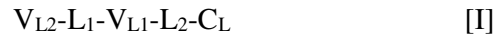
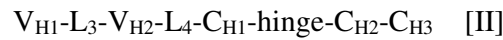


CLAIMS

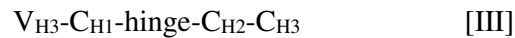
1. A ~~method for expanding virus specific memory T cells, comprising contacting a virus specific memory T cell with a binding protein, wherein the~~ binding protein ~~comprises~~ comprising four polypeptide chains that form ~~the~~ three antigen binding sites, wherein a first polypeptide chain of the binding protein comprises a structure represented by the formula:



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



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



and a fourth polypeptide chain of the binding protein 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;

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

wherein V_{H1} and V_{L1} form a first antigen binding site that binds a CD28 polypeptide, wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, and wherein V_{H3} and V_{L3} form a third antigen binding site that binds a CD38 polypeptide;

for use in expanding virus-specific memory T cells *in vivo* by contacting a virus-specific memory T cell with the binding protein.

1. 2. A method for *in vitro* or *ex vivo* expanding virus-specific memory T cells, comprising contacting a virus-specific memory T cell with a binding protein, wherein the binding protein comprises four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain of the binding protein comprises a structure represented by the formula:



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



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



and a fourth polypeptide chain of the binding protein 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;

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

wherein V_{H1} and V_{L1} form a first antigen binding site that binds a CD28 polypeptide, wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, and wherein V_{H3} and V_{L3} form a third antigen binding site that binds a CD38 polypeptide~~The method of claim 1, wherein the virus-specific memory T cell is contacted with the binding protein *in vitro* or *ex vivo*.~~

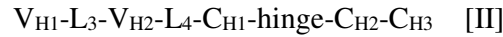
3. The ~~method-binding protein for use~~ of claim 1 ~~or claim 2~~, wherein contacting the virus-specific memory T cell with the binding protein causes activation and/or proliferation of virus-specific memory T cells.

4. The method of claim 2, wherein contacting the virus-specific memory T cell with the binding protein causes activation and/or proliferation of virus-specific memory T cells.

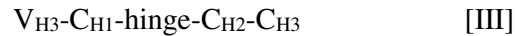
45. A method for expanding T cells, comprising contacting a T cell with a binding protein *in vitro* or *ex vivo*, wherein the binding protein comprises four polypeptide chains that form ~~the~~ three antigen binding sites, wherein a first polypeptide chain of the binding protein comprises a structure represented by the formula:



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



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



and a fourth polypeptide chain of the binding protein 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;

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

wherein V_{H1} and V_{L1} form a first antigen binding site that binds a CD28 polypeptide, wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, and wherein V_{H3} and V_{L3} form a third antigen binding site that binds a CD38 polypeptide.

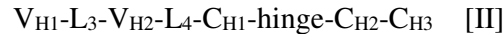
~~56.~~ The method of claim ~~45~~, wherein the T cell is a memory T cell or an effector T cell.

~~67.~~ The method of claim ~~45~~ or claim ~~56~~, wherein the T cell expresses a chimeric antigen receptor (CAR) on its cell surface or comprises a polynucleotide encoding a CAR.

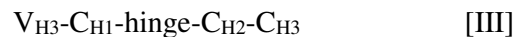
~~78.~~ A ~~method for treating chronic viral infection, comprising administering to an individual in need thereof an effective amount of a binding protein, wherein the~~ binding protein ~~comprises comprising~~ four polypeptide chains that form ~~the~~ three antigen binding sites ~~for treating chronic viral infection~~, wherein a first polypeptide chain ~~of the binding protein~~ comprises a structure represented by the formula:



and a second polypeptide chain ~~of the binding protein~~ comprises a structure represented by the formula:



and a third polypeptide chain ~~of the binding protein~~ comprises a structure represented by the formula:



and a fourth polypeptide chain ~~of the binding protein~~ 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;

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

wherein V_{H1} and V_{L1} form a first antigen binding site that binds a CD28 polypeptide, wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, and wherein V_{H3} and V_{L3} form a third antigen binding site that binds a CD38 polypeptide.

