffgrgsrlhikrtvaapsvfifppsdeq lkshtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsksdstylsstltlsk adyekhkvyacevthqglsspvtkfsnrgec	SEQ ID NO: 303
Heavy chain B	Qvqlvqsgaevvkpgasvkvscasgytftsyihwvrqapqgglewigs <i>ypgnvnt</i> nyaqkfqgratltvdsistaymelsrlrsddtavyyctrshyglw <i>nfdv</i> wgkgtvtvsssqvqlvesgggvvqpgrslrscasgytftkawmhw vrqapgkqlwvvaqikdknsyatyadsvkgrftisrddskntlylqmnsrlr aedtavyycrgvyyalspfdywgqgtltvssrtastkgpsvflapcsrstses taalgclvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpsssl gtktytcenvdhkpsntkvdrveskygppcpapeflggpsvflfppkp kdtlmsirtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfn tyrvsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepqvcl ppsqeemtknqvslscavkgyfypsdiavewesngqpennykttppvldsd gsfflvskltvdksrwqegnfvscsvmhhealhnhytqkslsislglk	SEQ ID NO: 304
Light chain B	Divmtqtplslsvtpgqpasiscskssqslvhnnantylswylqkpgqspqliykv nrfsgvpdrfsgsgsgtdftlkisrveaedvgvyycggtqypftfgsgtkveikgqpk aapdiqmtqspsslsasvgdrvtitcqasqniyvwlnwyqqkpgkapkliiykasnl htgvpsrfsgsgsgtdftltisslpediatyycqggqtypyftfggtkleiktgpsrtv aapsvfifppsdeqlkshtasvcllnnfypreakvqwkvdnalqsgnsqesvteqd skdstylsstltlskadyekhkvyacevthqglsspvtkfsnrgec	SEQ ID NO: 305
Binding Protein 32 Nucleotide Sequences		
Heavy chain A	agagccacctggtgcagctctggcaccgccatgaagaaccaggcgctctgtcgggt gtcctgtcagacaagcggctacacctcaccgccacatcctgttctggttcggcaggcc cctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtgaactt cggcgaggcttccgggatagagtaccctgacccgggacgtgtaccgcgagatcgcc tacatggacatccgggcctgaagcccgatgacaccgccgtgtactactgcgccagaga cagaagctacggcgacagcagctgggctctggatgcttggggccagggcacaaacctg gtggtgtctgccgctctacaaaggcccctcgggttccctctggccccttgacagagaa gcaccagcgaatctacagccgccctgggctgctcgtgaaggactacttcccagccccg tgaccgtgtctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgct ccagagcagcggcctgtactctgtagcagcgtcgtgacagtgccagcagcagcctgg gcaccaagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaa gcggttggaatctaagtacggccctccctgccctccttcccagcccctgaatttctgggc ggacctcctgttctgttccccaaagcccagacacctgatgatcagccggacc cccgaagtgacctgcgtggtggtggatgtgtcccagggaagatcccaggtgcagttcaat	SEQ ID NO: 306

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Binding Protein 33 Amino Acid Sequences		
Heavy chain A	Rahlvqsgtamkkpgasvrvcqtsgytftahilfwfrqapgrglewv gwikipqyga vnfgggfrdrvlttrdvreyaiymdirglkpddtavvyccardrsygdsswaldawggg ttvvvsaastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfp avlqssglyslssvvtvpssslgtkytcnv dhkpsntkvdkrveskygppcpcpape flggpsvflfppkpkdtl misrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktk preeqfnstyrvvsvltvlhqdwlngkeykckvsnkg lpsiektiskakgqprepqv ytlppcqeemtknqvslwclvkgfypsdiawesngqpennyktpplvdsdgsff lyskltvdksrwqegnvfscsvmhhealhnhytqkslsislglk	SEQ ID NO: 310
Light chain A	Yihvtqspsslsvisgdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedgvp srfsgsgfhtsfnltsldlqaddiatyycqlqffgrgsrlhikrtvaapsvfifppsdeqlks gtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdsdstyslsstltlskadye khkvyacevthqglsspvtksfnrgec	SEQ ID NO: 311
Heavy chain B	Qvqlqesgpglvkpsqtslslctctvsfslsdygvhwvrpppgkglewlgviwa gggtynpnlksrktiskdtsknqvslklssvtaadtavvyccardkgysyyysm dywgqgtttvtvsssqvqlvesgggvvqpgrslrlscaasgftfkawmhvwrq apgkqlwvaqikdksnsyatyadsvkgrftisrddskntlylqmnsiraedt avyyrcgvyyalspfdywgqgtlvtvssrtastkgpsvflapcsrstsestaalg clvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtkyt cnvdhkpsntkvdkrveskygppcpcpapeflggpsvflfppkpkdtl mis rtpvtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnstyrvvsvlt vlhqdwlngkeykckvsnkg lpsiektiskakgqprepqvctlpssqeemt knqvslscavkgfypsdiawesngqpennyktpplvdsdgsfflvskltv dksrwqegnvfscsvmhhealhnhytqkslsislglk	SEQ ID NO: 312
Light chain B	Divmtqtplsivtpgqpasickssqslvhnnantylswylqkpgqspqsllykvsnr fsgvpdrfsgsgsgtdftlkisrveaedvgvyycgqgtqypftfsgstkveikgqpkaa pdilvtqspaslavspgqratitcrasesveyyvtslmqwyqqkpgppklifaasn esgvparfsgsgsgtdftltinveandvanyycqsrkvpytfqggtkleiktgpsrt vaapsvfifppsdeqlksgtasvvcllnnfyreakvqwkvdnalqsgnsqesvteq skdstyslsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 313
Binding Protein 33 Nucleotide Sequences		
Heavy chain A	agagcccacctggtgcagctctggcaccgccatgaagaaaccaggcgctctgtgcgggt gtcctgtcagacaagcggtacacctcaccgcccacatcctgttctggttcggcaggcc cctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtgaactt cggcgagggtctccgggatagagtaccctgacccgggacgtgtaccgcgagatgcc tacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcgcagaga cagaagctacggcgacagcagctgggctctggatgcttggggccagggcacaaacctg gtggtgtctccgcctctacaaaggcccctcgggttccctctggccccttgacagcaga gcaccagcgaatctacagccgccctgggctgcctcgtgaaggactacttcccagccccg	SEQ ID NO: 314

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Light chain A	<p>Tacatccacgtgaccagagccccagcagcctgtccgtgtccatcgggcgacagagtgcacatcaactgccagacctctcagggcgtgggcagcgacctgcactggtatcagcacaagc</p> <p>ctggcagagcccccaagctgctgatccaccacacaagcagcgtggaagatggcgtgcc</p> <p>cagcagattttccggcagcggcttccacaccagcttcaacctgacctcagcgatctgcag</p> <p>ggcgacgacattgccacctactattgtcaggtgctgcagttcttcggcagaggcagcagac</p> <p>tgcacatcaagcgtacgggtggcgtcccagcgtgttcattctcccacctagcgacgagc</p> <p>agctgaagtcggcacagcctctgtcgtgtgctgctgaacaacttctacccccgcgagg</p> <p>ccaaagtgcagtggaggtggacaacgccctgcagagcggcaacagccaggaaagcg</p> <p>tgaccgagcaggacgaaggactccacctacagcctgagcagcacctgacactgag</p> <p>caaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccaggggcctg</p> <p>tctagccccgtgaccaagagcttcaaccggggcgagtgt</p>	<p>SEQ ID NO: 315</p>
Heavy chain B	<p>caggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagacctgagcct</p> <p>gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgactgggtgcgccagc</p> <p>cacctggaaaaggcctggaatggctggcgtgatctgggctggcggaggcaccacta</p> <p>caacccagcctgaagtcagaaagaccatcagcaaggacaccagcaagaaccaggtg</p> <p>tcctgaagctgagcagcgtgacagccgggataccgccgtgtactactgcgccagaga</p> <p>caagggtacagctactactacagcatggactactggggccagggcaccacctgaccg</p> <p>tgtatcctctcaggtgcagctggtggaatctggcggcggagtgtgacgctggcagaa</p> <p>gctgagactgagctgtgccgccagcggcttcaccttaccacaggcctggatgactggg</p> <p>tgcgccaggccccctggaaagcagctggaatgggtggcccagatcaaggacaagagcaa</p> <p>cagctacgccacctactacgccgacagcgtgaaggggcgggttcacctcagccgggac</p> <p>gacagcaagaacacctgtacctgcagatgaacagcctgcggggcggaggacaccgccg</p> <p>tgtactactgtcggggcgtgtactatgccctgagccccttcgattactggggccagggaac</p> <p>cctcgtgaccgtgtctagtgcggaccgttcgaccaagggcccatcggtgttccctctggcc</p> <p>ccttgagcagaagcaccagcgaatctacagccgccctgggctgcctcgtgaaggacta</p> <p>ctttccgagcccgtgacctgtcctggaactctggcgtctgacaagcggcgtgcacac</p> <p>ctttccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgacagtccc</p> <p>agcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagcaaca</p> <p>ccaaggtggacaagcgggtggaatctaagtacggccctccctgccctccttcccagccc</p> <p>ctgaatttctgggcggacctccgtgttctgttcccccaaaagcccaaggacacctgat</p> <p>gatcagccggacccccgaagtgcctgcgtgggtggatgtgtcccaggaagatccccg</p> <p>aggtgcagttcaattggtacgtggacggcgtggaagtgcacaacgccaagaccaagccc</p> <p>agagaggaacagttcaacagcacctaccgggtggtgtccgtgctgacctgctgcacca</p> <p>ggactggctgaacggcgaagagtacaagtgcaaggtgtccaacaaggcctgccagc</p> <p>tccatcgagaaaaccatcagcaaggccaaggccagccccgcgagcctcaagtgtgtac</p> <p>cctgccccctagccaggaagagatgaccaagaaccaggtgtccctgagctgtgccgtga</p> <p>aaggcttctaccccagcgacattgccgtggaatgggagagcaacggccagcccagaa</p> <p>caactacaagaccacccccctgtgctggacagcgacggctcatttctctggtgtccaag</p> <p>ctgacctggacaagagccgggtggcaggaaggcaacgtgttcagctgctccgtgatgca</p>	<p>SEQ ID NO: 316</p>

Light chain B	cgaggccctgcacaaccactacaccagaagtcctgtctctgtccctgggcaag gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccag catcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctgagct ggtatctgcagaagccccggccagagccccagtcctgatctacaaggtgtccaacagat tcagcggcgtgcccacagattctccggcagcggctctggcaccgacttcacctgaag atcagccgggtggaagccgaggacgtggcgtgtactattgtggccagggcacccagta ccccttcaccttggcagcggcaccaggtggaaatcaagggccagcccaaggccgcc cccgacatcgtgctgacacagagccctgctagcctggcgtgtctcctggacagagggc caccatcacctgtagagccagcagagcgtggaatattacgtgaccagcctgatgcagt gtatcagcagaagccccggccagcccccaagctgctgatttcgccccagcaacgtgg aaagcggcgtgccagccagatttccggcagcggctctggcaccgacttcacctgacca tcaaccccggtggaagccaacgacgtggccaactactactgccagcagagccggaaggt gccttacaccttggccagggcaccagctggaaatcaagaccaagggccccagccgta cgggtggcgtcccagcgtgtcatcttcccacctagcagcagcagctgaagtcggca cagcctctgtcgtgtgctgtgaacaacttctacccccgcaggccaaagtgcagtgg aggtggacaacgccctgcagagcggcaacagccaggaaagcgtgaccgagcaggac agcaaggactccactacagcctgagcagcaccctgacactgagcaaggccgactacg agaagcacaaggtgtacgcctgcgaagtgaccaccagggcctgtctagccccgtgacc aagagctcaaccggggcgaggt	SEQ ID NO: 317
Binding Protein 34 Amino Acid Sequences		
Heavy chain A	Qvhltqsgpevrkpgtsvkvsckapgnltktydlhwvrsvpqglqwmgwisheg dkkviverfkakvtidwdrstntaylqlsgltsgdtavyycakgskhrlrdyalydddga lnwavdvdylnlefwgqgtavtvssastkgpsvflpapsrstsestaalgclvkdyfp epvtvswngaltsgvhtfpavqlssglyslssvvtvpssslgtktytcnvdhkpsntkv dkrveskygppcpcpapeflggpsvflfppkpkdtlmsirtpevtcvvvdvsqedpe vqfnwyvdgvevhnaktkpreeqfnstyrvsvltvlhqdwlngkeykckvsnkgl pssiektiskakgqprepqvylppcqeemtknqvsllwclvkgyfypsdiawesng qpennykttppvldsdgsfflyskltvdksrwqegnvfscsvmhealnhytqksls lgk	SEQ ID NO:318
Light chain A	Dfvltqspshsvtpgesasisckssshlihgdrnnylawyvqkprspqliylasrras gvpdrfsgsgsdktlksirvetedvgyycmqgrespwtfgggtkvdkirtvaapsv fifppsdeqlksqtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstys lsstltlskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 319
Heavy chain B	Qvqlvqsgaevvkpgasvkvsckasgyftfsyyihwvrqapggglewigsy <i>pgnvnt</i> nayaqkfqgratlvtidsistaymelsrlrsddtavyyctrshyglwnf dvwkggtvtvsssqvqlvesgggvvqprslrslcaasgftfkawmhvwrq apgkqlewvaqikdksnsyatyyadsvkgrftisrddskntlylqmnslraedt avyycrgvyyspfdywgqgtlvtvssrtastkgpsvflpapsrstsestaalg clvkdyfpepvtvswngaltsgvhtfpavqlssglyslssvvtvpssslgtktyt cnvdhkpsntkvdkrveskygppcpcpapeflggpsvflfppkpkdtlms rtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnstyrvsvlt vlhqdwlngkeykckvsnkglpssiektiskakgqprepqvclppsqeemt knqvsllscavkgfypsdiawesngqpennykttppvldsdgsfflvskltv dksrwqegnvfscsvmhealnhytqkslsllgk	SEQ ID NO: 320
Light chain B	Divmtqtplslsvtpgpasiscskssqslvhnnantylswylqkpgqspqsliykvsnr fsgvpdrfsgsgsgtdftlksirveaedvgyycgaggtqyptfsgstkveikgqpkap diqmtqspsslsasvgrvtitcqasqniyvwlnwyqqkpgkapklliykasnlhtgv psrfsgsgsgtdftlisslpediatyyccqaggtypytfgggtkleiktgpsrtvaapsvf ifppsdeqlksqtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstys sstltlskadyekkhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 321
Binding Protein 34 Nucleotide Sequences		
Heavy chain A	caggtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaagg tgtcctgcaaggccccctggcaacacctgaaaacctacgacctgcactgggtgcgcagc	SEQ ID NO: 322

	<p>gtgccaggacagggactgcagtgatgggctggatcagccacgagggcgacaagaaa gtgatctgggaacggttcaaggccaaagtaccatcgactgggacagaagcaccaacac cgctacctgcagctgagcggcctgacctctggcgataccgccgtgtactactgcgcaa ggcgagcaagcaccggctgagagactacgccctgtacgacgatgacggcgccctgaac tgggccctggatgtggactacctgagcaacctggaattctggggccagggcacagccgt gaccgtgtcatctgcttcgaccaagggcccctcgggtgtccctctggccccttgacgaga agcaccagcgaaatctacagccgccctgggctgcctcgtgaaggactactttccgagccc gtgaccgtgtcttggaaactctggcgctctgacaagcggcggtgcacacctttccagccgtg ctccagagcagcggcctgtactctctgagcagcgtcgtgacagtgtccagcagcagcct gggcaccaagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggac aagcgggtggaatctaagtacggccctccctgccctccttgcccagcccctgaatttctgg gcggacctccgtgttctgttcccccaagcccaaggacacctgatgatcagccgga ccccgaagtgtacgtgcgtgggtggatgtgtccaggaagatcccaggtgcagtta attggtactgtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaaca gttaacagcacctaccgggtgtgttccgtgtgtgacctgtgtgtcaccaggactgggtgaa cggcaaaagagtacaagtgaaggtgtccaacaagggcctgccagctccatcgagaaa accatcagaaggccaaggggccagccccgcgagcctcaagtgtatacctgcccccttg ccaggaagagatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctaccc cagcgacattgccgtgggaatgggagagcaacggccagcccagaaacaactacaagacc acccccctgtgtgtgacagcgcagggctcatttctctgtactccaagctgacctgtggaca agagccggtggcaggaaggcaacgtgttcagctgtccctgtatgcacgagggccctgcac aaccactacaccagaagtccctgtctctgtccctgggcaag</p>	
Light chain A	<p>gacttcgtgtgacccagagccctcacagcctgagcgtgacacctggcgagagcgccag catcagctgcaagagcagccactccctgatccacggcgaccggaaacaactacctggctt ggtacgtgcagaagccccggcagatccccccagctgctgatctacctggccagcagcaga gccagcggcggtgcccgatagatttctggcagcggcagcgacaaggacttccacctgaa gatcagccgggtggaaccgaggacgtgggcacctactactgtatgcagggcagagag agccccctggaccttggccagggcaccaggtggacatcaagcgtacggtggccgctcc cagcgtgttcatcttccacctagcgacgagcagctgaagtccggcacagcctctgtcgtg tgcctgtgaacaacttctacccccgcgaggccaaagtgcagtggaaggtggacaacgc cctgcagagcggcaacagccaggaaagcgtgaccgagcaggacagcaaggactccac ctacagcctgagcagcacctgacactgagcaaggccgactacgagaagcacaaggtg tacgctgcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaaccg ggcgagtggt</p>	SEQ ID NO: 323
Heavy chain B	<p>caggtgcagctggtgcagctctggcgccgaggtcgtgaacctggcgccctctgtgaaggt gtcctgcaaggccagcggctacacctttaccagctactacatccactgggtgcgccaggc ccctggacagggactggaatggatcggcagcatctacccggcaacgtgaacaccaact acggccagaagtccaggcgagagccacctgacctgtgacaccagcatcagcaccgc ctacatggaactgagccggctgagaagcgacgacaccggcgtgtactactgcaccgggt ccactacggcctggattggaacttcgacgtgtggggcaagggcaccacctgacagt tctagcagccaggtgcagctggtggaatctggcggcgagtggtgcacctggcagaa gctgagactgagctgtgccgccagcggcttcaccttcaccaaggcctggatgcactggg tgcgccagggccccctggaaagcagctggaatgggtggcccagatcaaggacaagagcaa cagctacgccacctactacgccgacagcgtgaaggggcggttaccatcagccgggac gacagcaagaacacctgtacctgcagatgaacagcctgcggggccgaggacaccggcg tgtactactgtcggggcgtgtactatgccctgagccccctcgattactggggccagggaac cctcgtgacctgtctagtctggaccgccagcacaaggggcccatcggtgttccctctggc cccttgacgagaagcaccagcgaatctacagccgcctgggctgcctcgtgaaggact actttcccgagccgtgacctgtcctggaactctggcgctctgacaagcggcggtgcaca cctttccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgacagtcc cagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagcaac accaaggtggacaagcgggtggaatctaagtacggccctccctgcctccttgcccagcc cctgaatttctggggcgacctccgtgttctgttcccccaagcccaaggacacctga tgatcagccggacccccgaagtgcctgcgtggtggatgtgtccaggaagatccc</p>	SEQ ID NO: 324

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Light chain B	gacatcgtgatgacccagacccccctgagcctgagcgtgacacctggacagcctgccag catcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctgagct ggtatctgcagaagcccggccagagccccagtcctgatctacaaggtgtccaacagat tcagcggcgtgcccagagattctccggcagcggctctggcaccgacttcacctgaag atcagccgggtggaagccgaggacgtggcggtgtactattgtggccagggcacccagta ccccttcacctttggcagcggcaccgaaggtggaatcaaggccagcccaaggccgcc cccgacatccagatgaccagagccccagcagcctgtctgccagcgtggcgacagag tgaccatcacctgtcaggccagccagaacatctacgtgtggctgaactggtatcagcaga agcccggaagcccccaagctgctgatctacaaggccagcaacctgcacaccggcgt gcccagcagatttctggcagcggctccggcaccgacttcacctgacaatcagctccctg cagcccgaggacattgccactactactgccagcaggccagacctaccctacacctt ggccagggcaccaagctggaatcaagaccaaggccccagccgtacggtggccgct cccagcgtgtcatctccacctagcgacgagcagctgaagtccggcacagcctctgtc gtgtgctgctgaacaactctacccccgcgaggccaaagtgcagtggaaggtggacaa cgccctgcagagcggcaacagccaggaagcgtgaccgagcaggacagcaaggactc cacctacagcctgagcagcacctgacactgagcaaggccgactacgagaagcacaag gtgtacgctgcgaagtgaccaccaggcctgtctagccccgtgaccaagagcttaac cggggcgaggtg	SEQ ID NO: 325
Binding Protein 35 Amino Acid Sequences		
Heavy chain A	Qvhltsqspgpevrkpgtsvkvsckapgnltktydlhwvrsvpqglqwmgwisheg dkkviverfkakvtidwdrstntaylqlsgltsgdtaavyycakgskhrlrdyalydddga lnwavdvdylnlefwgqgtavtvssastkgpsvfplapcsrstsestaalgclvkdyfp epvtvswngaltsgvhtfpavlqssgylsslsvtvpssslgtktytcnvdhkpsntkv dkrveskygppcpapeflggpsvflfppkpkdtlmsrtpevtcvvvdvsqedpe vqfnwyvdgvevhnaktkpreeqfnstyrvsvltvlhqdwlngkeykckvsnkg pssiektiskakgqprepqvylppcqeemtknqvslwclvkgfypsdiawesng qpennykttppvldsdsfflyskltvdksrwqegnvfscsvmhealhnhytqksls lgk	SEQ ID NO: 326
Light chain A	Dfvltsphslsvtpgesasiscksshlihgdrnnylawyvqkpgrspqliylasrras gvpdrfsgsgsdktlksrvtetdvtyycmqgrespwtfgqgtkvdkrtvaapsv fifppsdeqlksgtasvcllnfybreakvqwkvdnalqsgnsqesvteqdskdstys lsstltlskadyekkhvyacevthqglsspvtksfnrgec	SEQ ID NO: 327
Heavy chain B	Qvqlqesgpglvkpsqtlstctvsfslsdygvhwvrqppgkglewlgviwa gggtynpnlksrktiskdtsknqvslklssvtaadtavyycardkgysyyysm dywgqgtvtvsssqvqlvesgggvvqpgsrslrscasgftfkawmhvwrq apgkqlwvraqikdksnsyatyyadsvkgrftisrddskntlylqmnslraedt avyyrcgvyyalspfdywgqgtlvtvssrtastkgpsvfplapcsrstsestaalg clvkdyfpepvtvswngaltsgvhtfpavlqssgylsslsvtvpssslgtktyt cnvdhkpntkvdkrveskygppcpapeflggpsvflfppkpkdtlms rtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnstyrvsvlt vlhqdwlngkeykckvsnkgpssiektiskakgqprepqvclppsqeemt knqvslscavkgfypsdiawesngqpennykttppvldsdsfflvskltv dksrwqegnvfscsvmhealhnhytqksls lgk	SEQ ID NO: 328
Light chain B	Divmtqtplsivtpgqpasisckssqslvhnnantylswylqkpgqspqsllykvsnr	SEQ ID

