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(54) **USES OF PDL1-BINDING PROTEINS**

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sion of application No. 16/601,825, filed on Oct. 15, 2019, now Pat. No. 11,566,078, which is a division of application No. 15/404,016, filed on Jan. 11, 2017, now Pat. No. 10,501,551.

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(52) **U.S. Cl.**

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(57) **ABSTRACT**

This invention relates generally to molecules that specifically engage 41BB, a member of the TNF receptor superfamily (TNFRSF). More specifically, this invention relates to multivalent and multispecific molecules that bind at least 41BB.

Specification includes a Sequence Listing.

FIG. 1

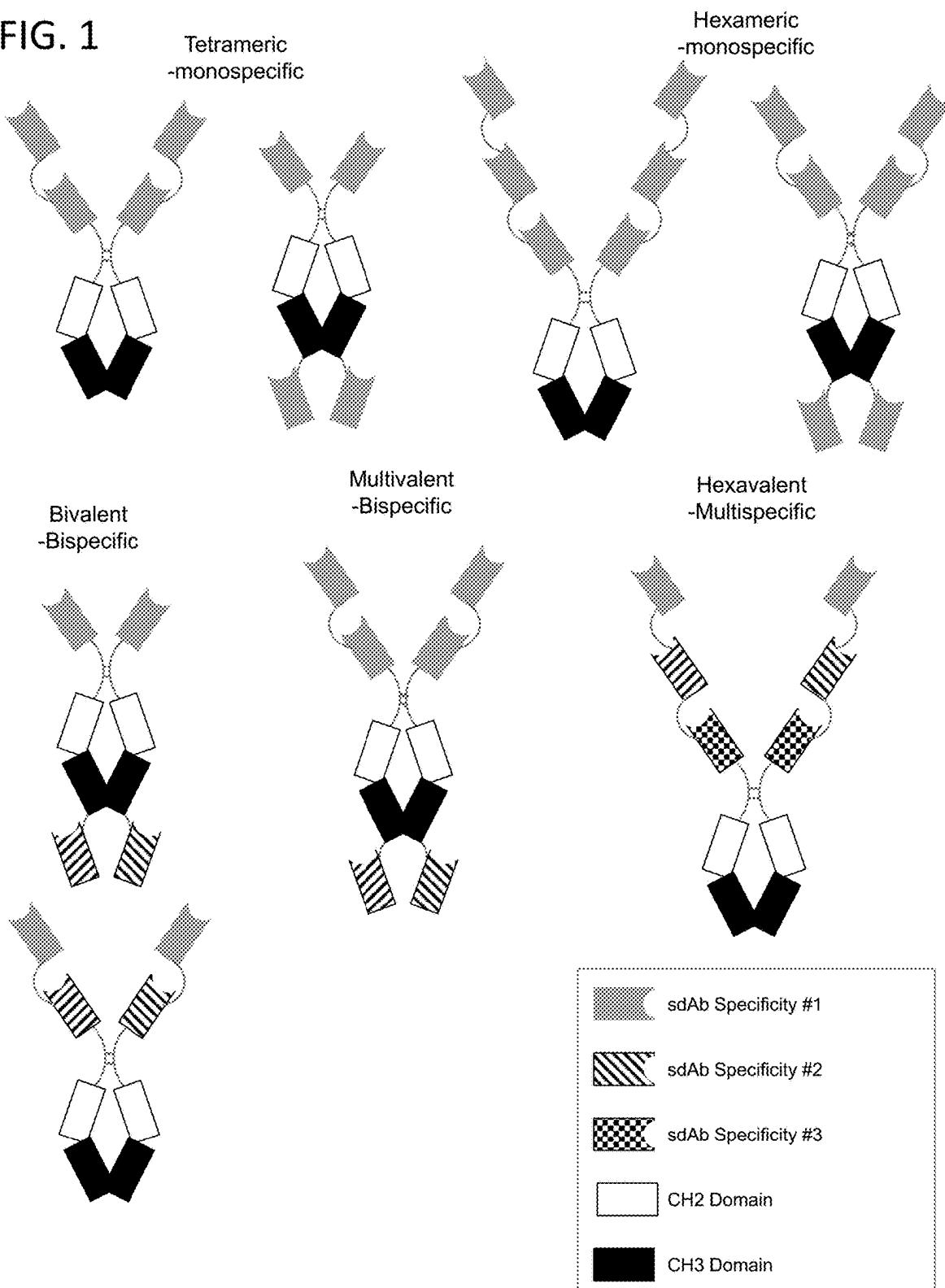


FIG. 2A

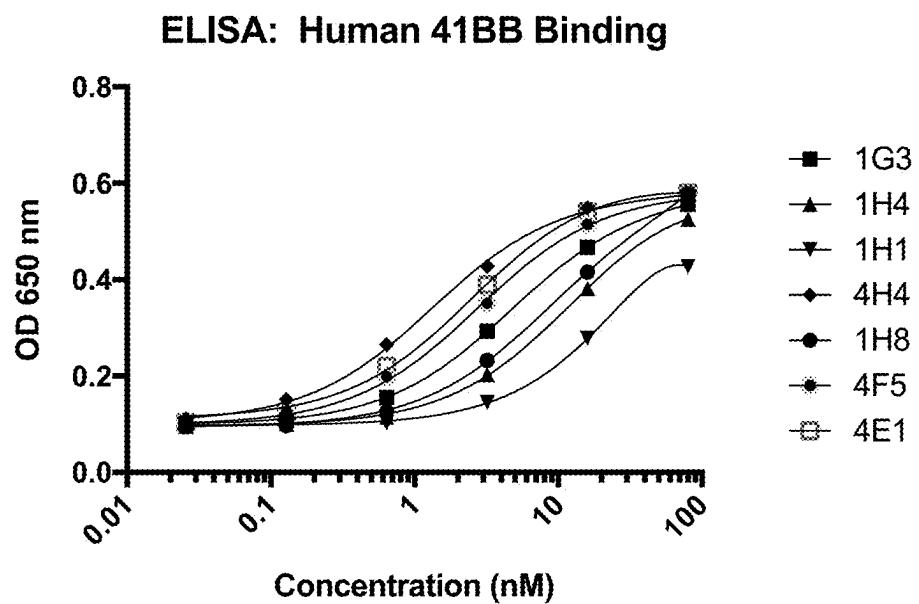


FIG. 2B

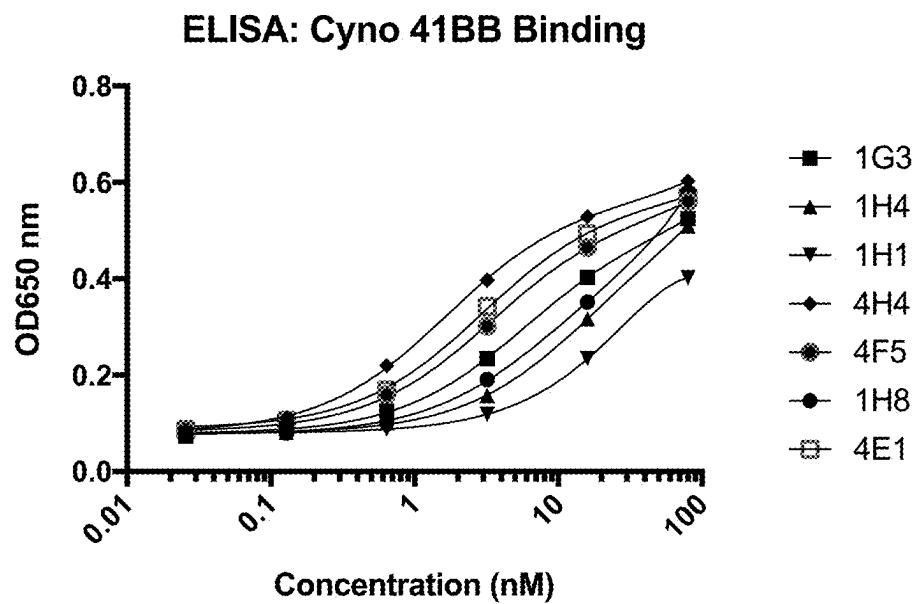


FIG. 3

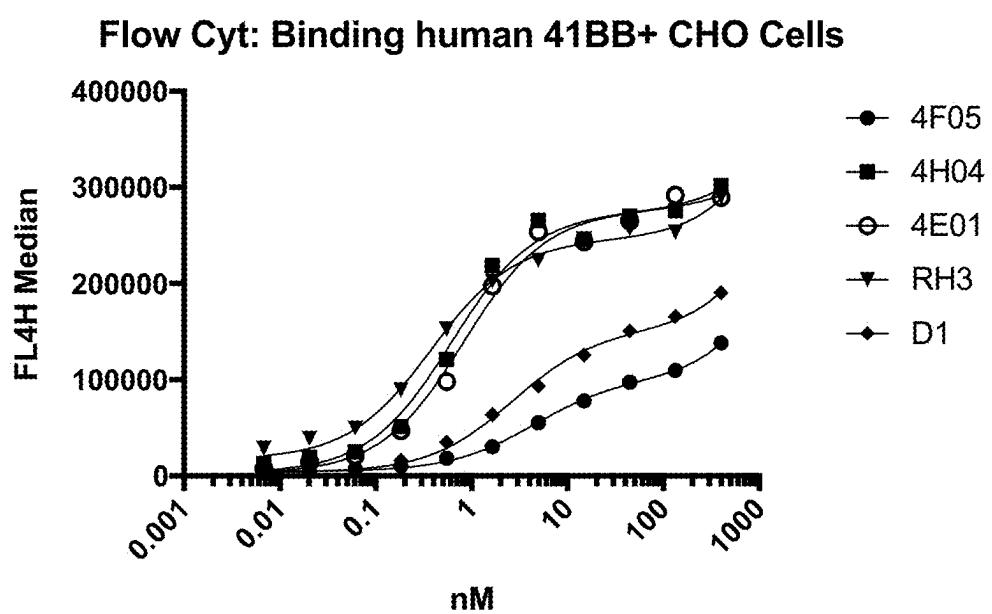


FIG. 4

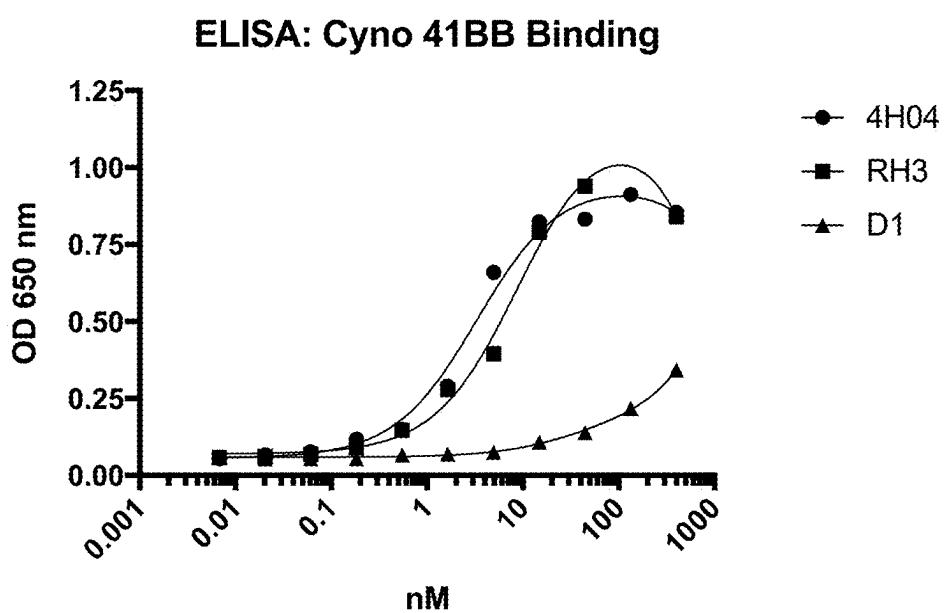


FIG. 5

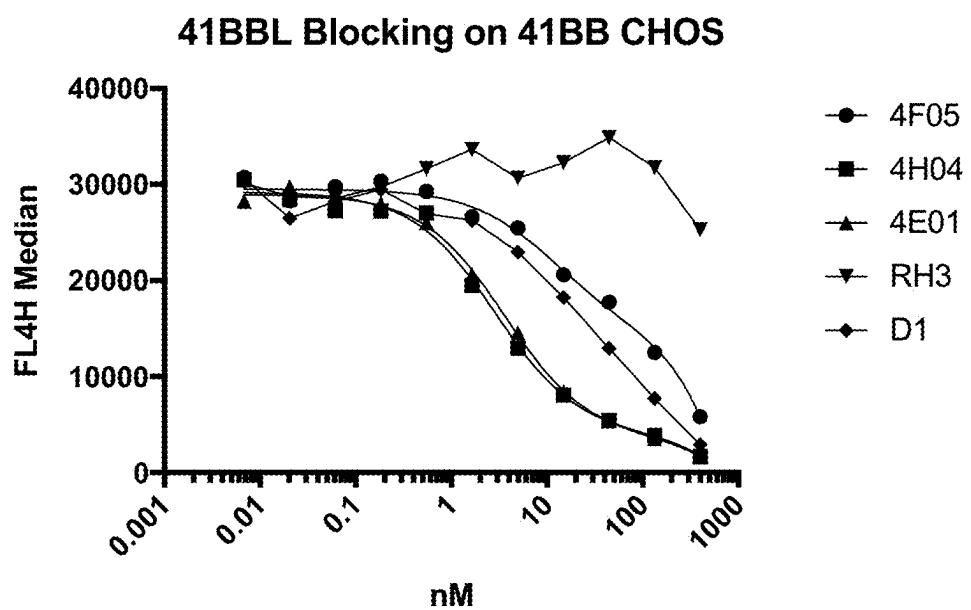


FIG. 6

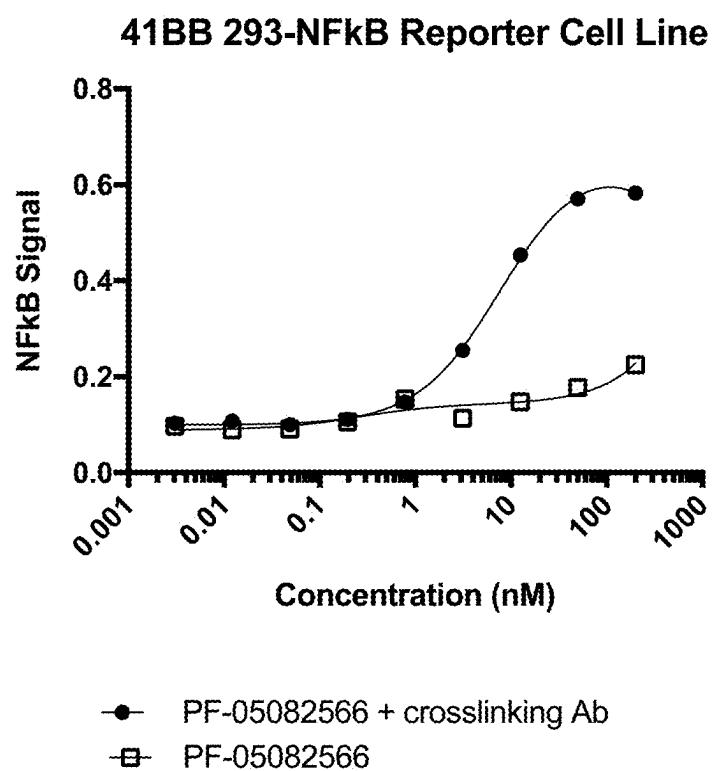