~~89.~~ The ~~method-binding protein for use~~ of claim ~~78~~, wherein the individual is a human.

~~910.~~ The ~~binding protein for use method~~ of claim ~~7-8~~ or claim ~~89~~, wherein the binding protein is to be administered to the individual in pharmaceutical formulation comprising the binding protein and a pharmaceutically acceptable carrier.

~~1011.~~ The ~~binding protein for use method~~ of any one of claims ~~7-98-10~~, wherein administration of the binding protein results in activation and/or proliferation of virus-specific memory T cells in the individual.

~~1112.~~ The ~~binding protein for use method~~ of any one of claims ~~1-6 and 101, 3, and 8-11~~, wherein the memory T cells are CD8+ or CD4+ memory T cells.

~~1213.~~ The ~~binding protein for use method~~ of any one of claims ~~1-6, 10, and 111, 3, 11, and 12~~, wherein the memory T cells are central memory T cells (T_{CM}) or effector memory T cells (T_{EM}).

~~13~~14. The binding protein for use method of any one of claims ~~1-12~~1, 3, and 8-13, wherein the CD28 polypeptide is a human CD28 polypeptide, wherein the CD3 polypeptide is a human CD3 polypeptide, and wherein the CD38 polypeptide is a human CD38 polypeptide.

~~14~~15. The binding protein for use method of any one of claims ~~1-13~~1, 3, and 8-14, wherein:

(a) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTSFN (SEQ ID NO:31), a CDR-H2 sequence comprising the amino acid sequence of IYPGNGGT (SEQ ID NO:32), and a CDR-H3 sequence comprising the amino acid sequence of ARTGGLRRAYFTY (SEQ ID NO:33), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of ESVDSYGNGF (SEQ ID NO:34), a CDR-L2 sequence comprising the amino acid sequence of LAS (SEQ ID NO:35), and a CDR-L3 sequence comprising the amino acid sequence of QQNKEDPWT (SEQ ID NO:36);

(b) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTSYA (SEQ ID NO:37), a CDR-H2 sequence comprising the amino acid sequence of IYPGQGGT (SEQ ID NO:38), and a CDR-H3 sequence comprising the amino acid sequence of ARTGGLRRAYFTY (SEQ ID NO:33), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSVSSYGQGF (SEQ ID NO:39), a CDR-L2 sequence comprising the amino acid sequence of GAS (SEQ ID NO:40), and a CDR-L3 sequence comprising the amino acid sequence of QQNKEDPWT (SEQ ID NO:36);
or

(c) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFSSYG (SEQ ID NO:41), a CDR-H2 sequence comprising the amino acid sequence of IWYDGSNK (SEQ ID NO:42), and a CDR-H3 sequence comprising the amino acid sequence of ARMFRGAFDY (SEQ ID NO:43), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QGIRND (SEQ ID NO:44), a CDR-L2 sequence comprising the amino acid sequence of AAS (SEQ ID NO:45), and a CDR-L3 sequence comprising the amino acid sequence of LQDYIYYPT (SEQ ID NO:46).

~~15~~16. The binding protein for use method of claim ~~14~~15, wherein:

(a) the V_{H3} domain comprises the amino acid sequence of
QVQLQQSGAELVRSGASVKMSCKASGYTFTSFNMHWVKETPGQGLEWIGYIYPGN
GGTNYNQKFKGKATLTADTSSSTAYMQISLTSEDSAVYFCARTGGLRRAYFTYWG

QGTLVTVS (SEQ ID NO:5), and the V_{L3} domain comprises the amino acid sequence of DIVLTQSPASLAVSLGQRATISCRASESVD SYGNGFMHWYQQKPGQPPKLLIYLASN LESGVPARFSGSGSRTDFTLTIDPVEADDAATYYCQQNKEDPWTFGGGGTKLEIK (SEQ ID NO:6);