	fsgvpdrfsgsgsgtdftlkisrveadvgyvycgqgtqypftfsgsgtkveikgqpkaa pdivltqspaslavspgqratitcrasesveyvvtslmqwyqqkpgqppkllifaasn esgvparfsgsgsgtdftlinpveandvanyycqsrkvpqyftfgggtkleiktgpsrt vaapsvfifppsdeqlksgtasvvcllnfybreakvqwkvdnalqsgnsqesvteqd skdstylsstitlkskadyekhkvyacevthqglsspvtksfnrgec	NO: 329
Binding Protein 35 Nucleotide Sequences		
Heavy chain A	cagggtgcacctgacacagagcggacccgaagtgcggaagcctggcacctctgtgaagg tgtcctgcaaggccccctggcaacaccctgaaaacctacgacctgcactgggtgcgcagc gtgccaggacagggactgcagtggatgggtggatcagccacgagggcgacaagaaa gtgatcgtggaacggttcaaggccaaagtaccatcgactgggacagaagcaccacac cgctacctgcagctgagcggcctgacctctggcgataccgccgtgtactactgcgcaa gggcagcaagcaccggctgagagactacgccctgtacgacgatgacggcgccctgaac tgggcccgtggatgtggactacctgagcaacctggaattctggggccaggggcacagcct gaccgtgtcatctgcttcaccaaggccccctgggtgttccctctggccccctgcagcaga agcaccagcgaattacagccgccctgggctgcctcgtgaaggactactttcccgagccc gtgaccgtgtcctggaaactctggcgctctgacaagcggcgtgcacacctttccagccgtg ctccagagcagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcct gggcaccaagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggac aagcgggtggaatctaagtacggccctccctgccctcctggccagccccctgaattctgg gcggacctccgtgttctgttcccccaagcccaaggacacctgatgatcagccgga ccccgaagtgcctgcgtgggtggatgtgtcccaggaagatcccaggtgcagtca attgtgtacgtggacggcgtggaagtgcacaacccaagaccaagcccagagaggaaca gttcaacagcacctaccgggtgtgtcctgtgtgacctgtgtgaccaggactggctgaa cggcaagagtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaa accatcagcaaggccaaggggccagccccgcgagcctcaagtgtataccctgccccctg ccaggaagagatgaccaagaaccaggtgtcctgtggtgtctcgtgaaaggcttacc cagcgacattgccgtggaatgggagagcaacggccagcccagacaactacaagacc acccccctgtgtggacagcgacggctattcttctgtactccaagctgacctggaca agagccggtggcaggaaggcaacgtgttcagctgtccgtgatgcacgagggcctgcac aaccactacaccagaagtccctgtctctgtcctgggcaag	SEQ ID NO: 330
Light chain A	gacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgagagcgcag catcagctgcaagagcagccactccctgatccacggcgaccggaacaactacctggtt ggtacgtgcagaagcccggcagatccccagctgctgatctacctggccagcagcaga gccagcggcgtgcccgatagattttctggcagcggcagcgacaaggacttcacctgaa gatcagccgggtggaaccgaggacgtgggcacctactactgtatgcagggcagagag agcccctggaccttggccagggcaccaaggtggacatcaagcgtacggtggcgctcc cagcgtgttcatcttcccactagcgacgagcagctgaagtccggcacagcctctgtctg tgctgtgaacaacttaccctggcagggccaaagtgcagtggaaaggtggacaacgc cctgcagagcggcaacagccaggaagcgtgaccgagcaggacagcaaggactccac ctacagcctgagcagcaccctgacctgagcaaggccgactacgagaagcacaaggtg tacgctgcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaaccg ggcgaggtgt	SEQ ID NO: 331
Heavy chain B	cagggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagacctgagcct gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgcactgggtgcgccagc cacctggaaaaggcctggaatggctggcgctgatctgggctggcgaggccaccaacta caacccagcctgaagtcagaaagaccatcagcaaggacaccagcaagaaccaggtg tcctgaagctgagcagcgtgacagccgccgataccgccgtgtactactgcgccagaga caagggtacagctactactacagcatggactactggggccagggcaccaccgtgaccg tgtcatcctctcaggtgcagctgggtggaatctggcgcgagtggtgcagcctggcagaa gcctgagactgagctgtccgccagcggcttcaccttaccacaggcctggatgactggg tgcgccagggccccctggaaagcagctggaatgggtggccagatcaaggacaagagcaa cagctacgccacctactacgccgacagcgtgaaggggcgggttcaccatcagccgggac gacagcaagaacacctgtacctgcagatgaacagcctcggggccgaggacaccgccg tgtactactgtcggggcgtgtactatgccctgagccccctcgattactggggccagggaac	SEQ ID NO: 332

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Light chain B	Divmtqtplsstvgqpasickss qslvhn nantylswylqkpgqspqsliykvsn rfsgvpdrfsgsgsgtdftlkisrveadvgyyyc gqgtqyp ftfsgtkveikgqpkaa pdigmtqspsslsasvgdrvtitcqas qniyvw lnwyqqkpgkapkliiykasnlhtg vpsrfsgsgsgtdftlisslpediatyyc qggqtypy ftfggtkleiktgpsrtvaaps vfifppsdeqlksgtasvcllnfybreakvqwkvdnalqsgnsqesvteqdkdst yslsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 337
Binding Protein 36 Nucleotide Sequences		
Heavy chain A	cagggtgcagctgggtgcagctctggcggccagatgaagaaccggcgagagcatgcgga tcagctgcagagccagcggctacgagttcatcgactgcacctgaactggatcagactgg cccctggcaagcggcctgagtgatgggatggctgaagcctagaggcggagccgtgaa ctacgccagacctctgcagggcagagtaccatgacccgggacgtgtacagcgataccg ccttctggaactgcggagcctgaccgtggatgataccgccgtgtacttctgcacccggg gcaagaactgcgactacaactgggacttcgagcactggggcagaggcaccctgtgatc gtgtcaagcgcgtcgaccaaggcccctcgggtgtccctctgccccttgacgagaagc accagcgaatctacagccgccctgggctgcctcgtgaaggactacttcccagcccgtg accgtgtcctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgtcc agagcagcggcctgtactctctgagcagcgtcgtgacagtgcccagcagcagcctgggc accaagacctacactgtaacgtggaccacaagcccagcaacaccaaggtggacaagc gggtggaatctaagtacggccctccctgccctccttgcccagcccctgaattcttgggcgg accctcgtgttctgttcccccaagcccaaggacacctgatgatcagccggacccc cgaagtgcctgcgtgggtggatgtgtcccaggaagatcccaggtgcagttaattg gtactgtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaaacgttc aacagcacctaccgggtgtgtccgtgctgaccgtgctgcaccaggactggctgaacgg caaagagtacaagtgaaggtgtccaacaaggcctgccagtcctatcgagaaaacca tcagcaaggccaaggccagccccgcagcctcaagtgtataacctgcccccttgccag gaagagatgaccaagaaccaggtgtccctgtgtgtctcgtgaaaggcttctaccccagc gacattgccgtggaatgggagagcaacggccagcccagaacaactacaagaccaccc cccctgtgctggacagcgacggctcatttctctgtactccaagctgaccgtggacaagag ccggtggcaggaaggcaacgtgttcagctgctcgtgatgcacgaggccctgcacaacc actacaccagaagtcctctgtctgtccctgggcaag	SEQ ID NO: 338
Light chain A	Gagatcgtgtgacacagagccctggcacctgagcctgtctccaggcgagacagccat catcagctgccggacaagccagtacggcagcctggcctggtatcagcagaggcctgga cagggccccagactcgtgatctacagcggcagcacaagagccgccgaatccccgata gattcagcggctccagatggggccctgactacaactgacctacagcaacctggaaagc ggcgacttcggcgtgtactactgccagcagctacgagttctcggccagggcaccaaggtg cagggtggacatcaagcgtacgggtggccgtcccagcgtgttcatttcccacctagcgac gagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaacttctacccccgc gaggccaaagtgcagtggaggtggacaacgccctgcagagcggcaacagccaggaa agcgtgaccgagcaggacagcaaggactccacctacagcctgagcagcacctgacac tgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccagggg cctgtctagccccgtgaccaagagcttcaaccggggcgagtg	SEQ ID NO: 339
Heavy chain B	cagggtgcagctgggtgcagctctggcggcaggtcgtgaaacctggcgccctctggaaggt gtcctgcaaggccagcggctacacctttaccagctactacatccactgggtgcgccaggc ccctggacagggactggaatggatcggcagcatctacccggcaacgtgaacaccaact acgcccagaagttccagggcagagccacctgaccgtggacaccagcatcagaccgc ctacatggaactgagccggctgagaagcgacgacaccgccgtgtactactgacccgggt cccactacggcctggattggaactcgacgtgtggggcaagggcaccaccgtgacagtg	SEQ ID NO: 340

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Light chain B	gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccag catcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctgagct ggatatctgcagaagcccggccagagccccagtcctgatctacaaggtgtccaacagat tcagcggcgtgcccacagattctccggcagcggctctggcaccgacttcacctgaag atcagccgggtggaagccgaggacgtgggcgtgtactattgtggccagggcaccagta ccccttcaccttggcagcggcaccaggtggaaatcaagggccagcccaaggccgcc cccacatccagatgaccagagccccagcagcctgtctgccagcgtgggcgacagag tgaccatcacctgtcaggccagccagaacatctacgtgtggtgaactggtatcagcaga agccccggaaggcccccaagctgctgatctacaaggccagcaacctgcacaccggcgt gcccagcagatttttgccagcggctccggcaccgacttcacctgacaatcagtcctctg cagcccaggacattgccactactactgccagcagggccagacctaccctacaccttt ggccagggcaccagctggaaatcaagaccaaggccccagccgtacggtggccgct cccagcgtgttcattctccacctagcgacgagcagctgaagtcggcacagcctctgtc gtgtgctgtgtgaacaactctacccccgcgaggccaaagtgcagtggaaaggtggacaa cgccctgcagagcggcaacagccaggaagcgtgaccgagcaggacagcaaggactc cacctacgcctgagcagcacctgacactgagcaaggccactacgagaagcacaag gtgtacgcctgcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaac cggggcgagtg	SEQ ID NO: 341
Binding Protein 37 Amino Acid Sequences		
Heavy chain A	Qvqlvqsggmkkpgesmriscrasgyefidctlnwirlapgkrpewmgwlkprg gavnyarplqgrvmtndrvysdtaflelrsltdvdyfctrknctdynwdfewhrg tpvivssastkgpsvfplapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfp avlqssglyslssvvtvpssslgtkytcnvdhkpstkvdkrveskygppcpcpape flggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnatk preeqfnstyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepqv ytlppcqemtknqvslwclvkgfypsdiavewesngqpennyktpvldsdgsff lyskltvdkrsrwqegnvfscsvmhelnhytqkslslslgk	SEQ ID NO: 342
Light chain A	Eivltqspgtlsispgetaiisrtsqygslawyqqrpqaprlviysgstraagipdrfsg srwgpdyntisnlesgdfgyyccqyeffgqgtkvqvdkrtvaapsvfifppsdeql ksqtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslstltskad yekhkvacevthqglsspvtksfnrgec	SEQ ID NO: 343

Heavy chain B	Qvqlqesgpglvkpsqtlstctvsqfslsdygvhwvrppgkglewlgviwa gggtynpnlksrktiskdtsknqvsllssvtaadtavyyccardkgysyyysm dywgqgtvtvsssqvqlvesgggvvqpgrslrlscaasgftfkawmhvwrq apgkqlwvaqikdknsyatyadsvkgrftisrddskntlylqmnsraedt avyyrcgvyyalspfdywgqgtlvtvssrtastkgpsvflapcsrstsestaalg clvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgtktyt cnvdhkpsntkvdkrveskygppcpcpapeflggpsvflfppkpkdtlmis rtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnstyrvvsvlt vlhqdwlngkeykckvsnkglpssiektiskakgqprepqvctlpssqeemt knqvslescavkgfypsdiavewesngqpennyktpvldsdsfflvskltv dksrwqegnvfscsvmhcalhnhytqkslslslgk	SEQ ID NO: 344
Light chain B	Divmtqtlslsvtpgqpasisckssqslvhnnantylswylkpgqspqsliykvsnr fsgvpdrfsgsgsgtdftlkisrveadvgyycgqgtqypftfsgtkveikgpkaa pdivltqspaslavspgqraticrasesveyvvtlsmqwyqqkpgqppkllifaasn esgvparfsgsgsgtdftltinpeandvanyycqqrkvpytfgqgtkleiktgpsrt vaapsvfifppsdeqlksgtasvcllnfybreakvqwkvdnalqsgnsqesvteqd skdstylsstltlskadyekkhvyacevthqglsspvtksfnrgec	SEQ ID NO: 345
Binding Protein 37 Nucleotide Sequences		
Heavy chain A	caggtgcagctggtgcagctctggcggccagatgaagaaacccggcgagagcatcgga tcagctgcagagccagcggctacaggttcacgactgcacctgaactggatcagactgg cccctggcaagcggcctgagtgatggatggctgaagcctagaggcggagccgtgaa ctacgccagacctctgcagggcagagtaccatgacccgggacgtgtacagcgataccg ccttctggaactgcggagcctgaccgtggatgataccgccgtgtacttctgacccggg gcaagaactgcgactacaactgggacttcgagcactggggcagaggcaccctgtgatc gtgtcaagcgcgtcgaccaagggccctcgggtgtccctctggcccttgcagcagaagc accagcgaatctacagccgccctgggctgcctcgtgaaggactacttcccagcccgtg accgtgtcctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgtcc agagcagcggcctgtactctgtgacagcgtcgtgacagtcccagcagcagcctgggc accaagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaagc gggtggaatctaagtacggccctccctgcctccttgcagccctgaattctgggcgg accctccgtgttctgttcccccaagcccaaggacacctgatgatcagccggacccc cgaagtgcacctgcgtggtggtggatgtgtcccaggaagatcccagagtgacgttaattg gtacgtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaaacagttc aacagcacctaccgggtggtgtccgtgtgacctgtgtgaccaggactgggtgaacgg caaagagtacaagtgcgaaggtgtccaacaaggcctgcccagctccatcgagaaaacca tcagcaaggccaaggccagccccgcgagcctcaagtgtataacctgcccccttgccag gaagagatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctacccagc gacattgccgtggaatgggagagcaacggccagcccagaaactacaagaccaccc cccctgtgtgacagcagcggctatttctctgtactccaagctgacctggacaagag ccggtggcaggaaggcaacgtgttcagctgtccgtgatgcagaggccctgcacaacc actacaccagaagtcctgtctgttccctgggcaag	SEQ ID NO: 346
Light chain A	Gagatcgtgtgacacagagccctggcaccctgagcctgtctccaggcgagacagccat catcagctgccggacaagccagtacggcagcctggcctgtatcagcagaggcctggac aggccccagactcgtgatctacagcggcagcacaagagccgccgaatccccgatag attcagcggctccagatggggccctgactacaacctgacctcagcaacctggaagcgc gcgacttcggcgtgtactactgccagcagtagagttcttcggcagggcaccaaggtgc aggtggacatcaagcgtacgggtggcgtcccagcgtgttcatttcccacctagcgacg agcagctgaagtccggcacagcctctgtcgtgtgcctgtgaacaacttctacccccga ggccaaagtgcagtgaaggtggacaacgcctgcagagcggcaacagccaggaaag cgtgaccgagcaggacagcaaggactccacctacagcctgagcagcaccctgacactg agcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccaggggc tgtctagccccgtgaccaagagcttcaaccggggcgaggtg	SEQ ID NO: 347
Heavy chain B	caggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagacctgagcct	SEQ ID

	<p>gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgactgggtgcccagcc acctggaaaaggcctggaatggctggcgctgatctgggctggcggaggcaccactaca acccagcctgaagtccagaaagaccatcagcaaggacaccagcaagaaccaggtgtc cctgaagctgagcagcgtgacagccgccgataccgccgtgtactactgcgccagagaca agggtacagctactactacagcatggactactggggccaggccaccaccgtgaccgtg tcactctcaggtgcagctgggtgaatctggcggcgagtggtgcagcctggcagaagc ctgagactgagctgtccgccagcggcttcacctcaccaaggcctggatgcactgggtg cgccaggccctggaaagcagctggaatgggtggccagatcaaggacaagagcaac agctacgccacctactacgccagacgctgaaggggcgttcaccatcagccgggacg acagcaagaacacctgtacctgcagatgaacagcctgcggggcaggacaccgccgt gtactactgtcggggcgtgtactatgccctgagcccttcgattactggggccagggaacc ctcgtgaccgtgtctagtcggaccgcttcgaccaaggggccatcgggtgtccctctggccc cttgacgcagaagcaccagcgaatctacagccgccctgggctgcctcgtgaaggactact ttccgagcccgtagccgtgtcctggaactctggcgtctgacaagcggcgtgcacacctt tccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgacagtcccag cagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagcaaacacc aaggtggacaagcgggtggaatctaagtacggccctccctgcctccttggccagccct gaatttctggggcgaccctccgtgttctgttcccccaagcccaaggacacctgatga tcagccggacccccgaagtacctgcgtggtggtgatgtgtccaggaaatcccagag gtgcagttcaattggtacgtggacggcgtggaagtgcacaacgccaagaccaagcccag agaggaacagttcaacagcacctaccgggtggtgtccgtgctgaccgtgtgcaccagg actggctgaacggcaaagagtacaagtgaaggtgtccaacaaggcctgccagctcc atcgagaaaaccatcagaaggccaagggccagccccgcgagcctcaagtgtgtacctt gccccctagccaggaagagatgaccaagaaccaggtgtccctgagctgtgccgtgaaag gctttaccccagcgacattgccgtggaatgggagagcaacggccagcccagaaaca ctacaagaccacccccctgtgctggacagcagggctcatttctctgtgtccaaagt accgtggacaagagccggtggcaggaaggcaacgtgttcagctgtccgtgatgcacga ggccctgcacaaccactacaccagaagtcctgtctgtccctgggcaag</p>	NO: 348
Light chain B	<p>gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccag catcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctgagct ggtatctgcagaagcccggccagagccccagtcctgatctacaaggtgtccaacagat tcagcggcgtgcccagagattctccggcagcggctctggcaccgacttcacctgaaga tcagccgggtggaagccgaggacgtggcgtgtactattgtggccagggcacccagtac cccttcacctttggcagcggcaccaaggtggaatcaaggggccagcccaaggccgccc cgacatcgtgctgacacagagccctgtagcctggcgtgtctcctggacagagggcca ccatcacctgtagagccagcagagcgtggaatattacgtgaccagcctgatgcagtgg atcagcagaagcccggccagcccccaagctgctgatttgcggccagcaacgtggaa agcggcgtgccagccagatttccggcagcggctctggcaccgacttcacctgaccatc aaccctgtggaagccaacgacgtggccaactactactgccagcagagccggaaggtgc cctacacctttggccaggggcaccagctggaatcaagaccaaggggccccagccgtacg gtggccgctcccagcgtgtcatcttccacctagcagcagcagctgaagtccggcaca gcctctgtcgtgtgctgctgaacaacttctacccccgcgaggccaaagtgcagtggaa gtggacaacgccctgcagagcggcaacagccaggaaagcgtgaccgagcaggacagc aaggactccacctacagcctgagcagcaccctgacactgagcaagggcactacgaga agcacaaggtgtacgcctgcgaagtgaccaccaggccctgttagccccgtgaccaag agcttcaaccggggcgagtg</p>	SEQ ID NO: 349
Binding Protein 38 Amino Acid Sequences		
Heavy chain A	<p>Qvqlvqsgaevvkpgasvkvscasgytftsyyihwvrqapgglewigsyipgnv ntnyaqkfgratltvdsistaymelsrlsddtavyyctrshyldwnfdvwgkgttv tvssastkgpsvflplapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpavl qssglyslssvvtvpssslgtkytcnvdhkpsntkvdkrveskyppcppepapeflg gpsvflfpkpkdtlmiisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpre eqfnstyrvsvltvlhqdwlngkeykckvsnkglpssiiektiskakgqprepvytlp pcqeemtknqvsllwclvkgfypsdiavewesngqpennyktpvldsdgsfflysk</p>	SEQ ID NO: 350

	ltvdksrwqegnvfscsvmhleahnhytqkslslslgk			
Light chain A	Diqmtqspsslsasvgrvtitcqasqniyvwlnwyqqkpgkapklliykasnlhtgv psrfsqsgsgtdftltisslqpeditayycqqgqtypytfqggtkleikrtvaapsvfifpps deqlksqsgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsksdstylsstlt skadyekhkvyacevthqglsspvtksfnrgec	SEQ NO: 351	ID	
Heavy chain B	Rahlvqsgtamkkpgasvrvscqtsgyftahilfwfrqapgrglewvlgwikip qygavnfgggfrdrvlttrdvreiaymdirglkpddtavyyccardrsygdssw aldawgggttvvvsasqvqlvesgggvvpgrslrlscaasgfttkawmhw vrqapgkqlwvaqikdksnsyatyyadsvkgrftisrddskntlylqmnslra edtavyyrcgvyyalspfdywgqgtlvtvssrtastkgpsvfplapcsrstsesta algclvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgk tytcnvdhkpsntkvdkrveskygppcpcpapeflggpsvflfppkpkdtl misrtpevtcvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnstyrvv svltvlhqdwlngkeykckvsnkglpssiektiskakgqprepqvctlppsquee mtknqvsiscavkgfypsdiavewesngqpennykttppvldsdsfvlvskl tvdksrwqegnvfscsvmhleahnhytqkslslslgk	SEQ NO: 352	ID	
Light chain B	Divmtqtplslsvtpgqpasisckssqslvhnnantylswylqkpgqspqsllykvsnr fsgvpdrfsqsgsgtdftlkisrveadvgyycgqgtqypftfsggtkveikgqpkaa pyihvtqspsslsvsigdrvttncqtsqgvgsdlhwyqhkgpgrapklilhtssvedgv psrfsqsgfhtsfntisdlqaddiatyycvqlffgrgsrlhiktkgpsrtvaapsvfifpp sdeqlksqsgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsksdstylsstlt lskadyekhkvyacevthqglsspvtksfnrgec	SEQ NO: 353	ID	
Binding Protein 38 Nucleotide Sequences				
Heavy chain A	caggtgcagctggtgcagctctggcgccgaggtcgtgaaacctggcgccctctgtgaaggt gtcctgcaaggccagcggctacacctttaccagctactacatccactgggtgcgccaggc ccctggacaggactggaatgatcggcagcatctacccggcaacctgaacaccaact acgccagaagtccagggcagagccacctgaccgtggacaccagcatcagaccgc ctacatggaactgagccggctgagaagcgacgacaccgccgtgtactactgcaccgg cccactacggcctggattggaacttcgacgtgtggggcaagggcaccaccgtgacagt ctagcgcgtcgaccaaggccccctcggtgtccctctggccccctgcagcagaagacca gcgaatctacagccgccctgggctgcctcgtgaaggactactttccgagccccgtgaccg tgtcttggaactctggcgctctgacaagcggcgtgcacaccttccagccgtgctccagag cagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcctgggcacca agacctacacctgtaactgtgaccacaagcccagcaacaccaaggtggacaagcgggt ggaatctaagtacggccctccctgccctcctgcccagccccgaatttctggcgaccc tccgtgttctgttcccccaagcccaaggacacctgatgatcagccggacccccgaa gtgacctgcgtggtgtggtgatgtgccaggaagatcccaggtgcagttaattggtacg tggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaacagttcaacag cacctaccgggtggtgtcctgtgaccgtgctgcaccaggactggctgaacggcaag agtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaaaccatcagc aaggccaagggccagccccgcgagcctcaagtgtataacctgcccccttgccaggaaga gatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctacccagcgacatt gccgtggaatgggagagcaacggccagcccgagaacaactacaagaccacccccct gtgctggacagcgacggctcatttctgtactccaagctgaccgtggacaagagccggt ggcaggaaggcaactgttcagctgtccgtgatgcagaggccctgcacaaccactac accagaagtcctgtctgtccctgggcaag	SEQ NO: 354	ID	
Light chain A	Gacatccagatgaccagagccccagcagcctgtctgccagcgtggcgacagagtga ccatcacctgtcaggccagccagaacatctacgtgtggctgaactggtatcagcagaagc ccggcaaggcccccaagctgctgatctacaaggccagcaacctgcacaccggcgtgcc cagcagattttctggcagcggctccggcaccgacttcacctgacaatcagctccctgcag cccaggagacattgccactactactgccagcagggccagacctacccctacaccttggc cagggcaccaagctggaaatcaagcgtacgggtgccgctcccagcgtgttcatttccca cctagcgacgagcagctgaagtcggcacagcctctgtcgtgtcctgctgaacaactct	SEQ NO: 355	ID	