FIG. 7A

Flow Cyt: 28A10 Binding human PD-L1+ Cells

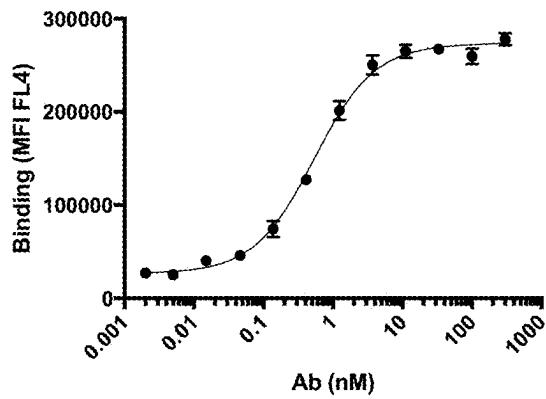


FIG. 7B

Flow Cyt: 28A10 Blocking PD1

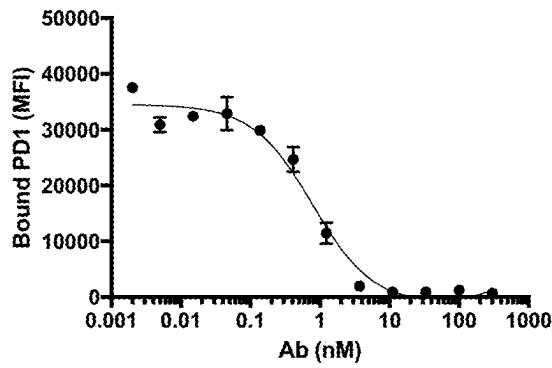
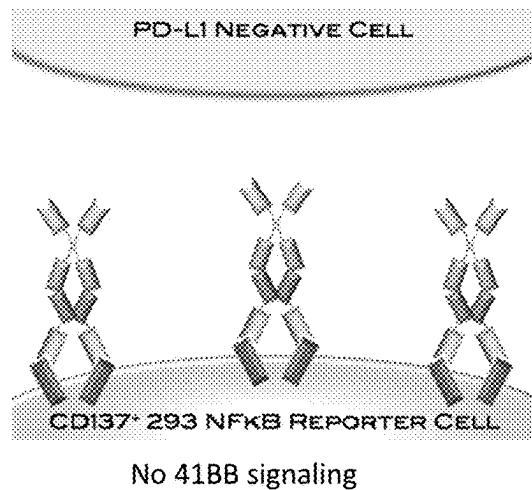
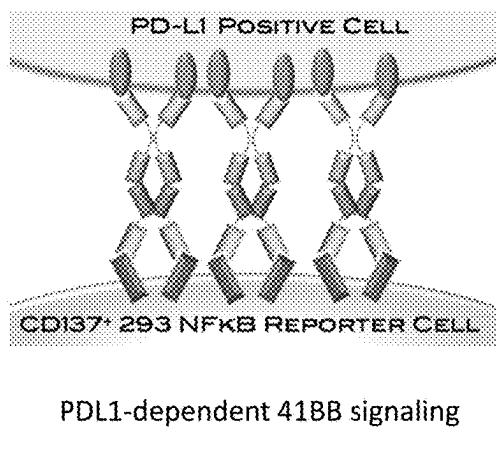


FIG. 8A



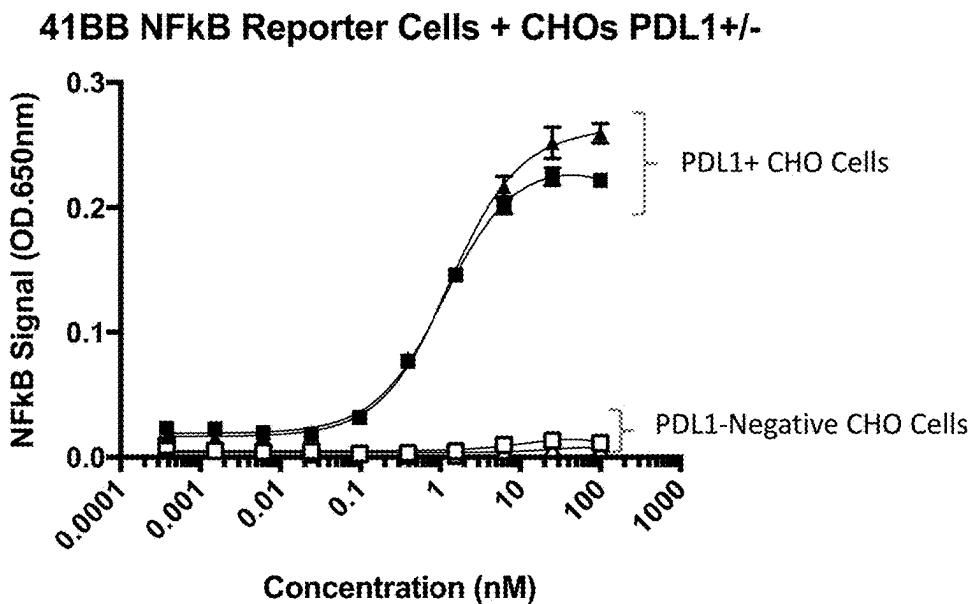
No 41BB signaling

FIG. 8B



PDL1-dependent 41BB signaling

FIG. 8C



- PDL1-CHO: 28A10-RH3 (PDL1 x 41BB)
- ▲ PDL1-CHO: 28A10-4E01 (PDL1 x 41BB)
- NT-CHO: 28A10-RH3 (PDL1 x 41BB)
- △ NT-CHO: 28A10-4E01 (PDL1 x 41BB)