(b) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKV SCKASGYTFTSYAMHWVKEAPGQRLEWIGYIYPGQ GGTNYNQKFQGRATLTADTSASTAYMELSSLRSED TAVYFCARTGGLRRAYFTYW GQGLTVTVSS (SEQ ID NO:13), and the V_{L3} domain comprises the amino acid sequence of DIVLTQSPATLSLSPGERATISCRASQSVSSYGQGF MHWYQQKPGQPPRLLIYGASSR ATGIPARFSGSGSGTDFTLTISP LEPEDFAVYYCQQNKEDPWTFGGGGTKLEIK (SEQ ID NO:14);

(c) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKV SCKASGYTFTSFNMHWVKEAPGQRLEWIGYIYPGN GGTNYNQKFQGRATLTADTSASTAYMELSSLRSED TAVYFCARTGGLRRAYFTYW GQGLTVTVSS (SEQ ID NO:17), and the V_{L3} domain comprises the amino acid sequence of DIVLTQSPATLSLSPGERATISCRASESVD SYGNGFMHWYQQKPGQPPRLLIYLASSR ATGIPARFSGSGSGTDFTLTISP LEPEDFAVYYCQQNKEDPWTFGGGGTKLEIK (SEQ ID NO:18);

(d) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVVKSGASVKV SCKASGYTFTSFNMHWVKEAPGQGLEWIGYIYPGN GGTNYNQKFQGRATLTADTSASTAYMEISSLRSED TAVYFCARTGGLRRAYFTYWG QGTLVTVSS (SEQ ID NO:21), and the V_{L3} domain comprises the amino acid sequence of DIVLTQSPATLSLSPGERATISCRASESVD SYGNGFMHWYQQKPGQPPRLLIYLASSR ATGIPARFSGSGSGTDFTLTISP LEPEDFAVYYCQQNKEDPWTFGGGGTKLEIK (SEQ ID NO:18);

(e) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKM SCKASGYTFTSFNMHWVKEAPGQRLEWIGYIYPGN GGTNYNQKFQGRATLTADTSASTAYMEISSLRSED TAVYFCARTGGLRRAYFTYWG QGTLVTVSS (SEQ ID NO:23), and the V_{L3} domain comprises the amino acid sequence of DIVLTQSPATLSLSPGERATISCRASESVD SYGNGFMHWYQQKPGQPPRLLIYLASSR ATGIPARFSGSGSGTDFTLTISP LEPEDFAVYYCQQNKEDPWTFGGGGTKLEIK (SEQ ID NO:18); or

(f) the V_{H3} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWDYGSNKYYADSVKGRFTISGDNSKNTLYLQMNSLRAEDTAVYYCARMFRGAFDYWGQGTLVTVSS (SEQ ID NO:9), and the V_{L3} domain comprises the amino acid sequence of AIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKLLIYAASSLQSGVPSRFGSGSGTDFTLTISGLQPEDSATYYCLQDYIYYPTFGQGTKVEIK (SEQ ID NO:10).

~~1617~~. The binding protein for use method of any one of claims ~~1-15~~ 1, 3, and 8-16, wherein:

(a) the V_{H1} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTSYY (SEQ ID NO:108), a CDR-H2 sequence comprising the amino acid sequence of IYPGNVNT (SEQ ID NO:109), and a CDR-H3 sequence comprising the amino acid sequence of TRSHYGLDWNFDV (SEQ ID NO:110), and the V_{L1} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QNIYVW (SEQ ID NO:111), a CDR-L2 sequence comprising the amino acid sequence of KAS (SEQ ID NO:112), and a CDR-L3 sequence comprising the amino acid sequence of QQGQTYPY (SEQ ID NO:113);
or

(b) the V_{H1} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFSLSDYG (SEQ ID NO:114), a CDR-H2 sequence comprising the amino acid sequence of IWAGGGT (SEQ ID NO:115), and a CDR-H3 sequence comprising the amino acid sequence of ARDKGYSYYYSM DY (SEQ ID NO:116), and the V_{L1} domain comprises a CDR-L1 sequence comprising the amino acid sequence of ESVEYYVTSL (SEQ ID NO:117), a CDR-L2 sequence comprising the amino acid sequence of AAS (SEQ ID NO:118), and a CDR-L3 sequence comprising the amino acid sequence of QQSRKVPYT (SEQ ID NO:119).