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Heavy chain B	<p> agagcccacctggtgcagcttggcaccgccatgaagaaaccaggcgccctgtgcgggt gtcctgtcagacaagcggctacacctaccgcccacatcctgttctggttcggcaggcc cctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtgaactt cggcggaggcttcgggatagagtaccctgaccgggacgtgtaccgcgagatgcct acatggacatccggggcctgaagccgatgacaccgctgtactactgcgcagagac agaagctacggcgacagcagctgggctctggatgcttggggccagggcacaaccgtgg tggtgtctgcctctcaggtgcagctggtggaatctggcggcgagtggtgcagcctggca gaagcctgagactgagctgtccgccagcggcttcacftcaccaaggcctggatgcact gggtgcccaggccccctggaagcagctggaatgggtggccagatcaaggacaaga gcaacagctacgccacctactacgccgacagcgtgaaggggccggttcaccatcagccgg gacgacagcaagaacacctgtacctgcagatgaacagcctgcgggccgaggacaccg ccgtgtactactgtcggggcgtgtactatgccctgagcccccttgattactggggccaggg aaccctcgtgaccgtgtctagtcggaccgcttgaccaaggggcccatcggtgttccctctg gccccctgcagcagaagcaccagcgaatctacagccgccctgggctgcctctgtgaagga ctactttcccgagcccgtagcgtgtcctggaactctggcgctctgacaagcggcgtgcac acctttccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgacagtgc ccagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagcaa caccaaggtggacaagcgggtggaatctaagtacggccctccctgccctcctgccagc ccctgaatttctggggcgaccctccgtgttctgttcccccaaaagccaaggacacctg atgatcagccggacccccgaagtgcctgcgtggtggtggtgtgtcccaggaagatccc gaggtgcagttcaattggtacgtggacggcgtggaagtgcacaacgccaagaccaagcc cagagaggaacagttcaacagcacctaccgggtggtgtccgtgctgaccgtgtgcacc aggactggctgaacggcaagagtagaagtgaaggtgtccaacaaggccctgccag ctccatcgagaaaacctacagcaaggccaaggggccagccccgcagcctcaagtgtgta ccctgccccctagccagggaagagatgaccaagaaccaggtgtccctgagctgtgccgtg aaaggcttctaccccagcgacattgccgtggaatgggagagcaacggccagcccgaga acaactacaagaccacccccctgtgtgtgacagcgacggctcattcttctggtgtcaa gctgaccgtggacaagagccgggtggcaggaaggcaacgtgttcagctgtccgtgatgc acgaggccctgcacaaccactacacccagaagtccctgtctctgtccctgggcaag </p>	<p> SEQ ID NO: 356 </p>
Light chain B	<p> Gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgcca gcatcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctgag ctggtatctgcagaagcccggcagagccccagtcctgtatctacaaggtgtccaacag attcagcggcgtgcccagacattctccggcagcggcctctggcaccgacttcacctgaa gatcagccgggtggaagccgaggacgtggcgtgtactattgtggccagggcacccagt accccttcacctttggcagcggcaccaaggtggaatcaaggggccagccaaggccgcc ccctacatccagtgaccagagccccagcagcctgtccgtgtccatcggcgacagagt gaccatcaactgccagacctctcaggcgtgggcagcgacctgcactggtatcagcaca agcctggcagagcccccaagctgctgatccaccacacaagcagcgtggaagatggcgt gcccagcagattttccggcagcggcttccacaccagcttcaacctgacctcagcgatctg caggccgacgacattgccacctactattgtcaggtgctgcagttcttcggcagaggcagca gactgcacatcaagaccaaggggccccagccgtacgggtggccgtccccagcgtgttcatct tcccacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgctgtgaaca acttctacccccgcaggccaaagtgcagtgggaaggtggacaacgccctgcagagcgg caacagccaggaaagcgtgaccgagcaggacagcaaggactccacctacagcctgag cagcaccctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaa gtgaccaccaggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt </p>	<p> SEQ ID NO: 357 </p>
Binding Protein 39 Amino Acid Sequences		
Heavy chain A	<p> Qvqlvqsgaevvkpgasvkvsckasgyftsyihwvrqapgglewigsiypgnv ntnyaqkfqratltdtsistaymelsrlrddtavyyctrshyglwdfvwwgkgttv tvssastkgpsvfplapcsrstsestaalgclvkdyfpepvtvswnsaltsgvhtfpavl </p>	<p> SEQ ID NO: 358 </p>

	qssglyslssvvtvpssslgtktytcnvdhkpstnkvdkrveskygppcpapeflg gpsvflfpkpkdltlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpre eqfnstyrvvsvltvlhqdwlngkeykckvsnkglpssiectiskakgqprepvytlp pcqeemtknqvslwclvkgfypsdiavewesngqpennyktppvldsdgsfflysk ltvdksrwqegnvfscsvmhleahnhytqkslsislglk	
Light chain A	Diqmtqspsslsasvgsdrvtitcqasqniyvwlnwyqqkpgkapklliykasnlhtgv psrfsqsgsgtdftltisslqpeditatyyccqggqtypytfqggtkleikrtvaapsvfifpps deqlksqsgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsksdstylsstltl skadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 359
Heavy chain B	Rahlvqsgtamkkpgasvrvscqtsgytftahilfwfrqapgrglewvkwikp qygavnfgggfrdrvltlrdvyreiaymdirglkpddtavyycardrsygdssw aldawgqgttvvvsadkthtqvqlvesgggvvqpgrslrlscaasgfttkaw mhwvrqapgkqlwvvaqikdksnsyatyyadsvkgrftisrddskntlylqm nslraedtavyycrgvyyalspfdywgqgtlvtvssdkthtastkgspsvfplapc srstsestaalgclvkdyppepvtvswngaltsgvhtfpavlqssglyslssvvt vpssslgtktytcnvdhkpstnkvdkrveskygppcpapeflggpsvflfp pkpkdltlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeq fnstyrvvsvltvlhqdwlngkeykckvsnkglpssiectiskakgqprepvc tlppsqeemtknqvslscavkgfypsdiavewesngqpennyktppvldsd gsfflvskltvdksrwqegnvfscsvmhleahnhytqkslsislglk	SEQ ID NO: 360
Light chain B	Divmtqtplslsvtpgqpasisckssqslvhnnantylswylqkpgqspqsllykvsnr fsgvpdrfsgsgsgtdftlkisrveaedvgvyycgqgtqypftfsggtkveikdkthtyih vtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapkllihhtssvedgvsrfs gsgfhtsfntisdlqaddiatyycqvlqffgrgsrlhikdkthtrtvaapsvfifppsdeql ksqsgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsksdstylsstltlksad yekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 361
Binding Protein 39 Nucleotide Sequences		
Heavy chain A	caggtgcagctggtgcagctctggcgccgaggtcgtgaaacctggcgccctctgtgaaggt gtcctgcaaggccagcggtacacctttaccagctactacatccactgggtgcgccaggc ccctggacagggactggaatggatcgagcagcatctacccggcaacgtgaacaccaact acgccagaagttccaggcgagagccaccctgaccgtggacaccagcatcagcaccgc ctacatggaactgagccggctgagaagcgacgacaccgccgtgtactactgcacccgggt cccactacggcctggattggaacttcgacgtgtggggcaagggcaccaccgtgacagtgt ctagcgctgcaccaaggggccctcggtgttcctctggcccttgagcagaagcacca gcaatctacagccgcccctgggctgcctcgtgaaggactacttcccagcccgtgaccg tgtcctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgctccagag cagcggcctgtactctctgagcagcgtcgtgacagtggcagcagcagcctgggcacca agacctacacgtgaactggaccacaagcccagcaacaccaaggtggacaagcgggt ggaatctaagtacggccctccctgcctccttggcagcccctgaatttctggcgggaccc tccgtgttctgtcccccaagcccaaggacaccctgatgatcagccggacccccgaa gtgacctgcgtggtggtgatgtgtcccaggaagatcccagggtgcagttaattggtacg tggacggcgtggaagtgcacaacgccaagaccaagcccagagagggaacagttaacag cacctaccgggtggtgctcctgctgaccgtgctgcaccaggactggctgaacggcaag agtacaagtgaaggtgtccaacaaggcctgcccagctccatcgagaaaaccatcagc aaggccaaggccagccccgcgagcctcaagtgtatacctgcccccttggcaggaaga gatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctacccagcgacatt gccgtggaatggagagcaacggccagcccagagaacaactacaagaccacccccct gtgtggacagcgacggctcattcttctgtactccaagctgaccgtggacaagagccgggt ggcaggaaggcaacgtgttcagctgctccgtgatgcagaggccctgcacaaccactac accagaagtcctgtctctgtccctgggcaag	SEQ ID NO: 362
Light chain A	gacatccagatgaccagagccccagcagcctgtctgccagcgtggcgacagagtga ccatcacctgtcaggccagccagaacatctacgtgtggctgaactggtatcagcagaagc ccggcaaggcccccaagctgtgatctacaaggccagcaacctgcacaccggcgtgcc	SEQ ID NO: 363

	cagcagattttctggcagcggctccggcaccgacttcacctgacaatcagtcctcgagcccaggacattgccactactactgccagcagggccagacctaccctacacctttggccagggcaccaagctggaaatcaagcgtacgggtggccgctcccagcgtgtcatcttcccaactagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaactctacccccgcgagggccaaggtgcagtgggaaggtggacaatgccctgcagagcggcaacagccaggaaagcgtgaccgagcaggacagcaaggactccactacagcctgagcagcacctgaccctgagcaaggccgactacgagaagcacaaggtgtacgctgcgaagtgacccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtg	
Heavy chain B	agagcccacctgggtgcagtctggcaccgccatgaagaaccaggcgctctgtgcgggtgtcctgtcagacaagcggctacacctaccgcccacatcctgttctgttccggcagggccctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtgaacttcggcgaggcttccgggatagtgaccctgaccggggacgtgtaccgcgagatcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcgccagagacagaagctacggcgacagcagctgggctctggatgcttggggccaggggcacaaccgtgtgtgtctgccgacaaaaccataccaggtgcagctggtggaatctggcggggagtggtgcagcctggcagaagcctgagactgagctgtgccgccagcgggttaccttcaccaaaggcctggatgactgggtgcgccaggccccctggaaagcagctggaatgggtggcccagatcaaggacaagagcaacagctacgccacctactacgccgacagcgtgaaggggccggtcaccatcagccgggacgacagcaagaacacctgtacctgcagatgaacagcctgcgggccgaggacaccgccgtgtactactgtcggggcgtgtactatgccctgagcccccttcgattactggggccagggaaccctcgtgaccgtgtctagtataagaccacaccgcttcgaccaaggccccatcggtttccctctggccccctgcagcagaagcaccagcgaatctacagccgccccgggtgcctcgtgaaggactacttcccagccccgtgaccgtgtcctggaactctggcgctctgacaagcggcgtgcacaccttccagccgtgtccagagcagcggcctgtactctgtgacgcgtcgtgacagtcccagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaagcgggtggaatctaagtacggccccctgcctccttggccagccccgaatttctggggcgaccctccgtgttctgttcccacaaagcccaaggacacctgatgatcagccggacccccgaagtgcctgcgtgtgtgtgatgtgtcccagggaagatcccaggtgcagttcaattgttacgtggacggcgtggaaagtgcacaacgccaaagaccaagcccagagaggaacagttcaacagcacctaccgggtgtgtccgtgtgaccgtgtgcaccaggactggctgaacggcgaagagtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaaaccatcagcaaggccaaggggcagccccgcgagcctcaagtgtgtaccctgccccctagccaggaagagatgaccaagaacaggtgtccctgagctgtgccgtgaaaggcttctaccccagcagattgccgtggaatgggagagcaacggccagcccagagaacaactacaagaccacccccctgtgtgacagcgacggctcattcttctgtgtccaagctgaccgtggacaagagccgggtggcagggaaggcaacgtgttcagctgtccgtgatgcagaggccctgcacaaccactacaccagaagtcccgtctctgtccctgggcaag	SEQ ID NO: 364
Light chain B	gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccagcatcagctgcaagagcagccagagcctggtgcacaacaacgcaacacctacctgagctggtatctgcagaagcccggccagagccccagtcctgatctacaaggtgtccaacagatcagcggcgtgcccagagattctccggcagcggctctggcaccgacttcacctgaagatcagccgggtggaagccgaggacgtggcgctgtactattgtggccaggggcacccagtacccctcacctttggcagcggcaccaaggtggaaatcaaggacaaaaccatacctacatcacgtgaccagagccccagcagcctgtccgtgtccatcggcgacagagtgacctcaaactgccagacctcagggcgtgggcagcagcctgcactggtatcagcacaagcctggcagagccccaaagctgctgatccaccacacaagcagcgtggaagatggcgtgcccagcagatttccggcagcggctccacaccagcttcaacctgacctcagcagctgtcagggccgacgacattgccacctactattgtcaggtgtcagttcttcggcagaggcagcagactgcacatcaaggataagaccatacccgtagcgtggccgctcccagcgtgtcatcttcccactagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaacttctacccccgcgaggccaaagtgcagtgggaaggtggacaacgccctgcagagcggcaacagccaggaaagcgtgaccgagcagagcaaggaactccactacagcctgagcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccag	SEQ ID NO: 365

	ggcctgtctagccccgtgaccaagagcttcaaccggggcgagtg	
Binding Protein 40 Amino Acid Sequences		
Heavy chain A	Qvqlvqsgaevvkgpaskvskasgytftsyihwvrqapggglewigsyppgnv ntnyaqkfqratltdtsistaymelsrlsddtavyyctrshyglwnfdvhwgkgttv tvssastkgpsvflapcsrstsestaalgclvkdyppepvtvswngaltsghvhtfpavl qssglyslssvvtvpssslgtkytcnvdhkpsntkvdkrveskygpppcppapeflg gpsvflfppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpre eqfnstyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepvytlp pcqeemtknqvslwclvkgyfypsdiavewesngqpennyktpvldsdsgsflysk ltvdksrwqegnvfscsvmhleahnhytqkslsislglk	SEQ ID NO: 366
Light chain A	Diqmtqspsslsasvgrvltitcasqniyvwlnwyqqkpgkapklliykasnlhtgv psrfsgsgsgtdftltisslqpeditayycqqgqtypytfqggtkleikrtvaapsvfifpps deqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslstltl skadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 367
Heavy chain B	Qvqlvesgggvvqpgrslrlscaasgftfkawmhvvrqapgkqlwvraqi kdknsnyatyyadsvkgrftisrddskntlylqmnsiraedtavyycrgvyayal spfdywgggtlvtvsssrhlvqsgtamkkpgasvrvscqtsgytftahilfwfr qapgrglewvgwikipqygavnfgggfrdrvlttrdvreiaymdirglkpdtd avyycardrsygdsswaldawgggttvvvsartastkgpsvflapcsrstsest aalglvkdyppepvtvswngaltsghvhtfpavlqssglyslssvvtvpssslgt kytcnvdhkpsntkvdkrveskygpppcppapeflggpsvflfppkpkdtl msrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnstyrv vsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepqvctlpssq eemtknqvslscavkgyfypsdiavewesngqpennyktpvldsdsgsfllvs kltdksrwqegnvfscsvmhleahnhytqkslsislglk	SEQ ID NO: 368
Light chain B	Yihvtqspsslsvsigdrvtincqtsqvgsgdlhwyqhkpgrapklhihtssvedgvp srfsgsgfhtsfntisdlqaddiatyycqvlqffgrgsrlhikgqpkapdivmtqtplsl svtpgqpasisckssqslvhnnantylswylqkpgqspqsllykvsnrfsgvpdrfsgs gsgtdftlkisrveaedvgvyycgggtqypftfgsgtkveiktgpsrtvaapsvfifpps deqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslstltl skadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 369
Binding Protein 40 Nucleotide Sequences		
Heavy chain A	caggtgcagctggtgcagctctggcgccgaggtcgtgaaacctggcgccctctgaaggt gtcctgcaaggccagcggctacacctttaccagctactacatccactgggtgcgccaggc ccctggacaggactggaatggatcggcagcatctacccggcaactgaacaccaact acgccagaagttccagggcagagccaccctgaccgtggacaccagcatcagaccgc ctacatggaactgagccggctgagaagcgacgacaccgccgtgtactactgacccgggt cccactacggcctggattggaacttcgacgtgtggggcaagggcaccaccgtgacagtgt ctagcgcgtcgaccaaggggcccctcggtgtccctctggccccttgacgagaagcacca gcgaatctacagccgcccctgggctgcctcgtgaaggactactttccgagcccgtgaccg tgtcctggaaactctggcgctctgacaagcggcgtgcacacctttccagccgtgtccagag cagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcctgggcacca agacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaagcgggt ggaatctaagtacggccctccctgcctccttgcccagcccctgaattctggcgcgacc tccgtgtcctgttcccccaagcccaaggacacctgatgatcagccggacccccgaa gtgacctgcgtggtggtgatgtgtcccaggaagatcccagggtgcagtcaattgtacg tggaaggcgtggaagtgcacaacgccaagaccaagcccagagaggaaacagttaacag cacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaaag agtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaaaccatcagc aaggccaagggccagccccgcgagcctcaagtgtataacctgcccccttgccaggaaga gatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctacccagcgacatt gccgtggaatggagagcaacggccagcccgagaacaactacaagaccacccccct gtgctggacagcgacggctcattctctgtactccaagctgaccgtggacaagagccgggt	SEQ ID NO: 370

	ggcaggaaggcaacgtgttcagctgctccgtgatgcacagggccctgcacaaccactac accagaagtcctgtctctgtccctgggcaag	
Light chain A	gacatccagatgaccagagccccagcagcctgtctgccagcgtggcgacagagtga ccatcacctgtcaggccagccagaacatctacgtgtggctgaactggtatcagcagaagc ccggcaaggcccccaagctgtgatctacaaggccagcaacctgcacaccggcgtgcc cagcagattttctggcagcggctccggcaccgacttcacctgacaatcagctccctgcag cccaggacattgccactactactgccagcaggggccagacctaccctacacctttggc caggggcaccaagctggaaatcaagcgtacggtggccgctccagcgtgttcattcttcca cctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgtgaacaactct acccccgcgagggcaaggtgcagtggaaggtggacaatgccctgcagagcggcaaca gccaggaagcgtgaccgagcaggacagcaaggactccacctacagcctgagcagca ccctgacctgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgc ccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 371
Heavy chain B	caggtgcagctggtggaatctggcggcggagtggtgcagcctggcagaagcctgagact gagctgtgccgccagcggcttcacctcaccaaggcctggatgactgggtgcgccagg ccctggaaagcagctggatgggtggccagatcaaggacaagagcaacagctacgc cacctactacgccgacagcgtgaaggggccggttcacctacagccgggacgacagcaag aacacctgtacctgcagatgaacagcctgcgggccgaggacaccgccgtgtactactgt cggggcggtgtactatgccctgagcccttcgattactggggccagggaacctctgtgacc gtgtctagtagcagagcccacctggtgcagctctggcaccgccatgaagaaaccaggcgc ctctgtcgggtgtctctgcagacaagcggctacaccttcaccgcccatcctgttctgtgt tccggcagggccctggcagaggactggaatgggtgggatggatcaagccccagtatgg cgccgtgaacttcggcggaggcttccgggatagagtaccctgacccgggacgtgtacc gcgagatcgctacatggacatccggggcctgaagcccgatgacaccgccgtgtactact gcccagagacagaagctacggcgacagcagctgggctctggatgcttggggccaggg cacaaccgtgggtgtgtctgccggaccgccagcacaaggggccatcggtgttccctct ggcccttgacagcagaagcaccagcgaatctacagccgcctgggctgcctcgtgaagg actactttcccgagcccggtgaccgtgtcctggaaactctggcgctctgacaagcggcgtgca cacctttccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgacagt cccagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagca acaccaaggtggacaagcgggtggaatctaagtacggccctccctgccctccttggccag ccctgaatttctggcgggacctccgtgttctgttcccccaaggccaaggacacct gatgatcagccggacccccgaagtacgtgcgtgggtggatgtgtcccaggaagatc ccgaggtgcagttcaattgtgtacgtggacggcgtggaagtgcacaacgccaagaccaag cccagagaggcaacagttcaacagcacctaccgggtggtgtccgtgctgacctgctgca ccaggactgggtgaacggcaagagtacaagtgaaggtgtccaacaaggcgctgcc agctccatcgagaaaaccatcagcaaggccaaggggccagccccgcgagcctcaagtgt gtaccttccccctagccagggaagatgaccaagaaccaggtgtccctgagctgtgcc gtgaaaggcttctaccccagcgacattgccgtggatgggagagcaacggccagcccga gaacaactacaagaccacccccctgtgtgtggacagcagggctcatttctctgtgtcc aagctgacctggacaagagccggtggcaggaaggcaacgtgttcagctgtccgtgat gcacgaggccctgcacaaccactacaccagaagtcctgtctgtccctgggcaag	SEQ ID NO: 372
Light chain B	tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacaga gtgaccatcaactgccagacctctcagggcgtgggcagcgacctgactggtatc agcacaagcctggcagagcccccaagctgtgatccaccacacaagcagcgtg gaagatggcgtgccagcagattttccggcagcggcttcacaccagcttcaacc tgacctcagcgatctgcaggccgacgacattgccacctactattgtcaggtgctg cagttcttcggcagaggcagcagactgcacatcaaggggccagcccaaggccgc ccccgacatcgtgatgccagacccccctgagcctgagcgtgacacctggaca gcctgccagcatcagctgcaagagcagccagagcctggtgcacaacaacgcca acacctacctgagctggtatctgcagaagcccggccagagccccagtcctgat ctacaaggtgtccaacagattcagcggcgtggccgacagattctccggcagcgg ctctggcaccgacttcacctgaagatcagccgggtggaagccgaggacgtggg	SEQ ID NO: 373