FIG. 9A

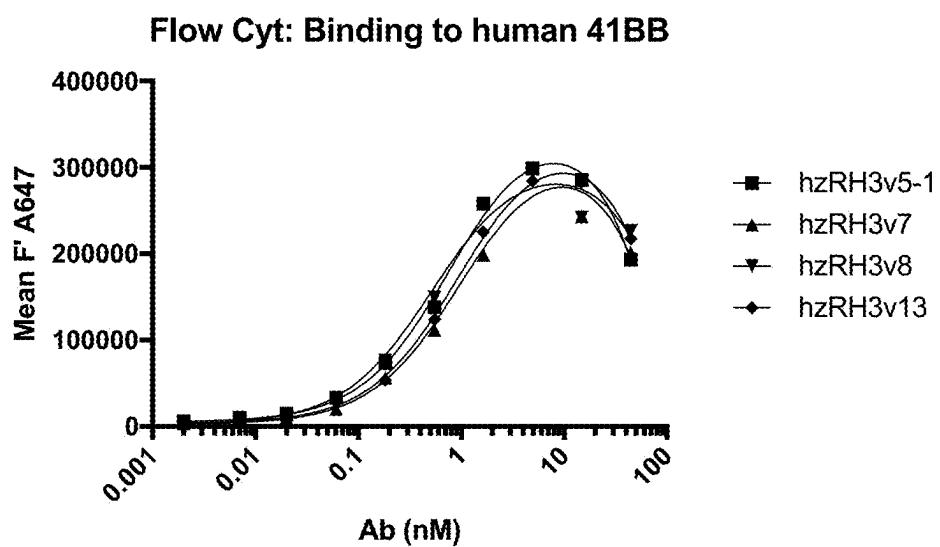


FIG. 9B

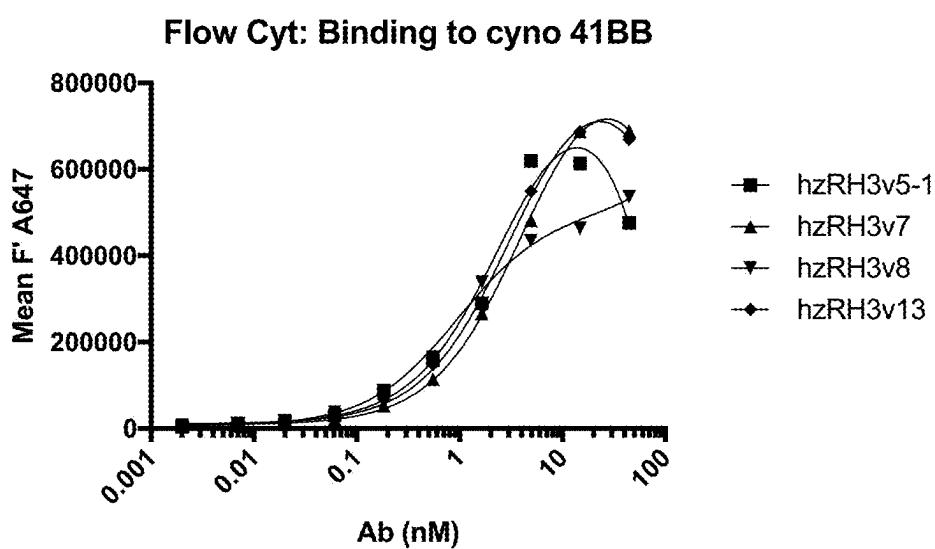


FIG. 9C

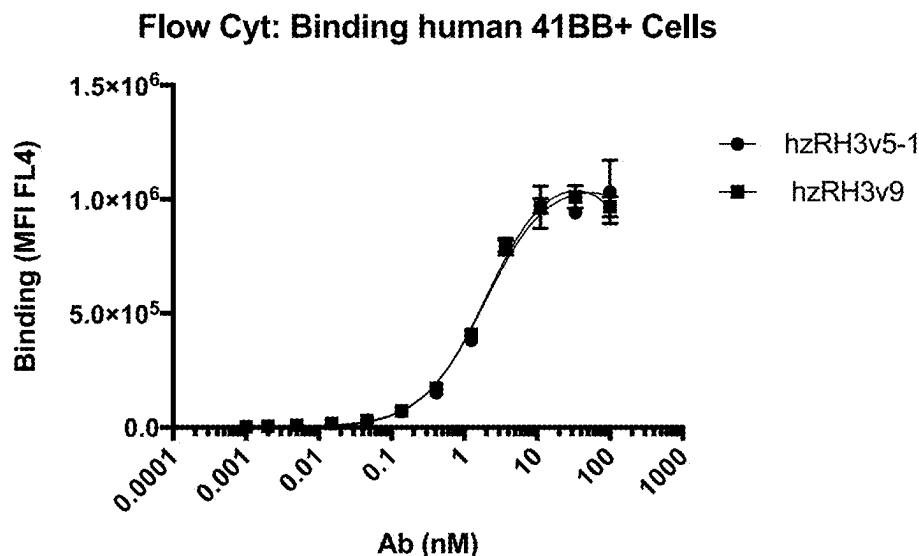


FIG. 9D

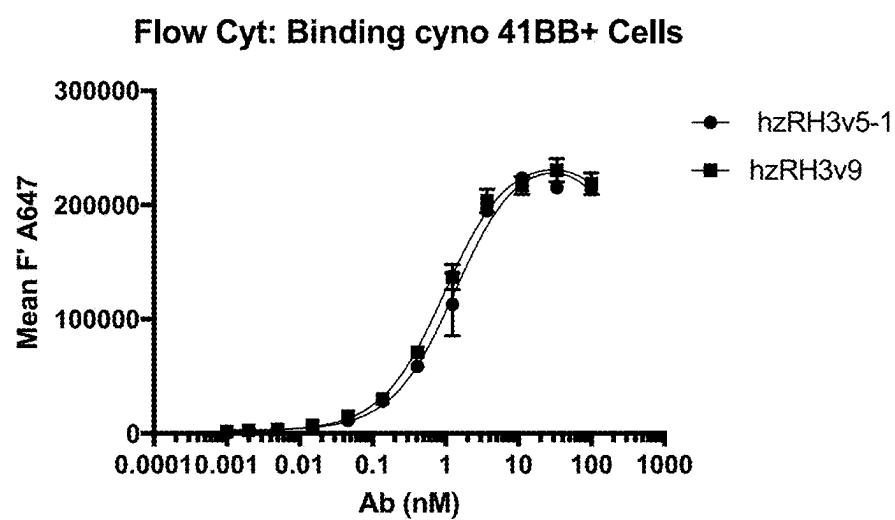


FIG. 9E

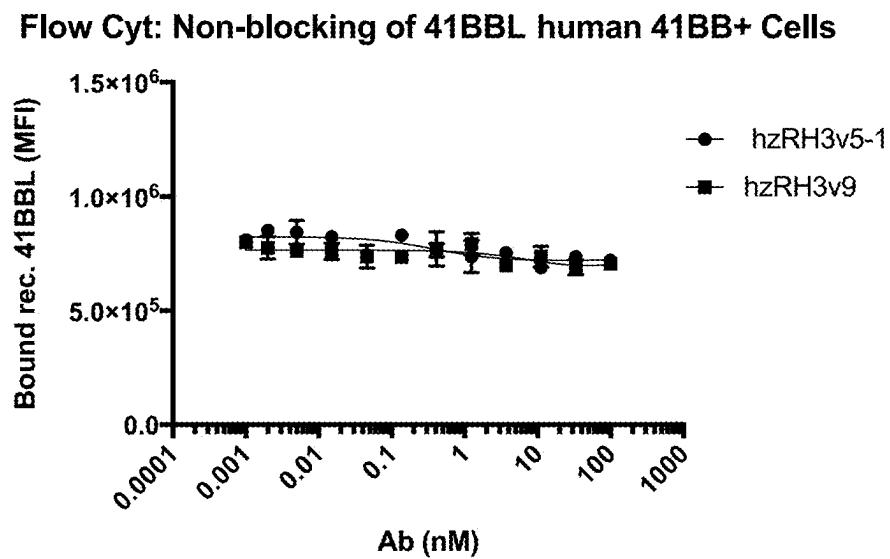


FIG. 10

Specific Binding: hzRH3v5-1: 41BB vs OX40 vs GITR CHO