~~1718~~. The binding protein for use method of claim ~~1617~~, wherein:

(a) the V_{H1} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKVSCASGYTFTSYYIHVVRQAPGQGLEWIGSIYPGNVNTNYAQKFQGRATLTVDTSISTAYMELSRLRSDDTAVYYCTRSHYGLDWNFDVWVGKTTVTVSS (SEQ ID NO:49), and the V_{L1} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCQASQNIYVWLNWYQQKPGKAPKLLIYKASNLTG

VPSRFSGSGSGTDFTLTISLQPEDATYYCQQGQTYPTFGQGTKLEIK (SEQ ID NO:50); or

(b) the V_{H1} domain comprises the amino acid sequence of QVQLQESGPGLVKPSQTLSTCTVSGFSLSDYGVHWVRQPPGKGLEWLGVIWAGGG TNYNPSLKSRTISKDTSKNQVSLKLSSVTAADTAVYYCARDKGYSYYYSMDYWG QGTTVTVS (SEQ ID NO:51), and the V_{L1} domain comprises the amino acid sequence of DIVLTQSPASLAVSPGQRATITCRASESVEYYVTSLMQWYQQKPGQPPKLLIFAASNV ESGVPARFSGSGSGTDFTLTINPVEANDVANYYCQQSRKVPYTFGQGTKLEIK (SEQ ID NO:52).

~~1819~~. The binding protein for use method of any one of claims ~~1-171~~, 3, and 8-18, wherein:

(a) the V_{H2} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFTKAW (SEQ ID NO:120), a CDR-H2 sequence comprising the amino acid sequence of IKDKSNSYAT (SEQ ID NO:121), and a CDR-H3 sequence comprising the amino acid sequence of RGVYYALSPFDY (SEQ ID NO:122), and the V_{L2} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHNNANTY (SEQ ID NO:123), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:124), and a CDR-L3 sequence comprising the amino acid sequence of GQGTQYPFT (SEQ ID NO:125); or

(b) the V_{H2} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFTKAW (SEQ ID NO:126), a CDR-H2 sequence comprising the amino acid sequence of IKDKSNSYAT (SEQ ID NO:127), and a CDR-H3 sequence comprising the amino acid sequence of GVYYALSPFDY (SEQ ID NO:128), and the V_{L2} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHNNGNTY (SEQ ID NO:129), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:130), and a CDR-L3 sequence comprising the amino acid sequence of GQGTQYPFT (SEQ ID NO:131).

~~1920~~. The binding protein for use method of claim ~~1819~~, wherein:

(a) the V_{H2} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWVRQAPGKQLEWVAQIKDKS NSYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCRGVYYALSPFDY

WGQGTSLTVSS (SEQ ID NO:53), and the V_{L2} domain comprises the amino acid sequence of

DIVMTQTPLSLSVTPGQPASISCKSSQSLVHNNANTYLSWYLQKPGQSPQSLIYKVS
NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID NO:54); or

(b) the V_{H2} domain comprises the amino acid sequence of

QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWRQAPGKGLEWVAQIKDKS
NSYATYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCRGVYYALSPFDY
WGQGTSLTVSS (SEQ ID NO:84), and the V_{L2} domain comprises the amino acid sequence of
DIVMTQTPLSLSVTPGQPASISCKSSQSLVHNNNGNTYLSWYLQKPGQSPQLLIYKVS
NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGGGTKVEIK (SEQ ID NO:85).

2021. The binding protein for use method of any one of claims 1-491, 3, and 8-20, wherein at least one of L_1 , L_2 , L_3 or L_4 is independently 0 amino acids in length.