	cgtgtactattgtggccagggcaccagtagcccttcacctttggcagcggcacca aggtggaatcaagaccaagggccccagccgtacggtggccgctcccagcgtg ttcatctcccacctagcgacgagcagctgaagtcggcacagcctctgtcgtgtg cctgtgaacaacttctacccccgcaggccaaagtgcagtggagggtggacaa cgccctgcagagcggcaacagccaggaaagcgtgaccgagcaggacagcaag gactccacctacagcctgagcagcaccctgacactgagcaaggccgactacgag aagcacaaggtgtacgcctgcgaagtgaccaccagggcctgtctagccccgtg accaagagcttcaaccggggcgagtgt	
Binding Protein 41 Amino Acid Sequences		
Heavy chain A	Qvqlvqsgaevvkpgasvkvscasgyftsyihwvrqapggglewigsyipgnv ntnyaqkfqgratltvdsistaymelsrlrddtavyyctrshyglwnfdvwgkgttv tvssastkgpsvfplapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpavl qssglyslssvvtvpssslgtkytcnvdhkpstnkvdkrveskygppcpapeflg gpsvflfpkpdktdlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpre eqfnstyrvsvltvlhqdwlngkeyckvsnkglpssiektiskakgpprepqvylp pcqeemtknqvslwclvkgyfypsdiavewesngqpennyktpvldsdgsfflysk ltvdksrwqegnvfscsvmhcalhnhytqkslsislglk	SEQ ID NO: 374
Light chain A	Diqmtqspsslsasvgrvtitcqsqniyvwlnwyqqkpgkapklliykasnlhtgv psrfsgsgsgtdftltisslpediatyycqqgqtypytfgggkcleikrtvaapsvfifpps deqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslstltl skadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 375
Heavy chain B	qvqlvesgggvvqpgrslrlscaasgftfkawmhwwvrqapgkqlewvaqik dksnsyatyyadsvkgrftisrddskntlylqmnsraedtavyyrcgvyyalsp fdywggqgtlvvtssdkthtrahlvqsgtamkkpgasvrvscqtsgytftahilfw frqapgrglewvlgwikipqygavnfgggfrdrvtltdvyreiaymdirglkpd dtavyycardrsygdsswaldawgggttvvvsadkthtastkgpsvfplapcsr stsestaalgclvkdyfpepvtvswngaltsgvhtfpavllqssglyslssvvtvp ssslgtkytcnvdhkpstnkvdkrveskygppcpapeflggpsvflfpkp pktdlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfns tyrvsvltvlhqdwlngkeyckvsnkglpssiektiskakgpprepqvctlp psqeemtknqvslscavkgyfypsdiavewesngqpennyktpvldsdgsf flvskltvdksrwqegnvfscsvmhcalhnhytqkslsislglk	SEQ ID NO: 376
Light chain B	Yihvtqspsslsvisgdrvtincqtsqvgvsgdlhwyqhkpgkapkllihhtssvedgvp srfsgsgfhtsfnltsldlqaddiatyycqvlqffgrgsrlhikdkthtdivmtqplslsvtp gqpasisckssqslvhnnantylswylqkpgqspqsllykvsnrfsqvpdrfsgsgsgt dftlkisrveaedvgyycgggtqypftfgsgtkveikdkthtrtaapsvfifppsdeql ksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslstltlkskad yekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 377
Binding Protein 41 Nucleotide Sequences		
Heavy chain A	cagggtgcagctgggtgcagctctggcgccgaggtcgtgaaacctggcgccctctgtgaaggt gtcctgcaaggccagcggctacacctttaccagctactacatccactgggtgcgccaggc ccctggacagggactggaatggatggcagcatctacccggcaacgtgaacaccaact acgcccagaagttccaggggcagagccaccctgaccgtggacaccagcatcagcacccgc ctacatggaactgagccggctgagaagcgacgacaccgccgtgtactactgcaccgggt cccactacggcctggattggaacttcgacgtgtggggcaagggcaccaccgtgacagtgt ctagcgctcgaccaagggcccctcggtgtccctctggccccttgacagcagaagcacca gcgaatctacagccgcccctgggctgcctcgtgaaggactacttcccagcccgtgaccg gtccttggaactctggcgctctgacaagcggcgtgcacaccttccagccgtgctccagag cagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcctgggcacca agacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaagcgggt ggaatctaagtacggccctccctgcctcctgcccagcccctgaatttctggcgggaccc tccgtgttcctgttcccccaagcccagacaccctgatgatcagccggacccccgaa	SEQ ID NO: 378

	cagcagattttccggcagcggcttcacaccagctcaacctgacctcagcgcgatctgcag gccgacgacattgccactactattgtcaggtgctgcagttcttcggcagaggcagcagac tgcacatcaaggacaaaaccataccgacatcgtgatgaccagacccccctgagcctga gctgacacctggacagcctgccagcatcagctgcaagagcagccagagcctggtgca caacaacgccaacacctactgagctggtatctgcagaagcccgccagagccccagct ccctgatctacaaggtgtccaacagattcagcggcggtgcccagcagattctccggcagcg gctctggcaccgacttcacctgaagatcagccgggtggaagccgaggacgtggcgctg tactattgtggccagggcaccagtagcccttcacctttggcagcggcaccaggtggaa atcaaggataagaccataccgtacggtggcgctcccagcgtgttcattctcccaccta gcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaactctacc cccgcgaggccaaagtgcagtggaaggtggacaacgcctgcagagcggcaacagcc aggaagcgtgaccgagcaggacagcaaggactccacctacagcctgagcagcacct gacactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccac cagggcctgttagccccgtgaccaagagctcaaccggggcgaggtg	
Binding Protein 42 Amino Acid Sequences		
Heavy chain A	Qvqlqesgpglvkpsqtlstctvsgfslsdygvhwvrpppgkglewlgviwagggt nynpslksrktiskdtsknqvslkssvtaadtavvycardkgyssyysmdywgqgtt vtvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgktytcnvdhkpstnkvdkrveskygppcpcpapefl ggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpr eeqfnstyrvvsvltvlhqdwlngkeyckvsnkglpssiektiskakgqprepqvyl ppcqemtnknqvsllwclvkgfypsdiavewesngqpennyktpplvdsdgsfflys kltdksrwqegnvfscsvmhhealhnhytqkslsislglk	SEQ ID NO: 382
Light chain A	Divltqspaslavspgqratitcrasesveyyvtlsmqwyqqkpgppklifaasve sgvparfsgsgsgtdftltinpeandvanyycqsrkvpvtyfgqgkcleikrtvaapsv fifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsdstys lssltliskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 383
Heavy chain B	Rahlvqsgtamkkpgasvrvcqtsgytftahilfwfrqapgrglewvlgwikp qygavnfgggfrdrvltldvryeiaymdirglkpddtavvycardrsygdssw aldawgggttvvvsasqvqlvesgggvvqpgrslrlscaasgfttkawmhw vrqapgkqlwvaqikdksnsyatyadsvkgrftisrddskntlylqmnsira edtavyycrgvyyalspfdywgqgtlvtvssrtastkgpsvflapcsrstsesta algclvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgk tytcnvdhkpstnkvdkrveskygppcpcpapeflggpsvflfppkpkdtl misrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnstyrvv svltvlhqdwlngkeyckvsnkglpssiektiskakgqprepqvctlppsquee mtknqvslscavkgfypsdiavewesngqpennyktpplvdsdgsfflvskl tvdksrwqegnvfscsvmhhealhnhytqkslsislglk	SEQ ID NO: 384
Light chain B	Divmtqtplsivtpgqpasisckssqslvhnnantylswylqkpgqspqsliykvsnr fsgvpdrfsgsgsgtdftlkisrveadvgyycgggtqypftfgsgtkveikgpkaa pyihvtqspsslsvsigdrvtincqtsqgvgsdlhwyqhkpgrapklhhtssvedgv psrfsgsgfhtsfntisdlqaddiatyycqlqffgrgsrlhiktkgpsrtvaapsvfifpp sdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdsdstyslssltl lskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 385
Binding Protein 42 Nucleotide Sequences		
Heavy chain A	caggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagaccctgagcct gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgcactgggtgcgccagc cacctggaaaaggcctggaatggctgggcgtgatctggcctggcggaggcaccaccta caacccagcctgaagtccagaaagaccatcagcaaggacaccagcaagaaccagtg tcctgaagctgagcagcgtgacagccgccgataccgccgtgtactactgcgccagaga caagggtacagctactactacagcatggactactggggccagggcaccaccgtgaccg tgtcatccgcgtcgaccaaggccccctcggtgtccctctggccccctgcagcagaagca ccagcgaatctacagccgcctgggctgcctcgtgaaggactacttcccagcccgtga	SEQ ID NO: 386

	ccgtgtcctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgtcca gagcagcggcctgtactctctgagcagcgtcgtgacagtgtccagcagcagcctgggca ccaagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaagcg ggtggaatctaagtagggccctccctgccctcctgtcccagcccctgaatttctggcgga ccctcctgttctgttcccccaagcccaaggacacctgatgatcagccggaccccc gaagtgtacgtggtggtggtggtgtgtccaggaagatcccaggtgcagttcaattggt acgtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaaacagttca acagcacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggc aaagagtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaaacct cagcaaggccaagggccagccccgcgagcctcaagtgtataacctgccccctgtccag gaagagatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctacccagc gacattgccgtggaatgggagagcaacggccagcccagaaactacaagaccaccc ccctgtgtgtgacagcgacggctcatttctctgtactccaagctgaccgtggacaagag ccggtggcaggaaggcaacgtgttcagctgctccgtgatgcacgagggcctgcacaacc actacaccagaagtccctgtctctgtccctgggcaag	
Light chain A	gacatcgtgtgacacagagccctgtgacctggcgtgtctcctggacagagggccac catcacctgtagagccagcgagagcgtggaatattacgtgaccagcctgatgcagtggta tcagcagaagcccggccagcccccaagctgtgtatttccgccagcaacgtgga ggcggtgtccagccagatttccggcagcggctgtggcaccgacttaccctgaccatca acccgtggaagccaacgacgtggccaactactactgccagcagagccggaaggtgcc ctacaccttggccagggcaccaagctggaaatcaagcgtacgggtggcgtctccagcg tgttcatcttccacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtcct gctgaacaacttctacccccgcgaggccaaggtgcagtgaaggtggacaatgcctgc agagcggcaacagccaggaagcgtgaccgagcaggacagcaaggactccacctaca gcctgagcagcacctgaccctgagcaaggccgactacgagaagcacaaggtgtacgc ctgcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcg agtgt	SEQ ID NO: 387
Heavy chain B	agagcccacctggtgcagtctggcaccgccatgaagaaccaggcgcctctgtgcgggt gtcctgtcagacaagcggctacacctaccgcccacatcctgttctggttccggcaggcc cctggcagaggactggaatgggtgggatggaatcaagccccagtatggcgccgtgaactt cggcgagggttccgggtagagtaccctgacccgggacgtgtaccgcgagatcgcc tacatggacatccggggcctgaagccgatgacaccgccgtgtactactgcgccagaga cagaagctacggcgacagcagctgggtcttgatgcttggggccagggcacaacctg gtggtgtctgcctctcaggtgcagctggtggaatctggcgccgagtggtgcagcctggc agaagcctgagactgagctgtgccgccagcggcttcaccttaccaaaggcctggatgca ctgggtgcgccaggcccctggaagcagctggaatgggtggccagatcaaggacaag agcaacagctacgccacctactacgccgacagcgtgaaggcgccggttaccatcagccg ggacgacagcaagaacacctgtacctgcagatgaacagcctgcggcgccgaggacacc ggcgtgtactactgtcggggcgtgtactatgccctgagccccttcgattactggggccagg gaacctcgtgaccgtgtctagtcggaccgcttgaccaaggggccatcggtgttccctct ggccccctgcagcagaagcaccagcgaatctacagccgccctgggctgcctcgtgaagg actacttcccagcccgtgaccgtgtcctggaactctggcgctctgacaagcggcgtgca caccttccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgacagt cccagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagca acaccaaggtggacaagcgggtggaatctaagtagggccctccctgccctcctgtcccag ccctgaatttctggcgacccctcctgttctgttcccccaagcccaaggacacct gatgatcagccggacccccgaagtgcctgctggtggtggtgtgtcccaggaagatc ccgaggtgcagttcaattgttacgtggacggcgtggaagtgcacaacgccaagaccaag cccagagaggaaacagttcaacagcacctaccgggtggtgtccgtgctgaccgtgctgca ccaggactggctgaacggcaagagtacaagtgaaggtgtccaacaaggcctgcc agctccatcgagaaaacctacgaaggccaaggccagccccgcgagcctcaagtgt gtacctgccccctagccaggaagatgaccaagaaccaggtgtccctgagctgtgcc gtgaaaggcttctacccagcgacattgccgtggaatgggagagcaacggccagcccc agaacaactacaagaccacccccctgtgtgacagcagcggtcatttctctggtgtc	SEQ ID NO: 388

	caagctgaccgtggacaagagccggtggcaggaaggcaacgtgttcagctgctccgtgatgcacgaggccctgcacaaccactacaccagaagtcctgtctctgctccctgggcaag	
Light chain B	gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccagcatcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctgagctggatatcgcagaagccccggccagagccccagtcctgatctacaagggtgccaacagattcagcggcggtgcccacagattctccggcagcggctctggcaccgacttcacctgaagatcagccgggtggaagccgaggacgtggcggtgtactattgtggccagggcaccagtaccccctcaccttggcagcggcaccaggtggaaatcaagggccagcccaaggccgccctcatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacagagtgaccatcaactgccagacctctcagggcggtgggcagcagctgcactggtatcagcagaagcctggcagagccccaaagctgctgatccaccacacaagcagcgtggaagatggcggtggccagcagatctccggcagcggctccacaccagcttcaacctgacctacgcagctgcagggcgacacattgccacctactattgtcaggtgctgcagttctcggcagaggcagcagactgcacatcaagaccaagggccccagccgtacggtggccgctcccagcgtgttcattctccacctagcagcagcagctgaagtccggcacagcctctgtcgtgtgctgtgtaacaactttacccccgcaggccaaaagtgacgtggaaggtggacaacgcctgcagagcggcaacagccaggaagcgtgaccgagcaggacagcaaggactccacctacagcctgagcagcacctgacactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccaggcgctgtctagccccgtgaccaagagcttcaaccggggcgagtg	SEQ ID NO: 389
Binding Protein 43 Amino Acid Sequences		
Heavy chain A	Qvqlqesgpglvkpsqtlslctctvsgfslsdygvhwvrppgkglewlgviwagggt nynpslksrktiskdtsknqvsllkssvtaadvayycardkgysyyysmdywgqgt vtvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgtktytcnvdhkpsntkvdkrveskygppppcpapefl ggpsvflfppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkp reeqfnstyrsvsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepvyt lppcqeemtknqvsllwclvkgyfypsdiavewesngqpennykttppvldsdgsffly skltvdkswqegnvfscsvmhealnhytqkslslslgk	SEQ ID NO: 390
Light chain A	Divltqspaslavspgqratitcrasesveyyvtlsmqwyqqkpgppklifaasve sgvparfsgsgsgtdftltinpeandvanyycqsrkvpvtyfgggtkleikrtvaapsv fifppsdeqlksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstys lsstltlaskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 391
Heavy chain B	Rahlvqsgtamkkpgasvrvcqtsgytftahilfwfrqapgrglewvgwik pqygavnfgggfrdrvtltdvyreiaymdirglkpddtavyyccardrsygdss waldawgqgttvvsadkthtqvqlvesgggvgppgrslrlscaasgftftka wmhwwrqpapgkqlwvaqikdksnsyatyadsvkgrftisrddskntlylq mnsdraedtavyyrcgvyyalspfdywgqgtlvtvssdkthtastkgpsvfla pcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpavlqssglyslssv vtvpssslgtktytcnvdhkpsntkvdkrveskygppppcpapeflggpsvfl fppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpre eqfnstyrsvsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepq vctlppsqeemtknqvsllscavkgfypsdiavewesngqpennykttppvld sdgsfflvskltvdkswqegnvfscsvmhealnhytqkslslslgk	SEQ ID NO: 392
Light chain B	Divmtqtplslsvtpgqpasisckssqslvhnnantylswylqkpgqspqsllykvsnr fsgvpdrfsgsgsgtdftlkisrveadvgyycgqgtqypftfsggtkveikdkhtyi hvtqspsslsvsigdrvtincqtsqvggsdlhwyqhkpgrapkllihhtssvedgvpsrf sgsgfhtsfnltilsqaddiatyycvqlqffgrgsrlhikdkthtrtaapsvfifppsdeq lksgtasvcllnnfypreakvqwkvdnalqsgnsqesvteqdskdstyslsstltlaska dyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 393
Binding Protein 43 Nucleotide Sequences		
Heavy chain A	cagggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagaccctgagcct gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgcactgggtgcgccagc cacctggaaaaggcctggaatggctggcgctgatctgggctggcggaggccaccaacta	SEQ ID NO: 394

	<p>caacccagcctgaagtccagaaagaccatcagcaaggacaccagcaagaaccaggtg tcctgaagctgagcagcgtgacagccgccgataccgccgtgtactactgcgccagaga caagggtacagctactactacagcatggactactggggccaggccaccaccgtgaccg tgtcatccgcgtcgaccaagggcccctcggtgttccctctggccccttcagcagaagca ccagcgaatctacagccgccctgggctgcctcgtgaaggactacttcccagcccgtga ccgtgtcctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgtcca gagcagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcctgggca ccaagacctacacctgaacgtggaccacaagcccagcaacaccaaggtggacaagcg ggtggaatctaagtacggccctccctgccctcctgccagcccctgaattctggcgga ccctccgtgttctgttcccccaagcccaaggacacctgatgatcagccggaccccc gaagtacactgcgtggtggtgatgtgtcccaggaagatcccaggtgcagttcaattggt acgtggacggcgtggaagtgcacaacccaagaccaagcccagagaggaacagttca acagcacctaccgggtggtgtccgtgtgaccgtgtgcaccaggactggtgaacggc aaagagtacaagtgaaggtgtccaacaagggcctgccagctccatcgagaaaaccat cagcaaggccaagggccagccccgcagcctcaagtgtataccctgccccctggccag gaagagatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctaccccagc gacattgccgtggaatgggagagcaacggccagcccagaacaactacaagaccaccc cccctgtgtgtgacagcgacggctcatttctctgtactccaagctgaccgtggacaagag ccggtggcaggaaggaacgtgttcagctgtccgtgatgcacgaggccctgcacaacc actacaccagaagtcctgtctctgtccctgggcaag</p>	
Light chain A	<p>gacatcgtgtgacacagagccctgtagcctggccgtgtctcctggacagagggccac catcacctgtagagccagcgagagcgtggaatattacgtgaccagcctgatgcagtggta tcagcagaagcccggccagcccccaagctgtgatttccgccagcaacgtgga gcccgtgccagccagatttccggcagcggctctggcaccgacttaccctgaccatca accccgtggaagccaacgacgtggccaactactactgccagcagagccggaagtgcc ctacaccttggccagggcaccaagctggaaatcaagcgtacggtggccgctccagcg tgttcatcttcccactagcgacgagcagctgaagtccggcacagcctctgtcgtgtcct gctgaacaacttctacccccgcgaggccaaggtgcagtggaaagtggaatgcctgc agagcgggaacagccaggaagcgtgaccgagcaggacagcaaggactccacctaca gcctgagcagcacctgacctgagcaaggccgactacgagaagcacaaggtgtacgc ctgcgaagtgaccaccagggcctgtctagccccgtgaccaagagcttcaaccggggcg agtgt</p>	SEQ ID NO: 395
Heavy chain B	<p>agagcccacctggtgcagtctggcaccccatgaagaaaccaggcgcctctgtgcgggt gtcctgtcagacaagcggctacaccttaccgcccacatcctgttctggttccggcaggcc cctggcagaggactggaatgggtgggatggatcaagccccagtatggcgccgtgaactt cggcggaggcttccgggatagagtaccctgacccgggacgtgtaccgcgagatgcc tacatggacatccggggcctgaagcccgatgacaccgccgtgtactactgcgccagaga cagaagctacggcgacagcagctgggctctggatgcttggggccagggcacaaccgtg gtggtgtctgccgacaaaaccataccaggtgcagctggtggaatctggcggcgaggt ggtgcagcctggcagaagcctgagactgagctgtgccccagcggcttacccttacca aggcctggatgactgggtgcgccaggcccctggaagcagctggaatgggtggcca gatcaaggacaagagcaacagctacgccactactacgccgacagcgtgaaggggcgg ttaccatcagccgggacgacagcaagaacacctgtacctgcagatgaacagcctgcg ggccgaggacaccgcccgtgtactactgtcggggcgtgtactatgccctgagccccctga ttactggggccagggaacctcgtgaccgtgtctagtataagaccacaccgcttcgac caaggggccatcgggtgttccctctggccccttcagcagaagcaccagcgaatctacagc cgccctgggctgcctcgtgaaggactacttcccagcccgtgaccgtgtcctggaactct ggcgtctgacaagcggcgtgcacaccttccagccgtgtccagagcagcggcctgta ctctctgagcagcgtcgtgacagtgccagcagcagcctgggcaccaagacctacact gtaacgtggaccacaagcccagcaacaccaaggtggacaagcgggtggaatctaagta cggccctccctgcccctcctgccagcccctgaattctggcgggaccctccgtgttctgt tcccccaagcccaaggacacctgatgatcagccggacccccgaagtacactgcgtg gtggtggatgtgtcccaggaagatcccaggtgcagttcaattggtacgtggacggcgtg gaagtgcacaacccaagaccaagcccagagaggaacagttcaacagcactaccgg</p>	SEQ ID NO: 396

	gtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaagagtacaagtgc caaggtgtccaacaagggcctgccagctccatcgagaaaaccatcagcaaggccaag ggccagccccgcgagcctcaagtgtgtaccctgccccctagccaggaagagatgacca agaaccaggtgtccctgagctgtgccgtgaaaggcttctaccccagcgacattgccgtgg aatgggagagcaacggccagcccagagaacaactacaagaccacccccctgtgtgga cagcgacggctcattcttctgtgtccaagctgaccgtggacaagagccggtggcagg aaggcaacgtgttcagctgtccgtgatgcacgaggccctgcacaaccactacaccag aagtcctgtctctgtccctgggcaag	
Light chain B	gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccag catcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctgagct ggtatctgcagaagcccggccagagccccagctcctgatctacaaggtgtccaacagat tcagcggcgtgcccagagattctccggcagcggctctggcaccgacttcacctgaag atcagccgggtggaagccgaggacgtggcggtgtactattgtggccagggcacccagta ccccttcaccttggcagcggcaccaggtggaatcaaggacaaaaccatacctacat ccacgtgacccagagccccagcagcctgtccgtgtccatcggcgacagagtaccatca actgccagacctctcagggcgtggcgagcgacctgcactggtatcagcacaagcctggc agagcccccaagctgctgatccaccacacaagcagcgtggaagatggcgtgcccagca gattttccggcagcggctccacaccagcttaacctgacctcagcgatctgcaggccga cgacattgccactactattgtcaggtgtgcagttcttcggcagaggcagcagactgcac atcaaggataagaccataccgtacggtggccgctcccagcgtgttcattctccacctta gcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgtgaacaacttctacc cccgcgaggccaaagtgcagtgaaggtggacaacgccctgcagagcggcaacagcc aggaaagcgtgaccgagcaggaaggaagactccacctacagcctgagcagcacct gacactgagcaaggccgactacgagaagcacaaggtgtacgcctgcgaagtaccac cagggcctgtctagccccgtgaccaagagcttcaaccggggcgagtgt	SEQ ID NO: 397
Binding Protein 44 Amino Acid Sequences		
Heavy chain A	Qvqlqesgpglvkpsqtlstctvsgfslsdygvhwvrppgkglewlgviwagggt nynpslksrktiskdtsknqvsllssvtaadtavyycardkgysyyysmdywgqgt vtvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgktytcnvdhkpstnkvdkrveskygppcpcpapefl ggpsvflfppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktpr eeqfnstyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakgpprepqvytl ppcqeeemtknqvslwclvkgfypsdiavewesngqpennyktppldsdgsfflys kltdksrwqegnvfscsvmhhealhnhytqkslsislsgk	SEQ ID NO: 398
Light chain A	Divltqspaslavspgqratitcrasesveyyvtslmqwyqqkpgppklifaasve sgvparfsgsgsgtdftltinpeandvanyycqsrkvpvpytgqgkcleikrtvaapsv fifppsdeqlksqtasvcllnfyreakvqwkvdnalqsgnsqesvteqdsdstys lsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 399
Heavy chain B	Qvqlvesgggvgpgrslrlscaasgftfkawmhvwrqapgkqllewvaqi kdksnsyatyyadsvkgrftisrddskntlylqmnsdraedtavyycrgvyyals pfdywgqgtlvtvssrahlvqsgtamkkpgasvrvscqtsgytftahilfwfrq apgrglewvfwikpqqygavnfgggfrdrvtltdvyreiaymdirglkpddta vyycardrsygdsswaldawgggttvvsartastkgpsvflapcsrstsesta algclvkdyfpepvtvswngaltsgvhtfpavlqssglyslssvvtvpssslgk tytcnvdhkpstnkvdkrveskygppcpcpapeflggpsvflfppkpkdtl msrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktprpreeqfnstyrvv svltvlhqdwlngkeykckvsnkglpssiektiskakgpprepqvctlpssqee mtknqvslscavkgyfypsdiavewesngqpennyktppldsdgsfflvskl tvdksrwqegnvfscsvmhhealhnhytqkslsislsgk	SEQ ID NO: 400
Light chain B	Yihvtqspsslsvisgdrvtincqtsqvgssdlhwyqhkpgrapkllihhtssvedgvp srfsgsgfhtsfntisdlqaddiatyycqvlqffgrgsrlhikgqpkaapdivmtqtplsls vtpgqpasisckssqslvhnnantylswylqkpgqspqsllykvsnrfsqvpdrfsgsg sgtdftlkisrveadvgyycgqgtqypftfgsgtkveiktkgpsrtvaapsvfifppsd	SEQ ID NO: 401