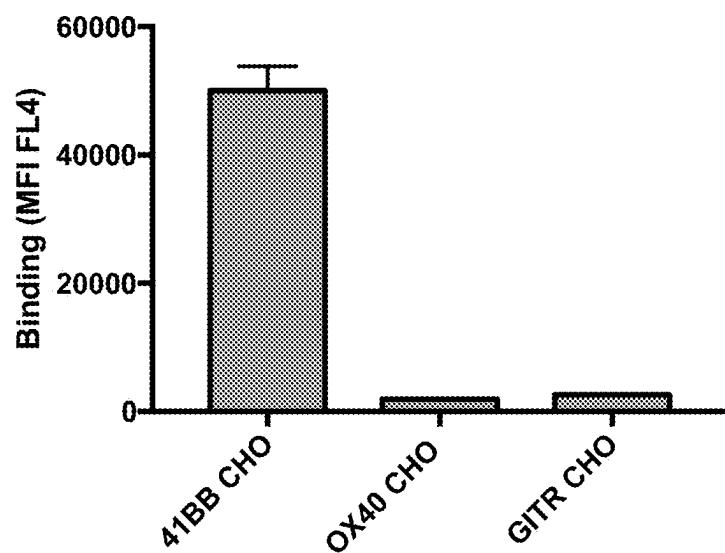


FIG. 11A

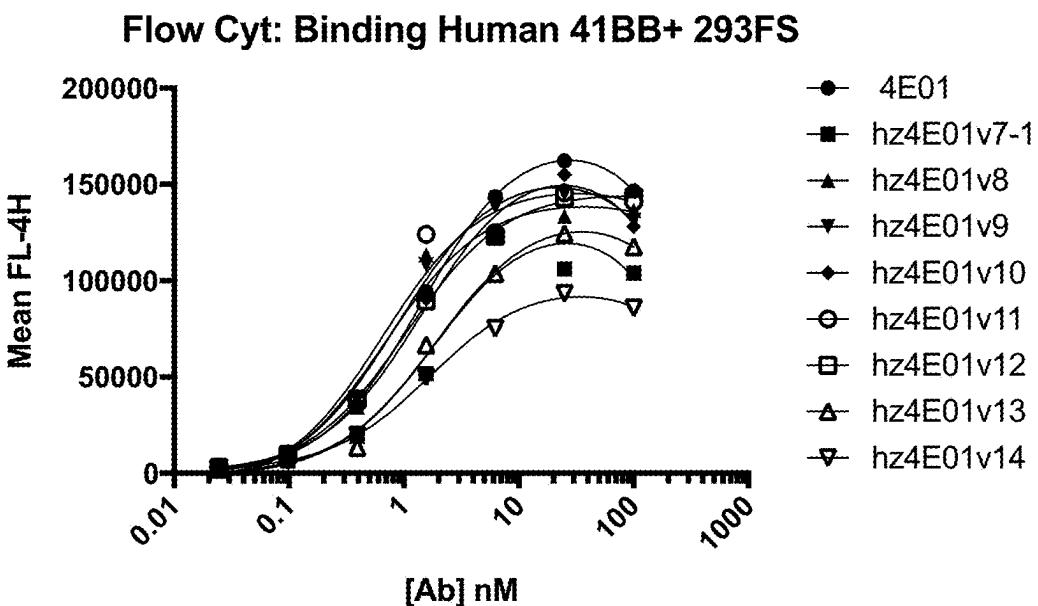


FIG. 11B

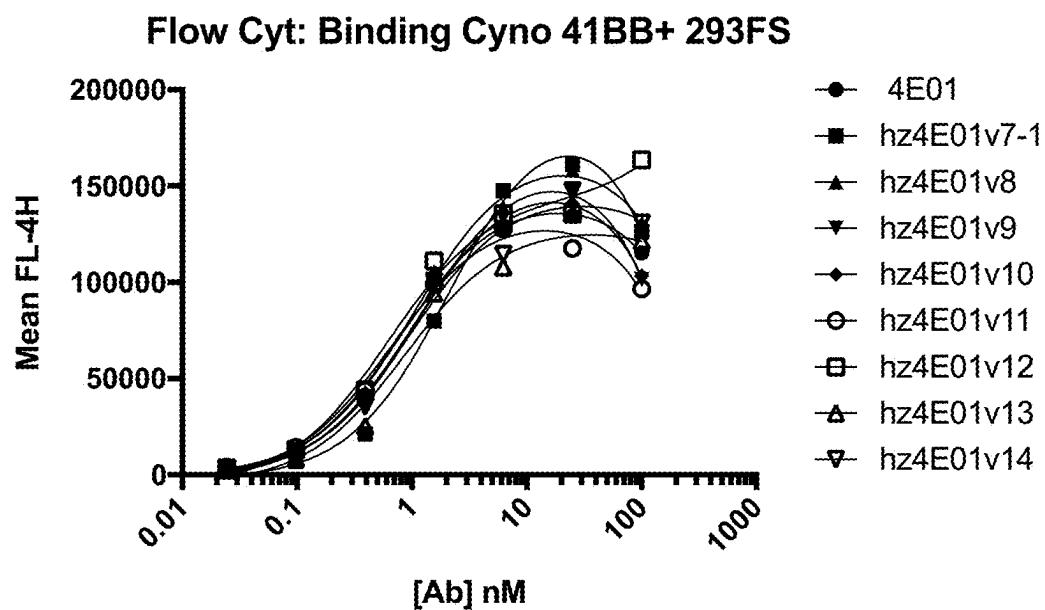


FIG. 11C

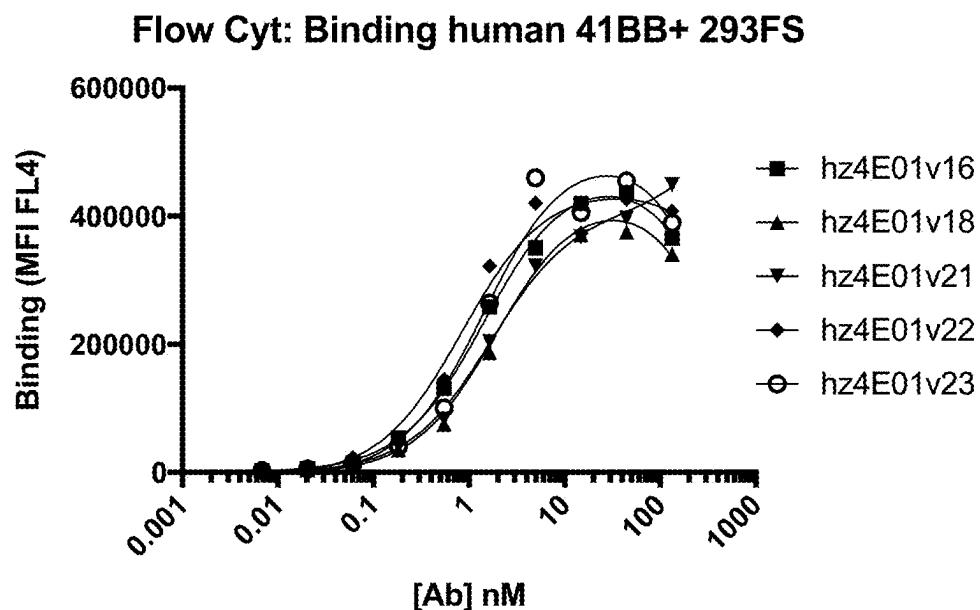


FIG. 11D

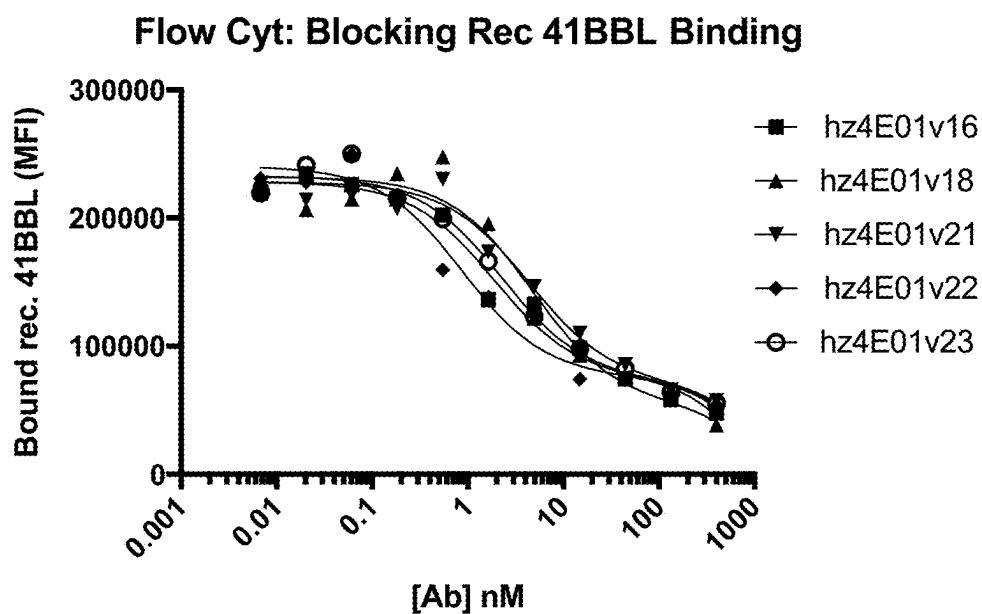


FIG. 12