2422. The binding protein for use method of any one of claims 1-491, 3, and 8-20, wherein (a) L_1 , L_2 , L_3 and L_4 each independently are zero amino acids in length or comprise a sequence selected from the group consisting of GGGGSGGGGS (SEQ ID NO:55), GGGGSGGGSGGGGS (SEQ ID NO: 56), S, RT, TKGPS (SEQ ID NO: 57), GQPKAAP (SEQ ID NO: 58), and GGSGSSGSGG (SEQ ID NO: 59); or (b) L_1 , L_2 , L_3 and L_4 each independently comprise a sequence selected from the group consisting of GGGGSGGGGS (SEQ ID NO:55), GGGGSGGGSGGGGS (SEQ ID NO:56), S, RT, TKGPS (SEQ ID NO:57), GQPKAAP (SEQ ID NO: 58), and GGSGSSGSGG (SEQ ID NO:59).

2223. The binding protein for use method of any one of claims 1-491, 3, and 8-20, wherein L_1 comprises the sequence GQPKAAP (SEQ ID NO: 58), L_2 comprises the sequence TKGPS (SEQ ID NO:57), L_3 comprises the sequence S, and L_4 comprises the sequence RT.

2324. The binding protein for use method of any one of claims 1-221, 3, and 8-23, wherein the hinge- C_{H2} - C_{H3} domains of the second and the third polypeptide chains are human IgG4 hinge- C_{H2} - C_{H3} domains, and wherein the hinge- C_{H2} - C_{H3} domains each comprise amino acid substitutions at positions corresponding to positions 234 and 235 of human IgG4 according to EU Index, wherein the amino acid substitutions are F234A and L235A.

2425. The binding protein for use method of any one of claims 1-221, 3, and 8-23, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG4 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ domains each comprise amino acid substitutions at positions corresponding to positions 233-236 of human IgG4 according to EU Index, wherein the amino acid substitutions are E233P, F234V, L235A, and a deletion at 236.

2526. The binding protein for use method of any one of claims 1-241, 3, and 8-25, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG4 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ domains each comprise amino acid substitutions at positions corresponding to positions 228 and 409 of human IgG4 according to EU Index, wherein the amino acid substitutions are S228P and R409K.

2627. The binding protein for use method of any one of claims 1-221, 3, and 8-23, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG1 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ domains each comprise amino acid substitutions at positions corresponding to positions 234, 235, and 329 of human IgG1 according to EU Index, wherein the amino acid substitutions are L234A, L235A, and P329A.

2728. The binding protein for use method of any one of claims 1-221, 3, and 8-23, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG1 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ domains each comprise amino acid substitutions at positions corresponding to positions 298, 299, and 300 of human IgG1 according to EU Index, wherein the amino acid substitutions are S298N, T299A, and Y300S.

2829. The binding protein for use method of any one of claims 1-271, 3, and 8-28, wherein the hinge-CH₂-CH₃ domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 or IgG4 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the hinge-CH₂-CH₃ domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 or IgG4 according to EU Index, wherein the amino acid substitutions are S354C and T366W.

2930. The binding protein for use method of any one of claims 1-271, 3, and 8-28, wherein the hinge-CH₂-CH₃ domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 or IgG4

according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the hinge-CH₂-CH₃ domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 or IgG4 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

~~3031~~. The binding protein for use of claim 1, wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:61, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:60, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:62, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:63;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:61, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:64, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:65, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:63;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:61, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:66, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:67, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:63;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:61, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:60, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:68, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:69;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:61, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:64, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:70, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:69; or

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:61, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:66, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:71, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:69.

31-32. The binding protein for use method of any one of claims ~~1-30~~ 1, 3, and 8-31, wherein the virus is a human immunodeficiency virus (HIV), influenza virus, cytomegalovirus (CMV), hepatitis B virus (HBV), human papillomavirus (HPV), Epstein-barr virus (EBV), human foamy virus (HFV), herpes simplex virus 1 (HSV-1), or herpes simplex virus 1 (HSV-2).