	eqlksgtasvvcllnnfybreakvqwkvdnalqsgnsqesvteqdsdstylsstlts kadyekkhkvyacevthqglsspvtksfnrgec	
Binding Protein 44 Nucleotide Sequences		
Heavy chain A	cagggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagaccctgagcct gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgactgggtgcccagc cacctggaaaaggcctggaatggctggcgctgatctgggctggcggaggcaccaacta caacccagcctgaagtccagaaagaccatcagcaaggacaccagcaagaaccaggtg tcctgaagctgagcagcgtgacagccgccgataccgccgtgtactactgcgcagaga caagggtacagctactactacagcatggactactggggccagggcaccaccgtgaccg tgtcatccgcgtcgaccaaggggccctcgggttccctctggccccttgacgcagaagca ccagcgaatctacagccgccctgggctgcctcgtgaaggactactttccgagcccgtga ccgtgtcctggaactctggcgtctgacaagcggcgtgcacacctttccagccgtgtcca gagcagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcctgggca ccaagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaagcg ggtggaatctaagtacggccctccctgccctccttgcccagcccctgaatttctggcgga ccctccgtgttctgttcccccaagcccaaggacacctgatgatcagccggaccccc gaagtgacctgcgtggtggtggtgatgtgtccaggaagatcccagggtgcagttcaattggt acgtggacggcgtggaagtgcacaacccaagaccaagcccagagaggaacagttca acagcacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactgggtgaacggc aaagagtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaaacct cagcaaggccaagggccagccccgcgagcctcaagtgtataacctgcccccttgccag gaagagatgaccaagaaccaggtgtccctgtggtgtctcgtgaaaggcttctacccagc gacattgccgtggaatgggagagcaacggccagcccagaacaactacaagaccaccc ccctgtgctggacagcgcagggctatttctctgtactccaagctgaccgtggacaagag ccggtggcaggaaggcaacgtgttcagctgctccgtgatgcagaggccctgcacaacc actacaccagaagtcctgtctctgtccctgggcaag	SEQ ID NO: 402
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Heavy chain B	cagggtgcagctggtggaatctggcggcggagtggtgcagcctggcagaagcctgagac tgagctgtgccccagcggcttcaccttcaccaaggcctggatgcactgggtgcccag gcccctggaaagcagctggaatgggtggcccagatcaaggacaagagcaacagctacg ccacctactacgccgacagcgtgaaggggccggttcacctacagccgggacgacagcaa gaacacctgtacctgcagatgaacagcctgcgggccgaggacaccgccgtgtactact gtcggggcgtgtactatgccctgagcccccttcgattactggggccagggaacctcgtga ccgtgtctagtagcagagcccacctggtgcagtctggcaccgccatgaagaaaccaggc gcctctgtcgggtgtcctgtcagacaagcggctacaccttcaccgcccacatcctgtctg gttccggcagggccctggcagaggactggaatgggtggatggatcaagccccagtatg gcggcgtgaacttcggcggaggttccgggatagagtaccctgacccgggacgtgtac cgcgagatgcctacatggacatccggggcctgaagcccgatgacaccgccgtgtacta ctgcgccagagacagaagctacggcgacagcagctgggctctggatgcttggggccag ggcacaacctgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgt tctggccccttgacgcagaagcaccagcgaatctacagccgccctgggctgcctcgtgaa ggactacttcccagcccgtgaccgtgtcctggaactctggcgtctgtgacaagcggcgt	SEQ ID NO: 404

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Light chain B	<p>tacatccacgtgaccagagccccagcagcctgtccgtgtccatcggcgacagagtgcacatcaactgccagacctctcagggcgtgggcagcgacctgcactggtatcagcacaagcctggcagagcccccaagctgctgatccaccacacaagcagcgtggaagtggcgtgccagcagattttccggcagcggcttccacaccagcttcaacctgacctacagcagatctgcaggccagcagattgccacctactattgtcaggtgctgcagttcttcggcagaggcagcagactgcacatcaaggacaaaaccataccgacatcgtgatgccagacccccctgagcctgagcgtgacacctggacagcctgccagcatcagctgcaagagcagccagagcctgggtgcaacaacgcccaacacctacctgagctggtatctgcagaagcccggccagagcccccagtccctgatctacaaggtgtccaacagattcagcggcgtgccgacagattctccggcagcggtctggcaccgacttcaccctgaagatcagccgggtggaagccgaggacgtggcgtgtactattgtggccagggcaccagtagcccccttcacctttggcagcggcaccgaaggtggaaatcaaggataagaccatacccgtaggtggcgtctccagcgtgttcatcttccacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtgcctgctgaacaacttctacccccgcgagggccaaagtgcagtggaggtggacaacgcctgcagagcggcaacagccaggaaagcgtgaccgagcagagcaaggactccacctacagcctgagcagccctgacactgagcaagccgactacgagaagcacaaggtgtacgctgcgaagtgcaccaggcgctgtctagccccgtgaccaagagcttcaaccggggcgagtg</p>	SEQ ID NO: 413
Binding Protein 46 Amino Acid Sequences		
Heavy chain A	<p>Qvqlvqsgaevvkpgasvkvskasgytftsyyihwvrqapggglewigsyypgnvntnyaqkfqratlrvtdtsistaymelsrlrddtavyyctrshyglidwnfdvbwkggtvtvssastkgpsvfplapcsrstsestaalgclvkdyfpepvtvswnsalgtsgvhtfpavlgssglyslssvvtvpssslgktytcnvdhkpsntkvdkrveskygppcpcpapeflggspsvflfppkpkdltmisrtpetvcvvvdvsqedpevfwnvyvdgvevhnaktkpreeqfnstyrvsvltvlhqdwlngkeyckvsnkglpssiektiskakgqprepvytlppcqeeemtknqvslwclvkgfypsdiavewesngqpennnyktpvldsdgsfflyskltvdksrwqegnvfscsvmhleahnhytqkslslslgk</p>	SEQ ID NO: 414
Light chain A	<p>Diqmtqspsslsasvgrvrtiteqasqniyvwlnwyqqkpgkapklliykasnlhtgvprrsfsgsgsgtdftltisslqpediatyycqqgqtypytfggqtkleikrtvaapsvfifppsdealksgtasvvcllnnfvpreakvqwkvdnalqsgnsaesvteadskdstvslsstltl</p>	SEQ ID NO: 415

	skadyekhkvyacevthqglsspvtksfnrgec			
Heavy chain B	Qvhltqsgpevrkpgtsvkvsckapgnltktydlhwvrsvpgqglqwmgwi shegdkkviverfkakvtidwdrstntaylqlsgltsgdtavyycakgskhrlrd yalydddgalnwavdvdylnlefwgqgtavtvsssqvqlvesgggvvpgr slrlscaasgftfkawmhwwrqapgkqlwvvaqikdksnsyatyyadsvkg rftisrddskntlylqmnsdraedtavyycrgvyyalspfdywgqgtlvtvssrta stkgpsvfplapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpavl qssglyslssvvtvpssslgtkytcnvdhkpsntkvdkrveskygppcppepa peflggpsvflfppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgve vhnaktkpreeqfnstyrvsvltvlhqdwlngkeykckvsnkglpssiektis kakgqprepqvctlppsqeemtknqvslescavkgfypsdiavewesngqpe nnykttppvldsdsfflvskltvdksrwqegnvfscsvmhealnhnytqksls lslgk	SEQ ID NO: 416		
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Binding Protein 46 Nucleotide Sequences				
Heavy chain A	cagggtgcagctgggtgcagctctggcgccgaggtcgtgaaacctggcgccctctgtgaaggt gtcctgcaaggccagcggctacacctttaccagctactacatccactgggtgcgccaggc ccctggacagggactggaatggatcggcagcatctacccggcaactgaacaccaact acgcccagaagttccagggcagagccacctgaccgtggacaccagcatcagcaccgc ctacatggaactgagccggctgagaagcgacgacaccgctgtactactgcaccgggt cccactacggcctggattggaacttcgacgtgtggggcaagggcaccaccgtgacagt tctagcgcgtcgaccaaggccccctcggtgtccctctggccccctgcagcagaagcacc agcgaatctacagccgccctgggtgcctcgtgaaggactacttcccagcccgtgacc gtgtcctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgtccaga gcagcggcctgtactctctgagcagcgtcgtgacagtgcccagcagcagcctgggcacc aagacctacacctgtaactgtgaccacaagcccagcaacaccaaggtggacaagcggg tggaatctaagtacggccctccctgccctcctgcccagccccgaatttctggcgggacc ctcctgtgtcctgttcccccaagcccaaggacacctgatgatcagccggacccccga agtgcacctgcgtggtggtgatgtgtcccaggaagatcccagggtgcagttcaattgttac gtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaaacagttcaac agcacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaa agagtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaaacctca gcaaggccaagggccagccccgcgagcctcaagtgtataacctgccccctggcagga agagatgaccaagaaccaggtgtccctgtggtgtctgtgaaaggcttctacccagcga cattgccgtggaatgggagagcaacggccagcccagagaacaactacaagaccaccccc cctgtgtcggacagcgacggctcattcttctgtactccaagctgaccgtggacaagagcc ggtggcaggaaggcaacgtgttcagctgtccgtgatgcacgaggccctgcacaaccac tacaccagaagtccctgtctctgtccctgggcaag	SEQ ID NO: 418		
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Binding Protein 47 Amino Acid Sequences			
Heavy chain A	Qvqlvqsgaevvkpgasvkvsckasgytftsyyihwvrqapggglewigsiypgnv ntnyaqkfqratltdtsistaymelsrlrddtavyyctrshyglwdnfdvwgkgttv tvssastkgpsvfplapcsrstsestaalgclvkdyfpepvtvswnsaltsgvhtfpavl	SEQ ID NO: 422	

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Light chain A	Diqmtqspsslsasvgrvtitcqasqniyvwlnwyqqkpgkapklliykasnlhtgv psrfsgsgsgtdftltisslqpdiatyycqqgqtypytfgggtkleikrtvaapsvfifpps deqlksqtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdsksdstylsstltl skadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 423
Heavy chain B	Qvhltqsgpevrkpgtsvkvsckapgnltkydlhwvrsvpqglqwmgi shgdkkviverfkakvtidwrstntaylqlsgltsgdavyycakgskhrlrd yalydddgalnwavdvdylnlefwgqgtavtvssdkthtqvqlvesgggvv qpgrslrlscaasgftfkawmhwwrqapgkqlwvaqikdksnsyatyad svkgrftisrddskntlylqmnsdraedtavyycrgvyyspfdywgqgtlvtv ssdkthtastkgpsvflapcsrstsestaalgclvkdyfepvvtvswngaltsg vhtfpavlqssglyslssvvtvpssslgtkytcnvdhkpsntkvdkrveskygp pccppcpapeflggpsvflfppkpkdtlmisrtpetcvvvdvsqedpevqfn wyvdgvevhnaktkpreeqfnstyrvvsvltvlhqdwlngkeykckvsnkg lpssieltiskakgqprepvytlppsqeemtknqvslscavkgfypsdiavew esngqpennyktppvldsdsfflvskltvdksrwqegnvfscsvmhealnh hytqkslsislglk	SEQ ID NO: 424
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Light chain A	gacatccagatgaccagagccccagcagcctgtctgccagcgtggcgacagagtga ccatcacctgtcaggccagccagaacatctacgtgtggctgaactggtatcagcagaagc	SEQ ID NO: 427

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Binding Protein 48 Amino Acid Sequences		
Heavy chain A	Qvqlvqsgaevvkpgasvkvsckasgyftsyihwvrqapggglewigsyypgnv ntnyaqkfqratlvtidsistaymelsrlrddtavyyctrshyglwnfdvbwgkgttv tvssastkgpsvfplapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpavl qssglyslssvvtvpssslgktytcnvdhkpsntkvdkrveskygppcpapeflg gpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpre eqfnstyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakgpprepqvytlp pcqeemtknqvslwclvkgfypsdiavewesngqpennykttppvldsdsfflysk ltvdksrwqegnvfscsvmhleahnhytqkslslglgk	SEQ ID NO: 430
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Binding Protein 48 Nucleotide Sequences		
Heavy chain A	caggtgcagctgggtgcagctctggcgccgaggtcgtgaaacctggcgctctgtgaaggt gtcctgcaaggccagcggctacacctttaccagctactacatccactgggtgcgccaggc ccctggacagggactggaatggatcggcagcatctacccggcaactgtaacaccaact acgcccagaagttccagggcagagccacctgaccgtggacaccagcatcagcaccgc ctacatggaactgagccggctgagaagcgacgacaccgccgtgtactactgacccgggt cccactacggcctggattggaacttcgacgtgtggggcaagggcaccaccgtgacagtgt ctagcgcgtcgaccaaggggccctcggtgtccctctggcccttgacagagaagacca gcgaatctacagccgcttggtgcctcgtgaaggactacttcccagcccggtgaccg tgtcctggaactctggcgctctgacaagcggcgtgcacacctttccagccgtgctccagag cagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcctgggcacca agacctacacctgtaactggaccacaagcccagcaacaccaagggtggacaagcgggt ggaatctaagtacggcctccctgcctccttgcacagcccctgaattctgggcggaccc tccgtgtcctgttcccccaagcccaaggacacctgatgatcagccggacccccgaa gtgacctgcgtggtgtggtgtgtccaggaagatcccagggtgcagttaattggtacg tggaaggcgtggaagtgcacaacgccaagaccaagcccagagaggaacagttcaacag cacctaccgggtggtgtcctgctgaccgtgctgcaccaggactggctgaacggcaag	SEQ ID NO: 434

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Heavy chain B	<p>caggtgcagctgtgtggaatctggcggcggagtgtgtcagcctggcagaagcctgagact gagctgtgccgccagcggcttcaccttcaccaaggcctggatgcactgggtgcgccagg cccctggaaagcagctggaatgggtggccagatcaaggacaagagcaacagctacgc cacctactacccgacagcgtgaaggggcgggttcacctacagccgggacgacagcaag aacacctgtacctgcagatgaacagcctgcgggcccaggacaccgccgtgtactactgt cggggcgtgtactatgccctgagcccttcgattactggggccagggaacctctgtgacc gtgtctagtagccaggtgcacctgacacagagcggaccgaaagtgcggaagcctggca cctctgtgaaggtgtcctgcaaggccccggcaacacctgaaaacctacgacctgcact gggtgcgcagcgtgccaggacaggactgcagtggatgggctggatcagccacagg gcgacaagaagtgatctgtgaacgggtcaaggccaaagtgacctgactgggacaga agcacaacaccgcctacctgcagctgagcggcctgaccttggcgataccgccgtgtat ctactgcgccaaggggcagcaagcaccggctgagagactacgcctgtacgacgatgac ggcgccctgaactgggcccgtggatgtgactacctgagcaacctggaattctggggcca gggacagccgtgaccgtgtcatctcggaccgccagcacaaggggcccatcggtgttc ctctggccccctgcagcagaagcaccagcgaatctacagccgccctgggctgcctctga aggactactttcccagcccgtgaccgtgtcctggaactctggcgtctgacaagcggcgt gcacacctttccagccgtgtccagagcagcggcctgtactcttgagcagcgtcgtgac agtggccagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagccc agcaacaccaaggtggacaagcgggtggaatctaagtacggccctccctgccctcctgc ccagccccgaatttctggcggaccctccgtgttctgttcccccaaggccaaggaca ccctgatgatcagccggacccccgaagtgacctgcgtggtgtggtggtgtcccaggaa gatcccagggtgcagttcaattgtacgtggacggcgtggaagtgcacaacgccaagac caagcccagagaggaacagttcaacagcacctaccgggtgtgtccgtgtgaccgtgc tgcaccaggactggctgaacggcgaagagtacaagtgaaggtgtccaacaaggcctg cccagctccatcgagaaaaccatcagcaaggccaaggccagccccgcgagcctcaag tgtgtacctgccccctagccaggaaagatgaccaagaaccaggtgtccctgagctgtg ccgtgaaaggcttctacccagcgacattgccgtggaatgggagagcaacggccagccc gagaacaactacaagaccacccccctgtgctggacagcgacggctcatttctctgtgt ccaagctgaccgtggacaagagccggtggcagggaaggcaacgtgttcagctgctccgtg atgcacgaggccctgcacaaccactaccccagaagtcctgtctgtccctgggcaag</p>	SEQ ID NO: 436
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Heavy chain A	Qvqlvqsgaevvkpgasvkvscasgytftsyyihwvrqapggglewigsiypgnv ntnyaqkfqratlvtidsistaymelsrlsddtavyyctrshyglwdfvngkgttv tvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpavl qssglyslssvvtvpssslgtkytcnvdhkpsntkvdkrveskyppcpapeflg gpsvflfppkpkdtlmsirtpvctvvvdvsqedpevqfnwyvdgvevhnaktkpre eqfnstyrvsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepvytlp pcqeemtknqvslwclvkgyfypsdiavewesngqpennyktppvldsdsfflysk ltvdksrwqegnvfscsvmhcalhnhytqkslsislglk	SEQ ID NO: 438
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Binding Protein 50 Amino Acid Sequences		
Heavy chain A	Qvqlqesgpglvkpsqtlsltctvsgfslsdygvhwvrppgkglewlgviwagggt nynpslksrktiskdtsknqyslssvtaadtavvycardkgysyyysmdywgqgtt vtvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgtktytcnvdhkpsntkvdkrveskygppcpcpapefl ggpsvflfppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpr eeqfnstyrvsvltvlhqdwlngkeykckvsnkgplssiectiskakgqprepqvyl ppcqemtknqvslwclvkgfypsdiavewesngqpennyktpvldsdgsfflys kltdksrwqegnvfscsvmhcalhnhytqksls	SEQ ID NO: 446
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Heavy chain B	Qvhltqsgpevrkpgtsvkvsckapgnltktydlhwvrsvpqglqwmgi shgdkkviverfkakvtidwdrstntaylqlsgltsgdtavvycakgskhrlrd yalydddgalnwavdvdylnlefwgqgtavtvsssqvqlvesgggvgvqgr slrlscaasgftfkawmhwwrqpqgkqlewvaqikdksnsyatyadsvk rftisrddskntlylqmnsiraedtavyycrgvyyspfdywgqgtlvtvssrta stkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpavl qssglyslssvvtvpssslgtktytcnvdhkpsntkvdkrveskygppcpcpapefl pelfggpsvflfppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgve vhnaktkpreeqfnstyrvsvltvlhqdwlngkeykckvsnkgplssiectis kakgqprepqvctlpssqemtknqvslscavkgyfypsdiavewesngqpe nnyktpvldsdgsfflvskltdksrwqegnvfscsvmhcalhnhytqksls ls	SEQ ID NO: 448
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Heavy chain B	caggtgcacctgacacagagcggaccggaagtgcggaagcctggcacctctgtgaagg tgtctgcaaggccccctggcaacacctgaaaacctacgacctgactgggtgcgagc gtgccaggacagggactgcagtggatgggctggatcagccacgagggcgacaagaaa gtgatcgtggaacggttcaaggccaaagtaccatcactgggacagaagcacaacac cgctacctgcagctgagcggcctgacctctggcgataccgccgtgtactactgcgcaa gggcagcaagcaccggctgagagactacgccctgtacgacgatgacggcgcctgaac tgggccgtggatgtggactacctgagcaacctggaattctggggccagggcacagcct gaccgtgtcatcttctcaggtgcagctgggtggaatctggcggcggagtgggtgcagcctgg cagaagcctgagactgagctgtgccgccagcggcttaccttcaacaggcctggatgca ctgggtgcccagggccctggaaagcagctggaatgggtggcccagatcaaggacaag agcaacagctacgccacctactacgccgacagcgtgaaggggcgggttaccatcagccg ggacgacagcaagaacacctgtacctgcagatgaacagcctgcggggccaggacacc ggcgtgtactactgtcggggcgtgtactatgccctgagcccccttgattactggggccagg gaacctcgtgaccgtgtctagtcggaccgttcgaccaaggggcccatcggtgttccctct ggccccctgcagcagaagcaccagcgaatctacagccgcctgggctgcctcgtgaagg actacttcccagcccgtgaccgtgtcctggaaactctggcgtctgacaagcggcgtgca caccttccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgacagt cccagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagcccagca acaccaaggtggacaagcgggtggaatctaagtacggccctccctgcctccttcccag	SEQ ID NO: 452