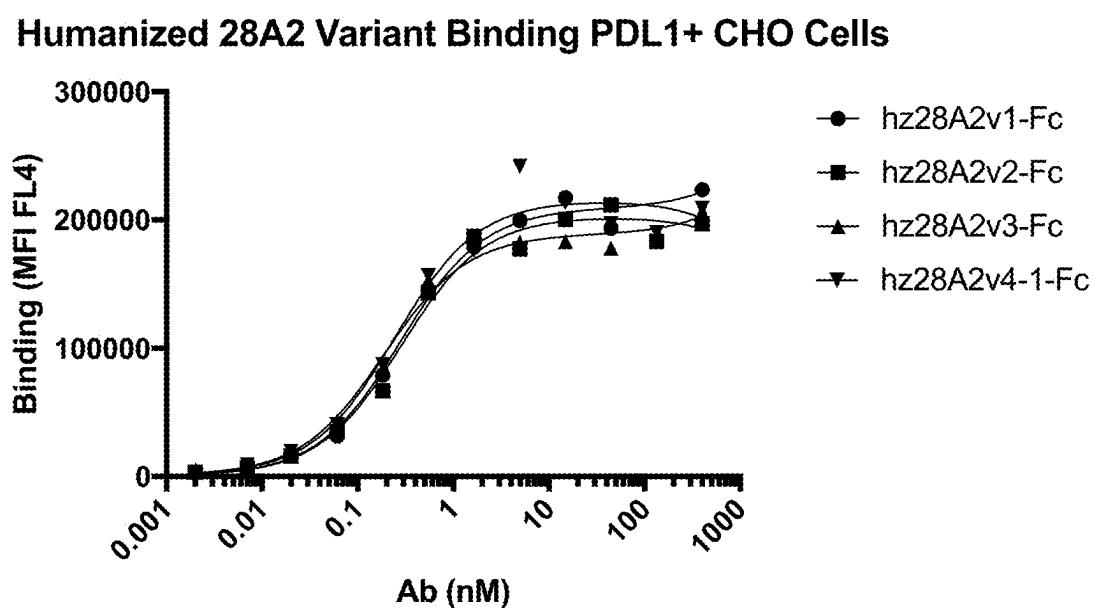


FIG. 13

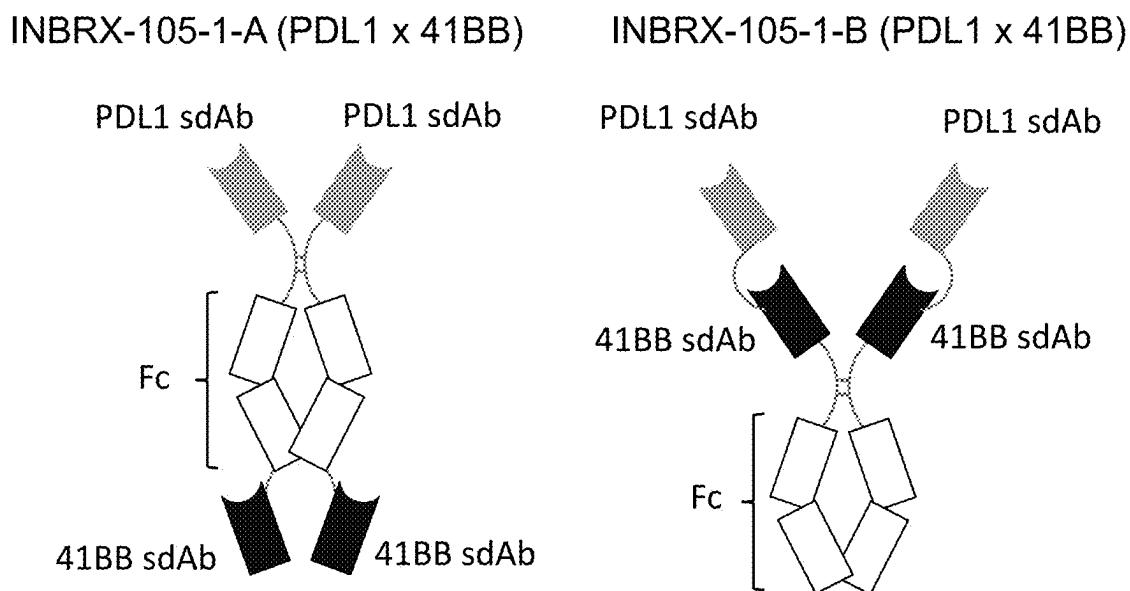


FIG. 14A

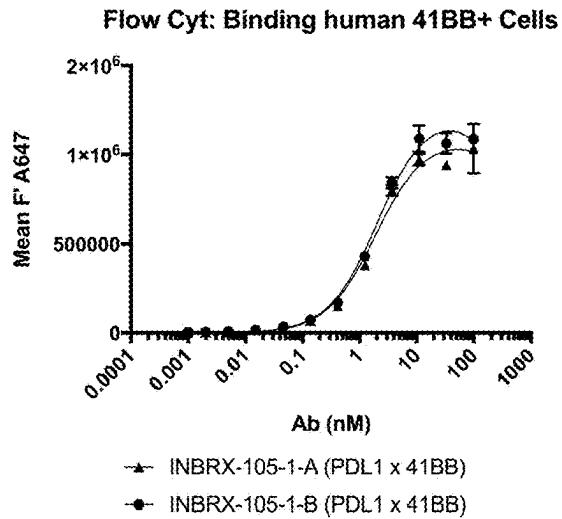


FIG. 14B

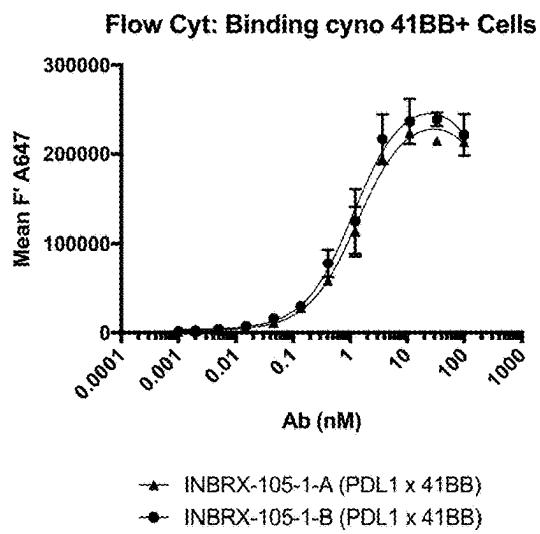


FIG. 14C

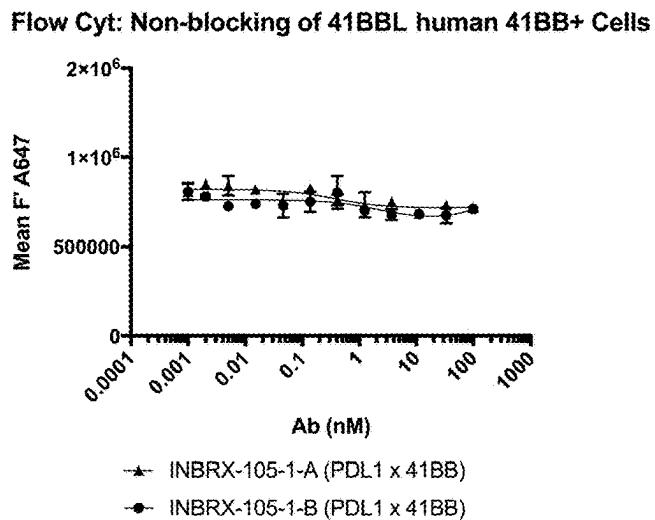


FIG. 15A

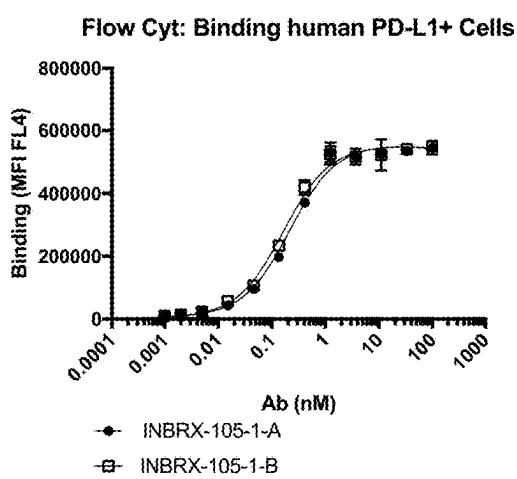