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Light chain B	gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccag catcagctgcaagagcagccagagcctggtgcacaacaacccaacacctacctgagct ggtatctgcagaagcccggccagagccccagtcctgatctacaaggtgtccaacagat tcagcggcgtgcccagagattctccggcagcggctctggcaccgacttcacctgaaga tcagccgggtggaagccgaggacgtggcgtgtactattgtggccagggcacccagtac cccttcacctttggcagcggcaccaaggtggaaatcaaggccagcccaaggccgcccc cgacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgagagcgcca gcatcagctgcaagagcagccactccctgatccacggcgaccggaacaactacctggctt ggtacgtgcagaagcccggcagatccccccagctgctgatctacctggccagcagcaga gccagcggcgtgcccgatagatttctggcagcggcagcgacaaggacttcacctgaa gatcagccgggtggaaccgaggacgtgggcacctactactgtatgcagggcagagag agccccctggacctttggccagggcaccaaggtggacatcaagaccaaggcccccagcc gtacggtggcgtccccagcgtgtcatcttccacctagcgacgagcagctgaagtccg gcacagcctctgtcgtgtgctgtgaacaacttctacccccgcaggccaaagtgcagt ggaaggtggacaacgcctgcagagcggcaacagccaggaaagcgtgaccgagcag gacagcaaggactccacctacagcctgagcagcaccctgacactgagcaaggccgact acgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcctgtctagccccgtg accaagagctcaaccggggcgaggtgt	SEQ ID NO: 453
Binding Protein 51 Amino Acid Sequences		
Heavy chain A	Qvqlqesgpglvkpsqtlstctvsgfslsdygvhwvrppgkglewlgviwagggt nynpslksrktiskdtsknqvslkssvtaadavyyccardkgysyyysmdywgqgtt vtvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgktytcnvdhkpstnkvdkrveskygppcpapefl ggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpr eeqfnstyrvsvltvlhqdwlngkeyckvsnkglpssiektiskakgqprepqvyl ppcqeemtnqvslwclvkgfypsdiavewesngqpennyktpvldsdgsfflys kltdksrwqegnvfscsvmhhealhnhtqkslsislglk	SEQ ID NO: 454
Light chain A	Divltqspaslavspgqratitcrasesveyyvtlsmqwyqqkpgqppkllifaasve sgvparfsgsgsgtdftltinpeandvanyycqsrkvpytfqggtkleikrtvaapsv fifppsdeqlksgtasvcllnfybreakvqwkvdnalqsgnsqesvteqdskdstys lsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 455
Heavy chain B	Qvhltqsgpevrkpgtsvkvsckapgnltktydlhwvrsvpqqlqwmgi shgdgkriverfkakvtidwrstntaylqlsgltsgdavyycaakgskhrlrd yalydddgalnwavdvdylnlefwggtavtvssdkthtqvqlvesgggvv qpgrslrlscaasgftfkawmhwwrqapgkqlwvvaqikdksnsyatyad svkgrftisrddskntlylqmnsdraedtavyycrgvyyalspfdywgqgtlvtv ssdkthtastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsg vhtfpavlqssglyslssvvtvpssslgktytcnvdhkpstnkvdkrveskygp pcppcpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfn wyvdgvevhnaktkpreeqfnstyrvsvltvlhqdwlngkeyckvsnkg pssiektiskakgqprepqvctlpssqeemtnqvslscavkgfypsdiavew	SEQ ID NO: 456

	esngqpennyktpvldsdgsfflvskltvdksrwqegnvfscsvmhcalhn hytqkslsislglk	
Light chain B	Divmtqtplslsvtpgqpasickssqslvhnnantylswylqkpgqspqsllykvsnr fsgvpdrfsgsgsgtdftlkisrveadvgyvycgqgtqypftfsgstkveikdkthtdf vltqspshslsvtpgesasickssshlihgdrnnylawyvkpgrspqliylasrasgv pdrfsgsgsdkdftlkisrvetdvgttycmqgrespwtfgggtkvdkdkthtrtvaa psvfifppsdeqlksgtasvvcllnnfympreakvqwkvdnalqsgnsqesvteqdskd styslsstltskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 457
Binding Protein 51 Nucleotide Sequences		
Heavy chain A	caggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagaccctgagcct gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgcactgggtgcccagcc acctggaaaaggcctggaatggctggcgctgatctggcgtggcggaggcaccacactaca acccagcctgaagtccagaaagaccatcagcaaggacaccagcaagaaccaggtgtc cctgaagctgagcagcgtgacagccgccgataccggcgtgtactactgcgccagagaca agggtctacgtactactacagcatggactactggggccaggcaccaccgtgaccgtg tcacccgctgcaccaaggggccctcgtgttcctctggcccttgcagcagaagcacc agcgaatctacagccgccctggcctcgtgaaggactactttccgagcccgtagcc gtgtcctggaactctggcgtctgacaagcggcgtgcacaccttccagcctgtccaga gcagcggcctgtactctctgagcagcgtcgtgacagtggccagcagcagcctgggcacc aagacctacacctgaacgtggaccacaagcccagcaacaccaaggtggacaagcggg tggaatctaagtacggccctccctgccctcctggccagccctgaattctggcgaggacc ctccgtgttctgttcccccaagcccaaggacaccctgatgatcagccggacccccga agtgcacctgcgtgggtggatgtgtcccaggaagatcccagggtgcagttcaattgtac gtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaaacagttcaaca gcacctaccgggtgtgtcctgctgaccgtgctgcaccagactggctgaacggcaaa gagtacaagtgaaggtgtcaacaaggccctgccagctccatcgagaaaaccatcag caaggccaaggccagccccgcgagcctcaagtgtataacctgccccctggcagggaag agatgaccaagaaccaggtgtccctgtgggtgtcgtgaaaggcttctacccagcgacat tgccgtggaatgggagagcaacggccagcccagagaactacaagaccacccccct gtgctggacagcgacggctcattctctgtactccaagctgaccgtggacaagagccggt ggcaggaaggcaacgtgttcagctgctccgtgatgcacgaggccctgcacaaccactac accagaagtccctgtctctgtccctgggcaag	SEQ ID NO: 458
Light chain A	gacatcgtgctgacacagagccctgtagcctggcctgtgtctctggacagagggccac catcacctgtagagccagcgagagcgtggaatattacgtaccagcctgatgcagtgtgat cagcagaagcccggccagcccccaagctgtgatttccgccagcaacgtggaaag cggcgtgccagccagatttccggcagcggctctggcaccgacttcacctgacctcaa ccccgtggaagccaacgacgtggccaactactactgccagcagagccggaaggtgcc tacaccttggccagggcaccaagctggaaatcaagcgtacgggtggcgtcccagcgt gttcatttccacctagcgacgagcagctgaagtcggcacagcctctgtcgtgtgcctg ctgaacaacttctacccccgcgaggccaaggtgcagtggaaaggtggacaatgccctgca gagcggcaacagccagggaagcgtgaccgagcaggacagcaaggactccacctacag cctgagcagcaccctgacctgagcaaggccgactacgagaagcacaaggtgtacgcct gcgaagtgaccaccaggccctgtctagccccgtgaccaagagcttcaaccggggcga gtgt	SEQ ID NO: 459
Heavy chain B	caggtgcacctgacacagagcggaccgcaagtgccgaagcctggcacctctgtgaagg tgtcctgcaaggccccctggcaacacctgaaacctacgacctgactgggtgcgcagc gtgccaggacagggactgcagtggatgggtggatcagccacgaggcgacagaagaaa gtgatcgtggaacggttcaaggccaaagtaccatcgactgggacagaagcaccacac cgctacctgcagctgagcggcctgacctctggcgataccggcgtgtactactgcgcaa gggcagcaagcaccggctgagagactacgccctgtacgacgatgacggcgccctgaac tgggccgtggatgtggactacctgagcaacctggaattctggggccagggcacagccgt gaccgtgtcatctgacaaaaccataccaggtgcagctggtggaatctggcggcggaggt	SEQ ID NO: 460

	<p>gggtgcagcctggcagaagcctgagactgagctgtgccgccagcggcttcacctcacca agggcctggatgactgggtgcccagggccctggaaagcagctggaatgggtggcca gatcaaggacaagagcaacagctacgccacctactacgccgacagcgtgaaggccgg ttaccatcagccgggacgacagcaagaacaccctgtacctgcagatgaacagcctgcg ggccgaggacaccgccgtgtactactgtcggggcgtgtactatgccctgagcccttga ttactggggccaggaaccctcgtgaccgtgtctagtataagaccacaccgcttcgac caaggggccatcggtgttccctctggcccttgagcagaagcaccagcgaatctacagc cgccctgggctgctcgtgaaggactactttcccgagcccgtagccgtgtcctggaactct ggcgtcttgacaagcggcgtgcacacctttccagccgtgtccagagcagcggcctgta ctctctgagcagcgtcgtgacagtggccagcagcagcctgggaccaagacctacacct gtaacgtggaccacaagcccagcaacaccaaggtggacaagcgggtggaatctaagta cggccctccctgccctccttgcccagccctgaatttctggcgccgaccctccgtgtcctgtt cccccaaaagcccaaggacacctgatgatcagccggacccccgaagtgcctgcgtg gtggtggatgtgtcccaggaagatcccaggtgcagttcaattggtacgtggacggcgtg gaagtgcacaagccaagaccaagcccagagaggaacagttcaacagcacctaccggg tggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcgaagagtacaagtga aggtgtccaacaagggcctgcccagctccatcgagaaaaccatcagcaaggccaagg ccagccccgcgagcctcaagtgtgtacctgccccctagccaggaagagatgaccaaga accaggtgtccctgagctgtgccgtgaaaggcttctacccagcgacattgccgtggaatg ggagagcaacggccagcccagacaactacaagaccacccccctgtgctggacagc gacggctcattctcctggtgtccaagctgaccgtggacaagagccggtggcaggaagg caacgtgttcagctgctccgtgatgcagaggccctgcacaaccactacaccagaagtc cctgtctctgtccctgggcaag</p>	
Light chain B	<p>gacatcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccag catcagctgcaagagcagccagagcctgggtgcacaacaacgccaacacctacctgagct ggtatctgcagaagcccggccagagccccagtcctgatctacaagggtgccaacagat tcagcggcgtgcccagacagattctccggcagcggcctgtggcaccgacttcacctgaaga tcagccgggtggaagccgaggacgtggcggtgtactattgtggccagggcaccagctac cccttcacctttggcagcggcaccaggtggaaatcaaggacaaaaccataccgacttc gtgtgacccagagccctcacagcctgagcgtgacacctggcgagagcgcagcatca gctgcaagagcagccactccctgatccacggcgaccggaacaactacctgcttggtac gtgcagaagcccggcagatccccagctgctgatctacctggccagcagcagagcca gcggcgtgcccgatagattttctggcagcggcagcgacaaggacttcacctgaagatca gccgggtggaaccgaggacgtgggcacctactactgtatgcaggcagagagagccc ctggacctttggccagggcaccaggtggacatcaaggataagaccatacccgtagcgt ggccgctcccagcgtgttcattctccacctagcgacgagcagctgaagtcggcagcgc ctctgtcgtgtgctgtgaacaacttctacccccgcgaggccaaagtgcagtggaaagtg gacaacgccctgcagagcggcaacagccaggaagcgtgaccgagcagcagacgaa ggactccacctacagcctgagcagcaccctgacactgagcaaggccgactacgagaag cacaaggtgtacgctgcgaagtgaccaccaggcgctgtctagccccgtgaccaagag cttcaaccggggcgagtg</p>	<p>SEQ ID NO: 461</p>
Binding Protein 52 Amino Acid Sequences		
Heavy chain A	<p>Qvqlqesgpglvkpsqtlstctvsgfslsdygvhwvrpppgkglewlgviwagggt nynpslksrktiskdtsknqvsllssvtaadtavyyccardkgyssyyssmdywgqgt vtvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsgvhtfpav lqssglyslssvvtvpssslgktytcnvdhkpstnkvdkrveskygppcpcpapefl ggpsvflfppkpkdtlmsrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpr eeqfnstyrvsvltvlhqdwlngkeykckvsnkglpssiektiskakgqprepvytl ppcqemtknqvslwclvkgfypsdiavewesngqpennyktpvldsdgsfflys kltdksrwqegnvfscsvmhcalhnyhtqkslsllgk</p>	<p>SEQ ID NO: 462</p>
Light chain A	<p>Divltqspaslavspggratitcrasesveyyvtlsmqwyqqkpgppkllifaasnve sgvparfsgsgsgtdftlinpveandvanyycqsrkvpptfqqgtkleikrtvaapsv fifppsdeqlksgtasvcllnfyprvakvqwkvdnalqsgnsqesvteqdsdstys lsstltlskadyekhkvyacevthqglsspvtksfnrgec</p>	<p>SEQ ID NO: 463</p>

Heavy chain B	Qvqlvesgggvvqpgrslrlscaasgfttkawmhvvrqapgkqlewvaqi kdknsnyatyadsvkgrftisrddskntlylqmnslraedtavyycrgvyyals pfdywggqglvtvsssqvhltsqgpevrkpgtsvkvsckapgnltktydlhwv rsvpgqglqwmgwishegdkkriverfkakvtidwdrstntaylqlsgltsgd tavyycakgskhrlrdyalydddgalnwavdvdylnlefwgggtavtvssrt astkgpsvflapcsrstsestaalgclvkdyfepvtvswnsгалтsgvhtfpav lqssglyslssvvtvpssslgtkytcnvdhkpstnkvdkrveskygppcp apeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgv evhnaktkpreeqfnstyrvvsvltvlhqdwlngkeykckvsnkglpssiekti skakgqprepqvctlpssqeemtknqvsalcavkgfypsdiavewesngqpe nnykttppvldsdsfflvskltvdksrwqegnvfscsvmhealnhnytqksls lslgk	SEQ ID NO: 464
Light chain B	Dfvltqsphslsvtpgesasisckssshlihgdrnnylawyvqkprspqliylasras gvprdfsgsgsdkdftlkisrvetedvgtyycmqgrespwtfgggtkvdikgqpkaap divmtqtplslsvtpgqpasisckssqslvhnnantylswylqkpgqspqsllykvsnr sgvprdfsgsgsgtdfllkisirveaedvgvyyccggtqypftfgsgtkveiktgpsrtv aapsvfifppsdeqlksqtasvvcllnnfypreakvqwkvdnalqsgnsqesvteqds kdstylsstltlskadyekkhkvacevthqglsspvtksfnrgec	SEQ ID NO: 465
Binding Protein 52 Nucleotide Sequences		
Heavy chain A	caggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagaccctgagcct gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgactgggtgcccagcc acctggaaaaggcctggaatggctggcgctgatctgggctggcggaggcaccactaca acccagcctgaagtccagaaaagaccatcagcaaggacaccagcaagaaccaggtgtc cctgaagctgagcagcgtgacagccgccgataccggcgtgtactactgcgccagagaca agggtacagctactactacagcatggactactggggccagggcaccaccgtgaccgtg tcaccgcgtcgaccaaggggccctcgggtgtccctctggcccttgccagcagaagcacc agcgaatctacagccgccctgggctgcctcgtgaaggactactttccgagcccgtagcc gtgtcctggaactctggcgtctgacaagcggcgtgcacacctttccagccgtgtccaga gcagcggcctgtactctctgagcagcgtcgtgacagtgccagcagcagcctgggcacc aagacctacacctgtaacgtggaccacaagcccagcaacaccaaggtggacaagcggg tggaatctaagtacggccctccctgccctcctgccagccctgaattctggggcgacc ctccgtgtcctgttcccccaagcccaaggacacctgatgatcagccggacccccga agtgacctgcgtggtggtggtgatgtgtcccaggaagatcccagggtgcagttcaattgtac gtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaaacagttcaaca gcacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaa gagtacaagtgaaggtgtccaacaaggccctgccagctccatcgagaaaaccatcag caaggccaagggccagccccgcagcctcaagtgtataacctgcccccttgccaggaag agatgaccaagaaccaggtgtccctgtggtgtctcgtgaaggcttctaccagcgcacat tgccgtggaatgggagagcaacggccagcccagaaactacaagaccacccccct gtgctggacagcagcggctcattctctgtactccaagctgaccgtggacaagagccggt ggcaggaaggcaacgtgttcagctgctcgtgatgcacaggccctgcacaaccactac accagaagtccctgtctctgtccctgggcaag	SEQ ID NO: 466
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	gtgt		
Heavy chain B	caggtgcagctggtggaatctggcggcggagtggtgcagcctggcagaagcctgagact gagctgtgccgccagcggcttcaccttcaccaaggcctggatgcactgggtgcgccagg cccttggaaagcagctggaatgggtggccagatcaaggacaagagcaacagctacgc cacctactacgccgacagcgtgaagggccggttcacatcagccgggacgacagcaag aacacctgtacctgcagatgaacagcctgcggggccaggacaccgccgtgtactactgt cggggcgtgtactatgccctgagccccttcgattactggggccagggaacctcgtgacc gtgtctagtagccaggtgcacctgacacagagcggaccggaagtgcggaagcctggca cctctgtgaagggtgctctgcaaggccccctggcaaacacctgaaaacctacgacctgact gggtgcgcagcgtgccaggacaggactgcagtggatgggtggtatcagccacgagg gcgacaagaaagtatcgtggaacggttcaaggccaaagtaccatcactgggacaga agcaccaacaccgcctacctgcagctgagcggcctgacctctggcgataccgccgtgt ctactgcgccaagggcagcaagcaccggctgagagactacgccctgtacgacgatgac ggcgccctgaactgggcccgtggatgtggactacctgagcaacctggaattctggggcca gggcacagccgtgaccgtgtcatctcgaccgccagcacaaggggcccatcgggtgttc ctctggccccttgacgcagaagcaccagcgaatctacagccgccctgggctgcctcgtga aggactactttcccagcccgtgaccgtgtcctggaactctggcgctctgacaagcggcgt gcacacctttccagccgtgtccagagcagcggcctgtactctctgagcagcgtcgtgac agtggccagcagcagcctgggcaccaagacctacacctgtaacgtggaccacaagccc agcaacaccaaggtggacaagcgggtggaatctaagtacggccctccctgccctccttgc ccagcccctgaatttctgggcggaccctccgtgttctgttcccccaaggcccaaggaca ccctgatgacagccggacccccgaagtgcctgcgtggtggtggtggtgtgtcccaggaa gatcccaggtgcagttcaattggtacgtggacggcgtggaagtgcacaacgccaagac caagcccagagaggaacagttcaacagcacctaccgggtggtgtccgtgctgaccgtgc tgcaccaggactggctgaacggcgaagagtacaagtgaagggtgtccaacaagggcctg cccagctccatcgagaaaacctacagcaaggccaagggccagccccgcgagcctcaag tgtgtaccctgccccctagccagggaagagatgaccaagaaccagggtgtccctgagctgtg ccgtgaaaggcttctaccccagcgacattgccgtggaatgggagagcaacggccagccc gagaacaactacaagaccacccccctgtgctggacagcgacgggtcattcttctgtgtg ccaagctgaccgtggacaagagccgggtggcaggaaggcaacgtgttcagctgtctccgtg atgcacgaggccctgcacaaccactacaccagaagtccctgtctctgtccctgggcaag	SEQ ID NO: 468	
Light chain B	gacttcgtgctgaccagagccctcacagcctgagcgtgacacctggcgagagcggcag catcagctgcaagagcagccactccctgatccacggcgaccggaacaactacctggcttg gtacgtgcagaagcccggcagatccccccagctgctgatctacctggccagcagcagag ccagcggcgtgcccgatagatttctggcagcggcagcgacaaggacttcacctgaag atcagccgggtggaaccgaggacgtgggcacctactactgtatgcagggcagagaga ggccctggacctttggccagggcaccaaggtggacatcaagggccagcccaaggccgc ccccgacatcgtgatgacctagacccccctgagcctgagcgtgacacctggacagcctg ccagcatcagctgcaagagcagccagagcctggtgcacaacaacgccaacacctacctg agctggtatctgcagaagcccggccagagccccagtcctgatctacaaggtgtccaac agattcagcggcgtgcccagacattctccggcagcggctctggcaccgacttcacctg aagatcagccgggtggaagccgaggacgtgggcgtgtactattgtggcaggggcaccc agtacccttcacctttggcagcggcaccgaaggtggaatcaagaccaagggccccagc cgtacggtggcgcctcccagcgtgttcattcttcccacctagcgacgagcagctgaagtcc ggcacagcctctgtcgtgtgcctgctgaacaacttctacccccgcgaggccaaagtgcag tggaaaggtggacaacgccttcagagcggcaacagccaggaaagcgtgaccgagcag gacagcaaggactccactacagcctgagcagcacctgacactgagcaaggccgact acgagaagcacaaggtgtacgcctgcgaagtgaccaccagggcctgtctagccccgtg accaagagcttcaaccggggcgagtgt	SEQ ID NO: 469	
Binding Protein 53 Amino Acid Sequences			
Heavy chain A	Qvqlqesgpglvkpsqtlstctvsgfslsdygvhwvrpppgkglewlgviwagggt nynpslksrktiskdtsknqvslklssvtaadtavvyecardkgyssyysmdywgqgtt vtvssastkgpsvflapcsrstsestaalgclvkdyfpepvtvswnsgaltsgvhtfpav lqssglyslssvvtvpssslgktytcnvdhkpsntkvdkrveskygnpcnncpapefl	SEQ ID NO: 470	

	ggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktpr eeqfnstyrvvsvltvlhqdwlngkeyckvsnkglpssiektiskakgqprepqvyl ppcqemtknqvslwclvkgfypsdiavewesngqpennyktpvldsdgsfflys kltvdksrwqegnvfscsvmhleahnhytqkslslslgk	
Light chain A	Divltqspaslavspgqratitcrasesveyyvtslmqwyqqkpgppklifaasve sgvparfsgsgsgtdftltinveandvanyycqsrkvpptfgggtkleikrtvaapsv fifppsdeqlksqtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdsdstys lsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 471
Heavy chain B	Qvqlvesgggvvqpgrslrlscaasgftftkawmhwwrqapgkqlwvaqi kdknsnyatyadsvkgrftisrddskntlylqmnslraedtavyycrgvyys pfdywgqgtlvtvssdkthtqvhltqsgpevrkpgtsvkvsckapgnltkydl hwwrsvpqgqlqwmgishegdkkviverfkakvtidwdrstntaylqlsgl tsgdtavyycakgskhrlrdyalydddgalnwavdvdylnlefwgqgtavtv ssdkthtastkgpsvflapcsrstsestaalgclvkdyfpepvtvswngaltsg vhtfpavlqssglyslssvvtvpssslgtkytcnvdhkpsntkvdkrveskygp pcppcpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfn wyvdgvevhnaktprreeqfnstyrvvsvltvlhqdwlngkeyckvsnkg lpssiektiskakgqprepqvctlpssqeemtknqvslscavkgfypsdiavew esngqpennyktpvldsdgsfflvscltvdksrwqegnvfscsvmhleah nhytqkslslslgk	SEQ ID NO: 472
Light chain B	Dfvltsphslsvtpgesasisckssshlihgdrnnylawyvqkprspqliylas rasgvpdrfsgsgsdktlktisrvetedvgtyycmqgrespwtfgggtkvdikdktdiv mtqtplsivtpgqpasisckssslvhnnantylswylqkpgqspqsllykvsnrfs gvpdrfsgsgsgtdftlktisrveadvgyycgqgtqypftfgsgtkveikdkttrtvaap svfifppsdeqlksqtasvvcllnnfyreakvqwkvdnalqsgnsqesvteqdsdst yslsstltlskadyekhkvyacevthqglsspvtksfnrgec	SEQ ID NO: 473
Binding Protein 53 Nucleotide Sequences		
Heavy chain A	caggtgcagctgcaggaatctggccctggcctcgtgaagcctagccagaccctgagcct gacctgtaccgtgtccggcttcagcctgagcgactacggcgtgcactgggtgcgccagcc acctggaaaaggcctggaatggctggcgctgatctggcgctggcggaggcaccacactaca acccagcctgaagtccagaaagaccatcagcaaggacaccagcaagaaccaggtgtc cctgaagctgagcagcgtgacagccgccgataccgccgtgtactactgcgccagagaca agggtacagctactactacagcatggactactggggccagggcaccaccgtgaccgtg tcacccgcgtcgaccaagggccctcgggtgtccctctggcccttgccagcagaagcacc agcgaatctacagccgccctgggctgcctcgtgaaggactactttcccgagcccgtagc gtgtctggaactctggcgtctgacaagcggcgtgcacaccttccagccgtgtccaga gcagcggcctgtactctgagcagcgtcgtgacagtgccagcagcagcctgggcacc aagacctacacctgaacgtggaccacaagcccagcaacaccaaggtggacaagcggg tggaatctaagtacggccctccctgccctcctgccagccctgaattctggcgaggacc ctccgtgttctgttcccccaagcccaaggacaccctgatgatcagccggacccccga agtgcacctgcgtggtggtggtgatgtgtccaggaagatcccagggtgcagttcaattggtac gtggacggcgtggaagtgcacaacgccaagaccaagcccagagagggaacagttcaaca gcacctaccgggtggtgtccgtgtgaccgtgtgcaccaggactggctgaacggcaca gagtacaagtgaaggtgtccaacaaggcctgccagctccatcgagaaaaccatcag caaggccaaggccagccccgcgagcctcaagtgtataacctgcccccttgccagggaag agatgaccaagaaccaggtgtccctgtggtgtctcgtgaaggcttctacccagcgacat tgccgtggaatgggagagcaacggccagcccgagaacaactacaagaccacccccct gtgctggacagcgacggctcattcttctgtactccaagctgaccgtggacaagagccggt ggcaggaaggcaacgtgttcagctgtccgtgatgcacgaggccctgcacaaccactac accagaagtccctgtctctgtccctgggcaag	SEQ ID NO: 474
Light chain A	gacatcgtgctgacacagagccctgtagcctggccgtgtctcctggacagagggccac catcacctgtagagccagcgagagcgtggaatattacgtgaccagcctgatgcagtgtat cagcagaagcccgccagcccccaagctgctgattttcgccgccagcaacgtggaaag	SEQ ID NO: 475