FIG. 15B

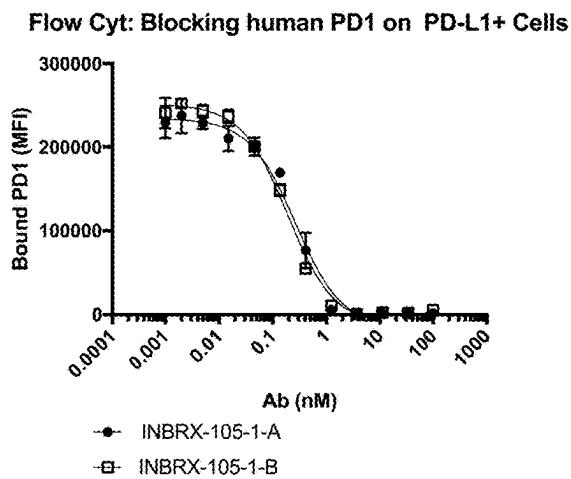


FIG. 15C

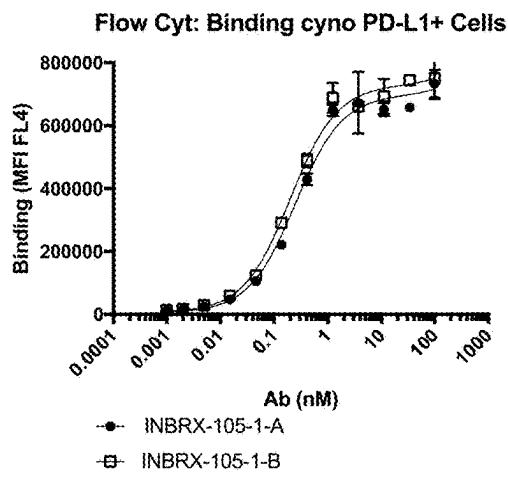


FIG. 15D

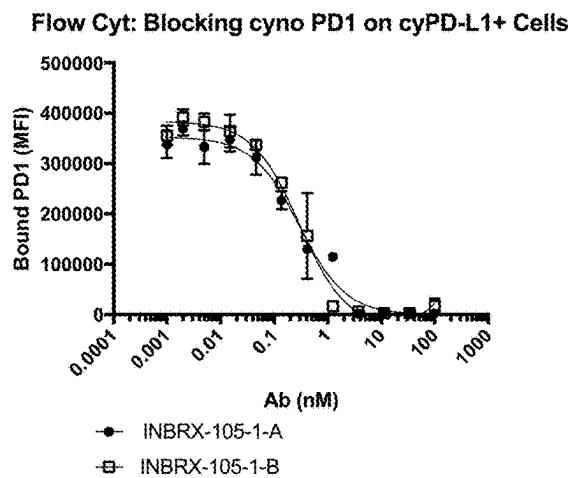


FIG. 16

PD-L1-Dependent 41BB Signaling: NF- κ B Reporter Cells

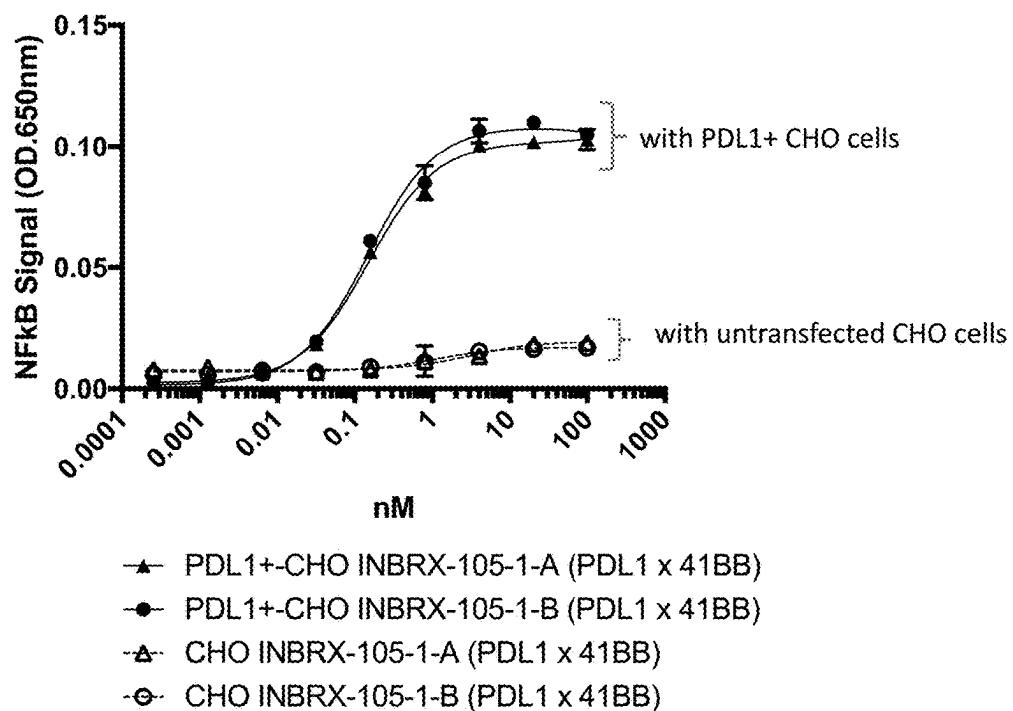


FIG. 17A