	cggcgtgccagccagattttccggcagcggctctggcaccgacttcaccctgaccatcaa ccccgtggaagccaacgacgtggccaactactactgccagcagagccggaaggtgcc tacacctttggccaggcaccagctggaaatcaagcgtacggtggccgctccagcgt gttcatcttccacctagcgacgagcagctgaagtccggcacagcctctgtcgtgtcctg ctgaacaacttctacccccgcgaggccaaggtgcagtggaaaggtggacaatgccctgca gagcggcaacagccaggaaagcgtgaccgagcaggacagcaaggactccacctag cctgagcagcacctgacctgagcaaggccgactacgagaagcacaaggtgtacgcct gcgaagtgacccaccaggcgctgtctagccccgtgaccaagagcttcaaccggggcga gtgt	
Heavy chain B	caggtgcagctggtggaatctggcggcgagtggtgcagcctggcagaagcctgagact gagctgtgccgccagcggcttacccttaccagcctggatgactgggtgcccagg ccctggaaagcagctggaatgggtggccagatcaaggacaagagcaacagctacgc cacctactacccgacagcgtgaaggccggttaccatcagccgggacgacagcaag aacacctgtacctgcagatgaacagcctgcgggcccaggacaccgccgtgtactactgt cggggcgctgtactatgccctgagcccttcgattactggggccagggaacctctgtgacc gtgtctagtgcacaaacccataccaggtgcacctgacacagagcggaccggaaagtgcg gaagcctggcacctctgtgaaggtgtcctgcaaggccctggcaacacctgaaaacct cgacctgcactgggtgcgcagcgtgccaggacaggactgcagtggatgggctggatc agccacgaggcgcacaagaaagtatcgtggaacggttcaaggccaaagtaccatcg actgggacagaagcacaacaccgcctacctgcagctgagcggcctgacctctggcgat accgccgtgtactactgcgcaagggcagcaagcaccggctgagagactacgccctgta cgacgatgacggcgcctgaactggccgtggatgtggactacctgagcaacctggaatt ctggggccagggcacagccgtgacctgtcatctgataagaccacaccgccagcaca aggggccatcggtgtccctctggcccttgcagcagaagcaccagcgaatctacagccg ccctgggctgctctgtgaaggactacttcccagccctgacctgtcctggaactctgg cgctctgacaagcggcgtgcacaccttccagcgtgtccagagcagcggcctgtactc tctgagcagcgtcgtgacagtgccagcagcagcctgggcaccaagacctacacctgta acgtggaccacaagcccagcaacaccaaggtggacaagcgggtggaatctaagtacgg ccctccctgcctccttggccagccctgaatttctgggcggaccctccgtgttctgttccc cccaaagcccaaggacacctgatgatcagccggacccccgaagtgcctgcgtggtg gtggatgtgtcccaggaagatcccagggtgcagttcaattgtactgtggacggcgtggaa gtgcacaacgccaaagaccaagcccagaggaacagttcaacagcacctaccgggtgg tgtccgtgctgacctgctgcaccaggactggctgaacggcaagagtacaagtgaag gtgtccaacaaggcctgccagctccatcgagaaaaccatcagcaaggccaaggcc agccccgcgacctcaagtgtgtacctgccccctagccagggaagagatgaccaagaac caggtgtccctgagctgtgccgtgaaaggcttctacccagcgacattgccgtggaatgg gagagcaacggccagcccagacaactacaagaccacccccctgtgtgacagcg acggctcattcttctggtgtcaagctgacctggacaagagccgggtggcagggaaggca acgtgttcagctgctcctgatgcagaggccctgcacaaccactacaccagaagtccc tgtctctgtccctgggcaag	SEQ ID NO: 476
Light chain B	gacttcgtgtgaccagagccctcacagcctgagcgtgacacctggcgagagcgcag catcagctgcaagagcagccactccctgatccacggcgaccggaacaactacctggcttg gtactgtcagaagcccggcagatccccccagctgtgtatctacctggccagcagcagag ccagcggcgtgcccgatagattttctgcagcggcagcgacaaggacttcacctgaag atcagccgggtggaaaccgaggacgtgggcacctactactgtatgcagggcagagaga gccccctggaccttggccagggcaccaaggtggacatcaaggacaaaaccataccgac atcgtgatgaccagacccccctgagcctgagcgtgacacctggacagcctgccagcat cagctgcaagagcagccagagcctggtgcacaacaacgcaaacctacctgagctggt atctgcagaagcccggccagagccccagtcctgatctacaaggtgtccaacagattca gcggcgtgcccagacattctccggcagcggctctggcaccgacttcacctgaagatca gcccgggtggaagccgaggacgtggcgtgtactattgtggcagggcaccagtagccc cttcaccttggcagcggcaccaaggtggaatcaaggataagaccatacccgtacgggt ggccgctcccagcgtgttcatcttccacctagcgacgagcagctgaagtccggcagac ctctgtcgtgtcctgtgaacaacttctacccccgcgaggccaagtgagtggaaggtg	SEQ ID NO: 477

	gacaacgccctgcagagcggcaacagccaggaaagcgtgaccgagcaggacagcaa ggactccacctacagcctgagcagcacctgacactgagcaaggccgactacgagaag cacaaggtgtacgcctgcgaagtgaccaccagggcctgtctagccccgtgaccaagag cttcaaccggggcgagtgt	
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Table A: CDR sequences of binding proteins

Ab	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
CD4BS "a"	dctln (SEQ ID NO: 248)	wlkprggavnyarplgg (SEQ ID NO: 249)	gkncdynwdfch (SEQ ID NO: 250)	rtsgygslla (SEQ ID NO: 266)	sgstraa (SEQ ID NO: 267)	qqyef (SEQ ID NO: 268)
CD4BS "b"	GYTFTAHI (SEQ ID NO: 251)	IKPQYGAV (SEQ ID NO: 252)	drsygdsswalda (SEQ ID NO: 253)	QGVGSD (SEQ ID NO: 269)	HTS (SEQ ID NO: 270)	qvlqf (SEQ ID NO: 271)
MPER	gfdfdnaw (SEQ ID NO: 254)	itgpggegwsv (SEQ ID NO: 255)	tgkyydfwsgyppgeeyfqd (SEQ ID NO: 256)	rgdslrshyas (SEQ ID NO: 272)	gknnrps (SEQ ID NO: 273)	ssrdksgrlsrv (SEQ ID NO: 274)
V1/V2 dir. "a"	GNTLKYD (SEQ ID NO: 257)	ISHEGDKK (SEQ ID NO: 258)	cakgskhrlrdyalydddgalnwavdvylsnlefw (SEQ ID NO: 259)	hslhgdrrny (SEQ ID NO: 275)	las (SEQ ID NO: 276)	cmqgrespwtf (SEQ ID NO: 277)
V3 dir.	SGASISDSY (SEQ ID NO: 260)	VHKSGDT (SEQ ID NO: 261)	ARTLHGRIYGIVAFNEWFTYFYMDV (SEQ ID NO: 262)	SLGSRA (SEQ ID NO: 278)	NNQ (SEQ ID NO: 279)	HIWDSRVPTKWV (SEQ ID NO: 280)
V1/V dir. "b"	QFRFDGYG (SEQ ID NO: 263)	ISHDGIKK (SEQ ID NO: 264)	CAKDLREDECEEWWSYDFGKQLPCA SRGGLVGIADNW (SEQ ID NO: 265)	TSNIGNNF (SEQ ID NO: 281)	ETD (SEQ ID NO: 282)	atwaaslsarv (SEQ ID NO: 283)

Ab	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
Anti-CD28	GYTFTSY (SEQ ID NO: 479)	IYPGNVNT (SEQ ID NO: 480)	trshyglwfnfdv (SEQ ID NO: 481)	QNIYVW (SEQ ID NO: 488)	KAS (SEQ ID NO: 489)	qqgqtypyt (SEQ ID NO: 490)
Anti-CD28	GFSLSDYG (SEQ ID NO: 482)	IWAGGGT (SEQ ID NO: 483)	ardkgyssyysmd (SEQ ID NO: 484)	ESVEYVTS (SEQ ID NO: 491)	AAS (SEQ ID NO: 492)	qgsrkvpvt (SEQ ID NO: 493)
Anti-CD3	GFTFTKAW (SEQ ID NO: 485)	IKDKSNS (SEQ ID NO: 486)	rgvyyspfdy (SEQ ID NO: 487)	QSLVHNNANTY (SEQ ID NO: 494)	KVS (SEQ ID NO: 495)	gggttyp (SEQ ID NO: 496)

Table B: CDR sequences of parental antibodies

Ab	CDR_H1	CDR_H2	CDR_H3	CDR_L1	CDR_L2	CDR_L3
CD4BS "a"	DCTLN (SEQ ID NO: 248)	LKPRGGAVNYARP LQ (SEQ ID NO: 497)	GKNC DYNWDFEH (SEQ ID NO: 250)	RTSQYGS LA (SEQ ID NO: 266)	SGSTRAA (SEQ ID NO: 267)	QQYEF (SEQ ID NO: 268)
CD4BS "b"	GYTFTAHI (SEQ ID NO: 251)	IKPQYGAV (SEQ ID NO: 252)	DRSYGDSSWALDA (SEQ ID NO: 253)	QGVGSD (SEQ ID NO: 269)	HTS (SEQ ID NO: 270)	QVLQF (SEQ ID NO: 271)
MPER	GFD FDN AW (SEQ ID NO: 254)	ITGPGEGWSV (SEQ ID NO: 255)	TGKYYDFW SGYP PGEEYFQ D (SEQ ID NO: 256)	SLRSHY (SEQ ID NO: 500)	GKN (SEQ ID NO: 501)	SSRDKSGSRLSV (SEQ ID NO: 274)
MPER_100W	GFD FDN AW (SEQ ID NO: 254)	ITGPGEGWSV (SEQ ID NO: 255)	TGKYYDFW WGYP PGEEYF QD (SEQ ID NO: 498)	SLRSHY (SEQ ID NO: 500)	GKN (SEQ ID NO: 501)	SSRDKSGSRLSV (SEQ ID NO: 274)
V1/V2 directe d "a"	GNTLKYD (SEQ ID NO: 257)	ISHEGDKK (SEQ ID NO: 258)	CAKGS KHLR DYAL YDDD GALN W AV DV DYLSNLEFW (SEQ ID NO: 259)	HSLIHGDRNNY (SEQ ID NO: 275)	LAS (SEQ ID NO: 276)	CMQGRESPWTF (SEQ ID NO: 277)
V1/V2 directe d "b"	QFRFDGYG (SEQ ID NO: 263)	ISHDGIKK (SEQ ID NO: 264)	CAKDLREDECEEWWSYDFGKQLPCA SRGGLVGIADNW (SEQ ID NO: 265)	TSNIGNNF (SEQ ID NO: 281)	ETD (SEQ ID NO: 282)	ATWAASLSAR V (SEQ ID NO: 283)
V3 directe	GASISDSY (SEQ ID NO: 499)	VHKSGDT (SEQ ID NO: 261)	ARTLHGRIYGIVAFNEWFTYFYMDV	SLGSRA (SEQ ID NO: 278)	NNQ (SEQ ID NO: 279)	HIWDSRVPTKW V

d			(SEQ ID NO: 262)			(SEQ ID NO: 280)
CD28	GYTFTSY (SEQ ID NO: 479)	IYPGNVNT (SEQ ID NO: 480)	TRSHYGLDWNFDV (SEQ ID NO: 481)	QNIYVW (SEQ ID NO: 488)	KAS (SEQ ID NO: 489)	QQGQTYPYT (SEQ ID NO: 490)
CD28_2	GFSLSDYG (SEQ ID NO: 482)	IWAGGGT (SEQ ID NO: 483)	ARDKGYSYYSM (SEQ ID NO: 484)	ESVEYYVTS (SEQ ID NO: 491)	AAS (SEQ ID NO: 492)	QQSRKVPYT (SEQ ID NO: 493)
CD3	GFTFTKAW (SEQ ID NO: 485)	IKDKSNS (SEQ ID NO: 486)	RGVYYALSPFDY (SEQ ID NO: 487)	QSLVHNNANTY (SEQ ID NO: 494)	KVS (SEQ ID NO: 495)	GQGTQYP (SEQ ID NO: 496)

Table C: Variable domain sequences of parental antibodies

Ab Name	V _H	V _L
CD4BS “a”	QVQLVQSGGQMKKPGESMRISCRASGYEFIDCTLNWLAP GKRPEWMGWLKPRGGAVNYARPLQGRVTMTRDVYSDTAF LELRSLTVDDTAVYFCTRGNKCDYNWDFEHWGRGTPVIVS S (SEQ ID NO: 502)	EIVLTQSPGTLSPGETAISCRTSQYGS LA WYQQ RPGQAPRLVIYSGSTRAAGIPDRFSGSRWGPDPYNL TISNLESGDFGVYYCQQYE FF GQGTKVQVDIK (SEQ ID NO: 512)
CD4BS “b”	RAHLVQSGTAMKKPGASVRVSCQTSGYTFTAHLFWFRQAP GRGLEWVGWIKPQYGAVNFGGGFRDRVTLTRDVYREIAY MDIRGLKPDDTAVYYCARD RSYGDSSWALDA WGQGTTVV VSA (SEQ ID NO: 503)	YIHVTQSPSSLSVSI G DRVTINCQTSQGVGSD L HW YQHKPGRAPKLLIH HTSS VEDGVPSRFS G SGFHTS FNLTISDLQADDIATYYCQVLQ FF GRGSR L HIK (SEQ ID NO: 513)
CD4BS “b” (Δglycan)	RAHLVQSGTAMKKPGASVRVSCQTSGYTFTAHLFWFRQAP GRGLEWVGWIKPQYGAVNFGGGFRDRVTLTRDVYREIAY MDIRGLKPDDTAVYYCARD RSYGDSSWALDA WGQGTTVV VSA (SEQ ID NO: 503)	YIHVTQSPSSLSVSI G DRVTINCQTSQGVGSD L HW YQHKPGRAPKLLIH HTSS VEDGVPSRFS G SGFHTS F Q L T ISDLQADDIATYYCQVLQ FF GRGSR L HIK (SEQ ID NO: 514)
CD4BS “b” (Δisomerization D55E)	RAHLVQSGTAMKKPGASVRVSCQTSGYTFTAHLFWFRQAP GRGLEWVGWIKPQYGAVNFGGGFRDRVTLTRDVYREIAY MDIRGLKPDDTAVYYCARD RSYGDSSWALDA WGQGTTVV VSA (SEQ ID NO: 503)	YIHVTQSPSSLSVSI G DRVTINCQTSQGVGSD L HW YQHKPGRAPKLLIH HTSS VE E GVPSRFS G SGFHTS FNLTISDLQADDIATYYCQVLQ FF GRGSR L HIK (SEQ ID NO: 515)
CD4BS “b” (Δisomerization)	RAHLVQSGTAMKKPGASVRVSCQTSGYTFTAHLFWFRQAP GRGLEWVGWIKPQYGAVNFGGGFRDRVTLTRDVYREIAY	YIHVTQSPSSLSVSI G DRVTINCQTSQGVGSD L HW YQHKPGRAPKLLIH HTSS VEDAVPSRFS G SGFHTS

n G56A)	MDIRGLKPDDTAVYYCARD <u>RSYGDSSWALDAWGQGT</u> TVV VSA (SEQ ID NO: 503)	FNLTISDLQADDIATYYC <u>QVLQFFGRGSRLHIK</u> (SEQ ID NO: 516)
CD4BS “b” (Δglycan / Δisomerization D55E)	RAHLVQSGTAMKKPGASVRVSCQTS <u>GYTFTAHLFWFRQAP</u> GRGLEWVGWIK <u>PQYGA</u> VNF GGG FRDRVTLTRDVYREIAY MDIRGLKPDDTAVYYCARD <u>RSYGDSSWALDAWGQGT</u> TVV VSA (SEQ ID NO: 503)	YIHVTQSPSSLSVSIGDRVTINCQTS <u>QGVGSDLHW</u> YQHKPGRAPKLLIH <u>HTSSVE</u> EGVPSRFSGSGFHTS F QLTISDLQADDIATYYC <u>QVLQFFGRGSRLHIK</u> (SEQ ID NO: 517)
MPER	EVRLVESGGGLVKPGGSLRLSCSASGFD <u>FDNAWMTWVRQP</u> PGKGLEWVGRI <u>TGP</u> GEGWSVDYAESVKGRFTISRDNKNTL YLEMNNVRTEDTGYYFCART <u>GKYYDFWSGYPPGEEYFQD</u> WGQGTLVIVSS (SEQ ID NO: 504)	ASELTQDPAVSVALKQTVTITCRGDS <u>SLRSHYASW</u> YQKKPGQAPVLLFY <u>GKNNRPSGIPDRFSGSASGN</u> RASLTITGAQAEDEADYYC <u>SSRDKSGSRLSVFGG</u> GTKLTVL (SEQ ID NO: 518)
MPER_100W	EVRLVESGGGLVKPGGSLRLSCSASGFD <u>FDNAWMTWVRQP</u> PGKGLEWVGRI <u>TGP</u> GEGWSVDYAESVKGRFTISRDNKNTL YLEMNNVRTEDTGYYFCART <u>GKYYDFW</u> GYPPGEEYFQD WGQGTLVIVSS (SEQ ID NO: 505)	ASELTQDPAVSVALKQTVTITCRGDS <u>SLRSHYASW</u> YQKKPGQAPVLLFY <u>GKNNRPSGIPDRFSGSASGN</u> RASLTITGAQAEDEADYYC <u>SSRDKSGSRLSVFGG</u> GTKLTVL (SEQ ID NO: 518)
V1/V2 directed “a”	QVHLTQSGPEVRKPGTSVKVSCKAPGNTL <u>KTYDLHWVRSV</u> PGQGLQWMGWIS <u>HEGDKK</u> VIVERFKAKVTIDWDRSTNTAY LQLSGLTSGDTAVYYCAKGSKHRLRDYALYDDDGALNWA VDVDYLSNLEFWGQGTAVTVSS (SEQ ID NO: 506)	DFVLTQSPHLSVTPGESASISCKSSH <u>SLIHGDRNN</u> YLAWYVQKPGRSPQLLIY <u>LASSRASGV</u> PDRFSGS GSDKDFTLKISRVEDVDVGTYYC <u>MQGRES</u> PWTFG QGTKVDIK (SEQ ID NO: 519)
V1/V2 directed “b”	QVQLVESGGGVVQPGTSLRLSCAASQFRFDGYGMHWVRQ APGKGLEWVASIS <u>HDGIKKY</u> HAEKVWGRFTISRDNKNTLY LQMNSLRPEDTALYYCAKDLREDECEEWWS SDYY DFGKQLP CAKSRGGLVGIADNWGQGTMTVTVSS (SEQ ID NO: 507)	QSVLTQPPSVSAAPGQKVTISCSGNTSNIGNNEVS WYQQRPGRAPQLLIY <u>ETDKRPSGIPDRFSASKSGT</u> SGTLAITGLQTGDEADYYC <u>CATWAASLSSARVFGT</u> GTKVIVL (SEQ ID NO: 520)
V3 directed	QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWSWIRRS PGKLEWIGYV <u>HKSGD</u> TNYSPLSKSRVNLSDTSKNQVSLSLV AATAADSGKYYCARTLHGRRIGIVAFNEWFTYFYMDVW GNGTQVTVSS (SEQ ID NO: 508)	SDISVAPGETARISCGEKS <u>LGSR</u> AVQWYQHRAGQ APSLIY <u>NNQDRPSGIPERFSGSPDSPFGTTATLTIT</u> SVEAGDEADYYC <u>HIWDSRVPTKWV</u> FGGGTTLTV L (SEQ ID NO: 521)
CD28	QVQLVQSGAEVVKPGASVKVSCKASGYTFTSY <u>YIH</u> WVRQA PGQGLEWIGSIY <u>PGNVNTNYA</u> QKFQGRATLTVDTSISTAYM	DIQMTQSPSSLSASVGDRVTITCQASQNIYVWLN WYQQKPGKAPKLLIY <u>KAS</u> NLHTGVPSRFSGSGSG

	ELSRLRSDDTAVYYC <u>TRSHYGLDWNFDVWGKGTTVT</u> VSS (SEQ ID NO: 509)	TDFTLTISLQPEDATYYC <u>QQGQ</u> TYPYTFGQGTK LEIK (SEQ ID NO: 522)
CD28_2	QVQLQESGPGLVKPSQTLSTCTVSG <u>FSLSDYGVHWVRQPP</u> GKGLEWLGVIWAGGGTNYNPSLKSRTISKDTSKNQVSLKL SSVTAADTAVYYC <u>ARDKGYSYYYSM</u> DYWGQGTTVTVSS (SEQ ID NO: 510)	DIVLTQSPASLAVSPGQRATITCRASESVEYYVTS <u>LMQWYQQKPGQPPKLLIFAA</u> SNVESGVPARFSGS GSGTDFTLTINPVEANDVANYYC <u>QQSRKVPYTFG</u> QGTKLEIK (SEQ ID NO: 523)
CD3	QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWVRQ APGKQLEWVAQIKDKSN <i>SY</i> ATYYADSVKGRFTISRDDSKNT LYLQMNSLRAEDTAVYYC <u>RGVYYALSPFDYWGQ</u> GLVTV SS (SEQ ID NO: 511)	DIVMTQTPLSLSVTPGQPASISCKSSQSLVHNNAN <u>TYLSWYLQKPGQSPQSLIYKV</u> SNRFSGVPDRFSGS GSGTDFTLKISRVEAEDVGVYYC <u>CGQGTQYP</u> FTFG SGTKVEIK (SEQ ID NO: 524)

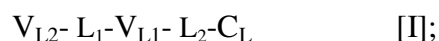
CDR sequences are underlined.

Variable domain modifications are shown in bold and italicized.

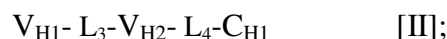
CLAIMS

What is claimed is:

1. A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



a second polypeptide chain comprises a structure represented by the formula:



a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain; and

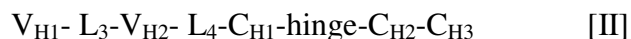
L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

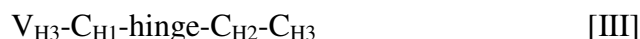
2. A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 and L_4 are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

3. The binding protein of claim 1 or claim 2, wherein the one or more HIV target protein is selected from the group consisting of glycoprotein 120, glycoprotein 41 and glycoprotein 160.

4. The binding protein of claim 1 or claim 2, wherein the binding protein is trispecific and capable of specifically binding three different epitopes on a single HIV target protein.

5. The binding protein of claim 1 or claim 2, wherein the binding protein is trispecific and capable of specifically binding two different epitopes on a first HIV target protein, and one epitope on a second HIV target protein, wherein the first and second HIV target proteins are different.

6. The binding protein of claim 1 or claim 2, wherein the binding protein is trispecific and capable of specifically binding three different antigen targets.

7. The binding protein of claim 1 or claim 2, wherein the binding protein is capable of inhibiting the function of one or more HIV target proteins.

8. The binding protein of any one of claims 1-7, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively.

9. The binding protein of any one of claims 1-7, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

10. The binding protein of any one of claims 1-9, wherein V_{L1} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

11. The binding protein of any one of claims 1-10, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively.

12. The binding protein of any one of claims 1-10, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

13. The binding protein of any one of claims 1-12, wherein V_{L2} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

14. The binding protein of any one of claims 1-13, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth

in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; or a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively.

15. The binding protein of any one of claims 1-13, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

16. The binding protein of any one of claims 1-15, wherein V_{L3} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, and 521.

17. The binding protein of any one of claims 1-16, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively.

18. The binding protein of any one of claims 1-16, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

19. The binding protein of any one of claims 1-18, wherein V_{H1} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.

20. The binding protein of any one of claims 1-19, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively.

21. The binding protein of any one of claims 1-19, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.
22. The binding protein of any one of claims 1-21, wherein V_{H2} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.
23. The binding protein of any one of claims 1-22, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; or a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively.
24. The binding protein of any one of claims 1-22, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.
25. The binding protein of any one of claims 1-24, wherein V_{H3} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, and 508.
26. The binding protein of any one of claims 1-25, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 266, a CDR-L2 comprising the sequence of SEQ ID NO: 267, and a CDR-L3 comprising the sequence of SEQ ID NO: 268; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the

sequence of SEQ ID NO: 259; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 248, a CDR-H2 comprising the sequence of SEQ ID NO: 497, and a CDR-H3 comprising the sequence of SEQ ID NO: 250.

27. The binding protein of any one of claims 1-25, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 512; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 502.

28. The binding protein of any one of claims 1-27, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 512; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 502.

29. The binding protein of any one of claims 1-25, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of

SEQ ID NO: 256; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

30. The binding protein of any one of claims 1-25, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

31. The binding protein of any one of claims 1-25 and 29-30, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

32. The binding protein of any one of claims 1-25, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 275, a CDR-L2 comprising the sequence of SEQ ID NO: 276, and a CDR-L3 comprising the sequence of SEQ ID NO: 277; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 500, a CDR-L2 comprising the sequence of SEQ ID NO: 501, and a CDR-L3 comprising the sequence of SEQ ID NO: 274; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO:

271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 257, a CDR-H2 comprising the sequence of SEQ ID NO: 258, and a CDR-H3 comprising the sequence of SEQ ID NO: 259; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 254, a CDR-H2 comprising the sequence of SEQ ID NO: 255, and a CDR-H3 comprising the sequence of SEQ ID NO: 256; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

33. The binding protein of any one of claims 1-25, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 519; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 518; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 506; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 504; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

34. The binding protein of any one of claims 1-25 and 32-33, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 519; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 518; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 506; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 504; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

35. The binding protein of claim 1, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

36. The binding protein of claim 1, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

37. The binding protein of claim 1, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

38. The binding protein of claim 1, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

39. The binding protein of claim 1, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid

substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

40. The binding protein of claim 2, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

41. The binding protein of claim 2, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

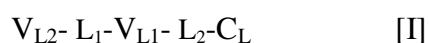
42. The binding protein of claim 2, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

43. The binding protein of claim 1 or claim 2, wherein at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length.

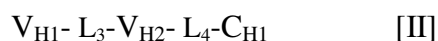
44. The binding protein of claim 1 or claim 2, wherein L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length.

45. The binding protein of any one of claims 1-44, wherein L₁ comprises Asp-Lys-Thr-His-Thr (SEQ ID NO: 525).

46. A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124, 130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and

wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 10, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123,

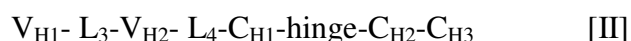
129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265.

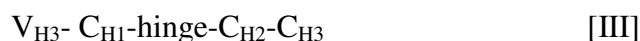
47. A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 , and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 10, 12, 18, 20, 26, 28, 34, 36,

42, 44, 50, 52, 58, 60, 66, 68, 74, 76, 82, 84, 90, 92, 98, 100, 106, 108, 114, 116, 122, 124, 130, 132, 138, 140, 146, 148, 154, 156, 162, 164, 170, 172, 178, 180, 186, 188, 194, 196, 202, 204, 210, 212, 218, 220, 226, 228, 233, 235, 241, 243; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-283; and
wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 9, 11, 17, 10, 25, 27, 33, 35, 41, 43, 49, 51, 57, 59, 65, 67, 73, 75, 81, 83, 89, 91, 97, 99, 105, 107, 113, 115, 121, 123, 129, 131, 137, 139, 145, 147, 153, 155, 161, 163, 169, 171, 177, 179, 185, 187, 193, 195, 201, 203, 209, 211, 217, 219, 225, 227, 232, 234, 240, 242; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-265.

48. The binding protein of claim 46, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

49. The binding protein of claim 46, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

50. The binding protein of claim 46, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1} , the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and

407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

51. The binding protein of claim 46, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

52. The binding protein of claim 46, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

53. The binding protein of claim 47, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

54. The binding protein of claim 47, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are

Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

55. The binding protein of claim 47, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

56. The binding protein of claim 46 or claim 47, wherein at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length.

57. The binding protein of claim 46 or claim 47, wherein L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length.

58. The binding protein of any one of claims 46-57, wherein L₁ comprises Asp-Lys-Thr-His-Thr (SEQ ID NO: 525).

59. A binding protein comprising a first polypeptide chain, a second polypeptide chain, a third polypeptide chain and a fourth polypeptide chain wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 4; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 3 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 3; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 1 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 2;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 12; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 11 or an amino acid sequence that is at least 95% identical to the amino acid sequence of

SEQ ID NO: 11; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 9; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 10 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 10;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 20; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 19 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 19; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 17 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 17; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 18 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 18;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 28 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 28; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 27 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 27; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 25 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 25; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 26 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 26;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 36 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 36; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 35 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 35; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 33 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 33; and the fourth polypeptide chain comprises the amino acid sequence of SEQ

ID NO: 34 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 34;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 44 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 44; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 43 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 43; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 41 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 41; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 42 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 42;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 52 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 52; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 51 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 49 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 49; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 50 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 60 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 60; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 59 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 59; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 57 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 57; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 58 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 58;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 68 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ

ID NO: 68; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 67 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 67; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 65 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 65; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 66 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 66;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 76 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 76; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 75 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 75; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 73 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 73; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 74 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 74;

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 84 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 84; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 83 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 83; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 81 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 81; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 82 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 82;

(l) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 92 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 92; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 91 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 91; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 89 or an amino acid sequence that is at least 95% identical to the amino acid sequence of

SEQ ID NO: 89; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 90 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 90;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 100 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 100; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 99 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 99; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 97 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 97; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 98 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 98;

(n) the first polypeptide comprises the amino acid sequence of SEQ ID NO: 108 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 108; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 107; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 105 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 105; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 106;

(o) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 116 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 116; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 115; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 113 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 113; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 114;

(p) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 124 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 124; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 123 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 123; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 121 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 121; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 122 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 122;

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 132 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 132; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 131 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 131; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 129 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 129; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 130 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 130;

(r) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 140 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 140; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 139 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 139; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 137; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 138;

(s) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 148 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 148; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 147 or an amino acid sequence that is at least 95% identical to the amino acid sequence

of SEQ ID NO: 147; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 145 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 145; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 146 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 146;

(t) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 156 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 156; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 155 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 155; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 153 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 153; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 154 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 154;

(u) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 164 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 164; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 163 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 163; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 161 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 161; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 162 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 162;

(v) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 172 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 172; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 171 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 171; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 169 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 169; and the fourth polypeptide chain comprises the amino acid

sequence of SEQ ID NO: 170 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 170;

(w) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 180 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 180; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 179 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 179; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 177 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 177; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 178 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 178;

(x) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 188 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 188; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 187 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 187; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 185 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 185; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 186 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 186;

(y) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 196 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 196; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 195 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 195; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 193 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 193; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 194 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 194;

(z) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 204 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ

ID NO: 204; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 203 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 203; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 201 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 201; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 202 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 202;

(aa) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 212 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 212; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 211 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 211; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 209 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 209; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 210 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 210;

(bb) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 220 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 220; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 219 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 219; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 217 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 217; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 218 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 218;

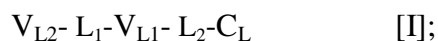
(cc) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 228 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 228; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 227 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 227; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 225 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 225; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 226 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 226;

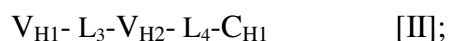
(dd) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 235 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 235; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 234 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 234; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 232 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 232; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 233 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 233; or

(ee) first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 243 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 243; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 242 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 242; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 240 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 240; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 241 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 241.

60. A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins and one or more T cell target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



a second polypeptide chain comprises a structure represented by the formula:



a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L₁, L₂, L₃, and L₄ are amino acid linkers;

and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair.

61. A binding protein comprising four polypeptide chains that form three antigen binding sites that specifically bind one or more HIV target proteins and one or more T cell target proteins, wherein a first polypeptide chain comprises a structure represented by the formula:



a second polypeptide chain comprises a structure represented by the formula:



a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and
L₁, L₂, L₃, and L₄ are amino acid linkers;
and wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over
light chain-heavy chain pair.

62. The binding protein of claim 60 or claim 61, wherein the one or more HIV target proteins are selected from the group consisting of glycoprotein 120, glycoprotein 41 and glycoprotein 160.

63. The binding protein of claim 60 or claim 61, wherein the one or more T cell target proteins are CD3 or CD28.

64. The binding protein of claim 60 or claim 61, wherein the binding protein is trispecific and capable of specifically binding an HIV target protein and two different epitopes on a single T cell target protein.

65. The binding protein of claim 60 or claim 61, wherein the binding protein is trispecific and capable of specifically binding an HIV target protein and two different T cell target proteins.

66. The binding protein of claim 60 or claim 61, wherein the binding protein is trispecific and capable of specifically binding a T cell target protein and two different epitopes on a single HIV target protein.

67. The binding protein of claim 60 or claim 61, wherein the binding protein is trispecific and capable of specifically binding a T cell target protein and two different HIV target proteins.

68. The binding protein of claim 60 or claim 61, wherein the first and second polypeptide chains form two antigen binding sites that specifically target two T cell target proteins, and the third and fourth polypeptide chains form an antigen binding site that specifically binds an HIV target protein.

69. The binding protein of any one of claims 60-68, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a

sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively.

70. The binding protein of any one of claims 60-68, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

71. The binding protein of any one of claims 60-70, wherein V_{L1} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

72. The binding protein of any one of claims 60-71, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively.

73. The binding protein of any one of claims 60-71, wherein V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

74. The binding protein of any one of claims 60-73, wherein V_{L2} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

75. The binding protein of any one of claims 60-74, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 comprising a sequence as set forth in SEQ ID NOs: 266, 267, and 268, respectively; a sequence as set forth in SEQ ID NOs: 269, 270, and 271, respectively; a sequence as set forth in SEQ ID NOs: 500, 501, and 274, respectively; a sequence as set forth in SEQ ID NOs: 275, 276, and 277, respectively; a sequence as set forth in SEQ ID NOs: 281, 282, and 283, respectively; a sequence as set forth in SEQ ID NOs: 278, 279, and 280, respectively; a sequence as set forth in SEQ ID NOs: 488, 489, and 490, respectively; a sequence as set forth in SEQ ID NOs: 491, 492, and 493, respectively; or a sequence as set forth in SEQ ID NOs: 494, 495, and 496, respectively.

76. The binding protein of any one of claims 60-74, wherein V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

77. The binding protein of any one of claims 60-76, wherein V_{L3} comprises a light chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, and 524.

78. The binding protein of any one of claims 60-77, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively.

79. The binding protein of any one of claims 60-77, wherein V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

80. The binding protein of any one of claims 60-79, wherein V_{H1} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

81. The binding protein of any one of claims 60-80, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively.

82. The binding protein of any one of claims 60-80, wherein V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

83. The binding protein of any one of claims 60-82, wherein V_{H2} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

84. The binding protein of any one of claims 60-83, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 comprising a sequence as set forth in SEQ ID NOs: 248, 497, and 250, respectively; a sequence as set forth in SEQ ID NOs: 251, 252, and 253, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 256, respectively; a sequence as set forth in SEQ ID NOs: 254, 255, and 498, respectively; a sequence as set forth in SEQ ID NOs: 257, 258, and 259, respectively; a sequence as set forth in SEQ ID NOs: 263, 264, and 265, respectively; a sequence as set forth in SEQ ID NOs: 499, 261, and 262, respectively; a sequence as set forth in SEQ ID NOs: 479, 480, and 481, respectively; a sequence as set forth in SEQ ID NOs: 482, 483, and 484, respectively; or a sequence as set forth in SEQ ID NOs: 485, 486, and 487, respectively.

85. The binding protein of any one of claims 60-83, wherein V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

86. The binding protein of any one of claims 60-85, wherein V_{H3} comprises a heavy chain variable domain comprising a sequence selected from the group consisting of SEQ ID NOs: 502, 503, 504, 505, 506, 507, 508, 509, 510, and 511.

87. The binding protein of any one of claims 60-86, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 488, a CDR-L2 comprising the sequence of SEQ ID NO: 489, and a CDR-L3 comprising the sequence of SEQ ID NO: 490; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 494, a CDR-L2 comprising the sequence of SEQ ID NO: 495, and a CDR-L3 comprising the sequence of SEQ ID NO: 496; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 479, a CDR-H2 comprising the sequence of SEQ ID NO: 480, and a CDR-H3 comprising the sequence of SEQ ID NO: 481; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 485, a CDR-H2 comprising the sequence of SEQ ID NO: 486, and a CDR-H3 comprising the sequence of SEQ ID NO: 487; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

88. The binding protein of any one of claims 60-86, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 522; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 524; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 509; V_{H2} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 511; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a

heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

89. The binding protein of any one of claims 60-88, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 522; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 524; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 509; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 511; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

90. The binding protein of any one of claims 60-86, wherein V_{L1} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 494, a CDR-L2 comprising the sequence of SEQ ID NO: 495, and a CDR-L3 comprising the sequence of SEQ ID NO: 496; V_{L2} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 488, a CDR-L2 comprising the sequence of SEQ ID NO: 489, and a CDR-L3 comprising the sequence of SEQ ID NO: 490; V_{L3} comprises a CDR-L1 comprising the sequence of SEQ ID NO: 269, a CDR-L2 comprising the sequence of SEQ ID NO: 270, and a CDR-L3 comprising the sequence of SEQ ID NO: 271; V_{H1} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 485, a CDR-H2 comprising the sequence of SEQ ID NO: 486, and a CDR-H3 comprising the sequence of SEQ ID NO: 487; V_{H2} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 479, a CDR-H2 comprising the sequence of SEQ ID NO: 480, and a CDR-H3 comprising the sequence of SEQ ID NO: 481; and V_{H3} comprises a CDR-H1 comprising the sequence of SEQ ID NO: 251, a CDR-H2 comprising the sequence of SEQ ID NO: 252, and a CDR-H3 comprising the sequence of SEQ ID NO: 253.

91. The binding protein of any one of claims 60-86, wherein V_{L1} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 524; V_{L2} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 522; V_{L3} comprises a CDR-L1, CDR-L2, and CDR-L3 of a light chain variable domain comprising the light chain variable domain sequence of SEQ ID NO: 513; V_{H1} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 511; V_{H2} comprises a CDR-H1, CDR-H2,

and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 509; and V_{H3} comprises a CDR-H1, CDR-H2, and CDR-H3 of a heavy chain variable domain comprising the heavy chain variable domain sequence of SEQ ID NO: 503.

92. The binding protein of any one of claims 60-86 and 90-91, wherein V_{L1} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 524; V_{L2} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 522; V_{L3} comprises a light chain variable domain comprising the sequence of SEQ ID NO: 513; V_{H1} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 511; V_{H2} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 509; and V_{H3} comprises a heavy chain variable domain comprising the sequence of SEQ ID NO: 503.

93. The binding protein of claim 60, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

94. The binding protein of claim 60, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

95. The binding protein of claim 60, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1} , the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

96. The binding protein of claim 60, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1} , the first Fc region comprising an immunoglobulin

hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

97. The binding protein of claim 60, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

98. The binding protein of claim 61, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

99. The binding protein of claim 61, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

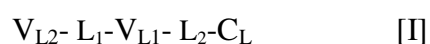
100. The binding protein of claim 61, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

101. The binding protein of claim 60 or claim 61, wherein at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length.

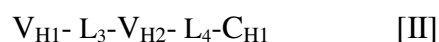
102. The binding protein of claim 60 or claim 61, wherein L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length.

103. The binding protein of any one of claims 60-102, wherein L₁ is Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299).

104. A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain; and

L₁, L₂, L₃, and L₄ are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;

wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383, 385, 391, 393, 399, 401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and

wherein:

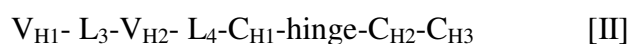
(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

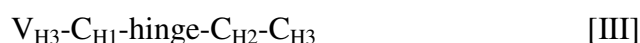
105. A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;
 V_{H2} is a second immunoglobulin heavy chain variable domain;
 V_{H3} is a third immunoglobulin heavy chain variable domain;
 C_L is an immunoglobulin light chain constant domain;
 C_{H1} is the immunoglobulin C_{H1} heavy chain constant domain;
 C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;
 C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;
hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and
 L_1 , L_2 , L_3 , and L_4 are amino acid linkers;
wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair;
wherein:

(a) V_{L1} , V_{L2} and V_{L3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 303, 305, 311, 313, 319, 321, 327, 329, 335, 337, 343, 345, 351, 353, 359, 361, 367, 369, 375, 377, 383, 385, 391, 393, 399, 401, 407, 409, 415, 417, 423, 425, 431, 433, 439, 441, 447, 449, 455, 457, 463, 465, 471, 473; or

(b) V_{L1} , V_{L2} and V_{L3} each independently comprise light chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 266-271, 275-277, 488-496; and
wherein:

(a) V_{H1} , V_{H2} , and V_{H3} are each independently a variable domain derived from an amino acid sequence as set forth in any one of SEQ ID NOs: 302, 304, 310, 312, 318, 320, 326, 328, 334, 336, 342, 344, 350, 352, 358, 360, 366, 368, 374, 376, 382, 384, 390, 392, 398, 400, 406, 408, 414, 416, 422, 424, 430, 432, 438, 440, 446, 448, 454, 456, 462, 464, 470, 472; or

(b) V_{H1} , V_{H2} , and V_{H3} each independently comprise heavy chain complementarity determining regions of a variable domain comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 248-253, 257-259, 479-487.

106. The binding protein of claim 104, wherein the second polypeptide chain further comprises an Fc region linked to C_{H1} , the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

107. The binding protein of claim 104, wherein the third polypeptide chain further comprises an Fc region linked to C_{H1}, the Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains.

108. The binding protein of claim 104, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

109. The binding protein of claim 104, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the first Fc region comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, wherein the second Fc region comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

110. The binding protein of claim 104, wherein the second polypeptide chain further comprises a first Fc region linked to C_{H1}, the first Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains, and wherein the third polypeptide chain further comprises a second Fc region linked to C_{H1}, the second Fc region comprising an immunoglobulin hinge region and C_{H2} and C_{H3} immunoglobulin heavy chain constant domains; wherein the first and second Fc regions comprise amino acid

substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

111. The binding protein of claim 105, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

112. The binding protein of claim 105, wherein the C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the C_{H3} domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

113. The binding protein of claim 105, wherein the C_{H3} domains of the second and the third polypeptide chains both comprise amino acid substitutions at positions corresponding to positions 428 and 434 of human IgG1 according to EU Index, wherein the amino acid substitutions are M428L and N434S.

114. The binding protein of claim 104 or claim 105, wherein at least one of L₁, L₂, L₃, or L₄ is independently 0 amino acids in length.

115. The binding protein of claim 104 or claim 105, wherein L₁, L₂, L₃, or L₄ are each independently at least one amino acid in length.

116. The binding protein of any one of claims 104-115, wherein L₁ is Gly-Gln-Pro-Lys-Ala-Ala-Pro (SEQ ID NO: 299).

117. A binding protein comprising a first polypeptide chain, a second polypeptide chain, a third polypeptide chain and a fourth polypeptide chain wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 305 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 305; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 304 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 304; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 302 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 302; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 303 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 303;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 313 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 313; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 312 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 312; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 310 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 310; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 311 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 311;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 321 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 321; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 320 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 320; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 318 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 318; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 319 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 319;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 329 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 329; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 328 or an amino acid sequence that is at least 95% identical to the amino acid sequence

of SEQ ID NO: 328; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 326 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 326; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 327 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 327;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 337 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 337; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 336 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 336; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 334 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 334; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 335 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 335;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 345 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 345; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 344 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 344; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 342 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 342; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 343 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 343;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 353 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 353; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 352 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 352; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 350 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 350; and the fourth polypeptide chain comprises the amino acid

sequence of SEQ ID NO: 351 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 351;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 361 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 361; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 360 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 360; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 358 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 358; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 359 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 359;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 369 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 369; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 368 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 368; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 366 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 366; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 367 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 367;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 377 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 377; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 376 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 376; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 374 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 374; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 375 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 375;

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 385 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ

ID NO: 385; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 384 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 384; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 382 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 382; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 383 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 383;

(l) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 393 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 393; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 392 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 392; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 390 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 390; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 391 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 391;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 401 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 401; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 400 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 400; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 398 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 398; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 399 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 399;

(n) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 409 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 409; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 408 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 408; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 406 or an amino acid sequence that is at least 95% identical to the amino acid

sequence of SEQ ID NO: 406; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 407 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 407;

(p) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 417 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 417; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 416 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 416; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 414 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 414; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 415 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 415;

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 425 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 425; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 424 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 424; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 422 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 422; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 423 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 423;

(r) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 433 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 433; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 432 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 432; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 430 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 430; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 431 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 431;

(s) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 441 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 441; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 440 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 440; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 438 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 438; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 439 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 439;

(t) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 449 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 449; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 448 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 448; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 446 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 446; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 447 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 447;

(u) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 457 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 457; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 456 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 456; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 454 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 454; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 455 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 455;

(v) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 465 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 465; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 464 or an amino acid sequence that is at least 95% identical to the amino acid sequence

of SEQ ID NO: 464; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 462 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 462; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 463 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 463; or

(w) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 473 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 473; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 472 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 472; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO: 470 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 470; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO: 471 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 471.

118. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the binding protein of any one of claims 1-117.

119. An expression vector comprising the nucleic acid molecule of claim 118.

120. An isolated host cell comprising the nucleic acid molecule of claim 118.

121. An isolated host cell comprising the expression vector of claim 119.

122. The isolated host cell of claim 120 or claim 121, wherein the host cell is a mammalian cell or an insect cell.

123. A vector system comprising one or more vectors encoding a first, second, third, and fourth polypeptide chain of a binding protein of any one of claims 1-117.

124. The vector system of claim 123, wherein the vector system comprises a first vector encoding the first polypeptide chain of the binding protein, a second vector encoding the second polypeptide chain of the binding protein, a third vector encoding the third polypeptide chain of the binding protein, and a fourth vector encoding the fourth polypeptide chain of the binding protein.

125. The vector system of claim 123, wherein the vector system comprises a first vector encoding the first and second polypeptide chains of the binding protein, and a second vector encoding the third and fourth polypeptide chains of the binding protein.

126. The vector system of any one of claims 123-125, wherein the one or more vectors are expression vectors.

127. An isolated host cell comprising the vector system of any one of claims 123-126.

128. The isolated host cell of claim 127, wherein the host cell is a mammalian cell or an insect cell.

129. A method of producing a binding protein, the method comprising:

a) culturing a host cell of any one of claims 120-122 and claims 127-128 under conditions such that the host cell expresses the binding protein; and

b) isolating the binding protein from the host cell.

130. A method of preventing and/or treating HIV infection in a patient comprising administering to the patient a therapeutically effective amount of at least one binding protein of any one of claims 1-117.

131. The method of claim 130, wherein the binding protein is co-administered with standard anti-retroviral therapy.

132. The method of claim 130 or claim 131, wherein administration of the at least one binding protein results in the neutralization of one or more HIV virions.

133. The method of any one of claims 130-132, wherein administration of the at least one binding protein results in the elimination of one or more latently and/or chronically HIV-infected cells in the patient.

134. The method of any one of claims 130-133, wherein the patient is a human.

135. The binding protein of any one of claims 1-117 for the prevention or treatment of an HIV infection in a patient.

136. The binding protein of claim 135, wherein the binding protein is co-administered with standard anti-retroviral therapy.
137. The binding protein of claim 135 or claim 136, wherein the binding protein causes the neutralization of one or more HIV virions in the patient.
138. The binding protein of any one of claims 135-137, wherein the binding protein causes the elimination of one or more latently and/or chronically HIV-infected cells in the patient.
139. The binding protein of any one of claims 135-138, wherein the patient is a human.