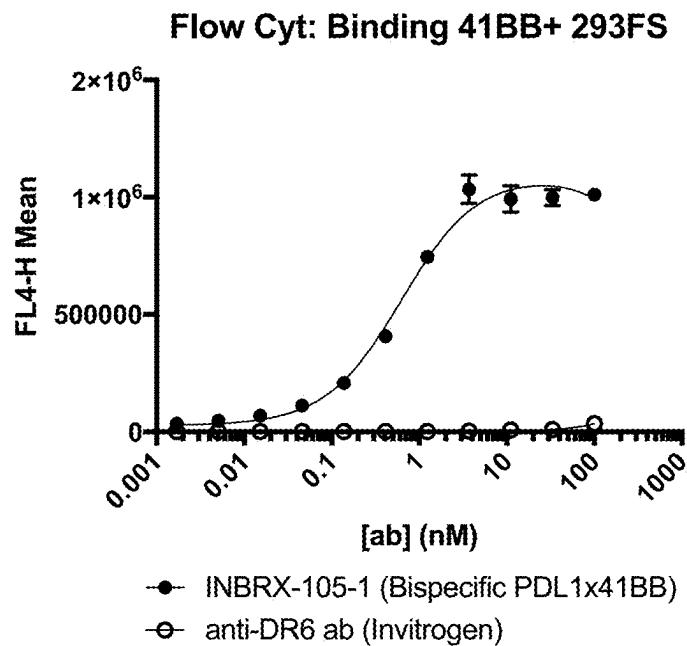


FIG. 17B

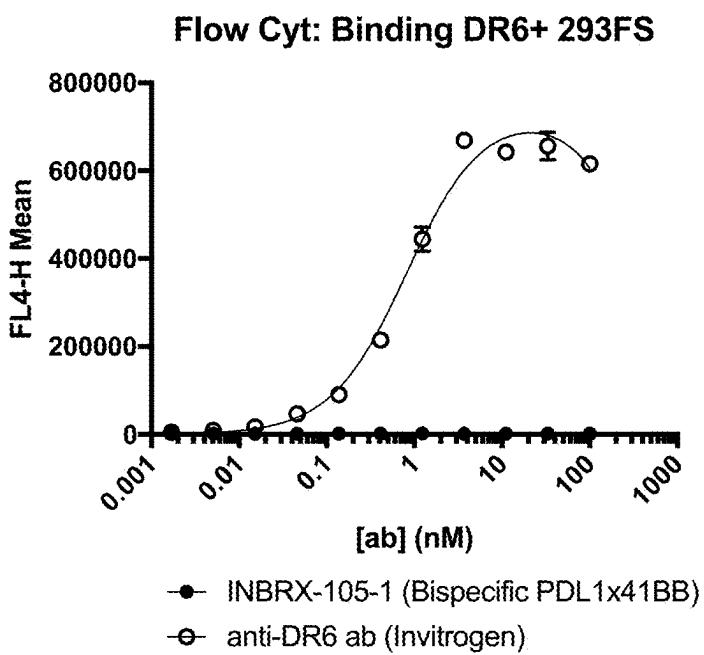


FIG. 18A

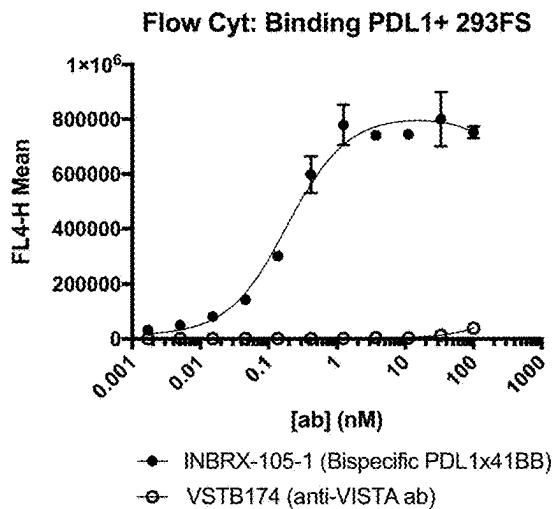


FIG. 18B

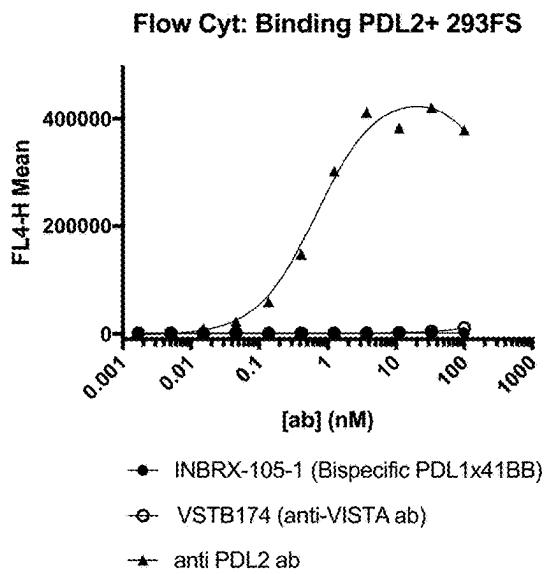


FIG. 18C

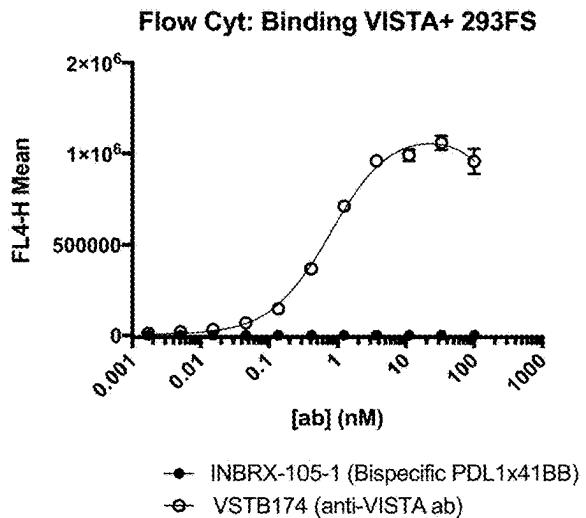


FIG. 19A

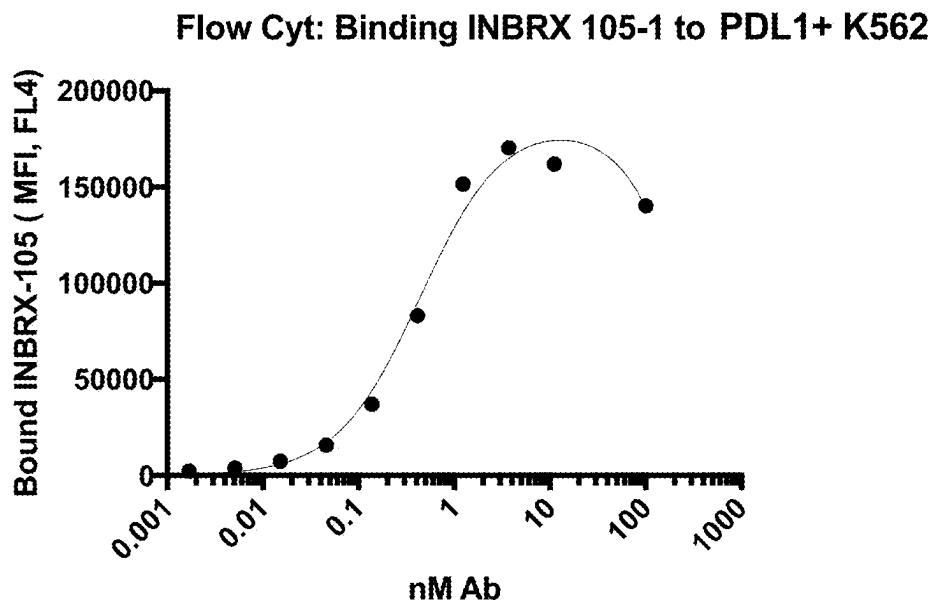


FIG. 19B

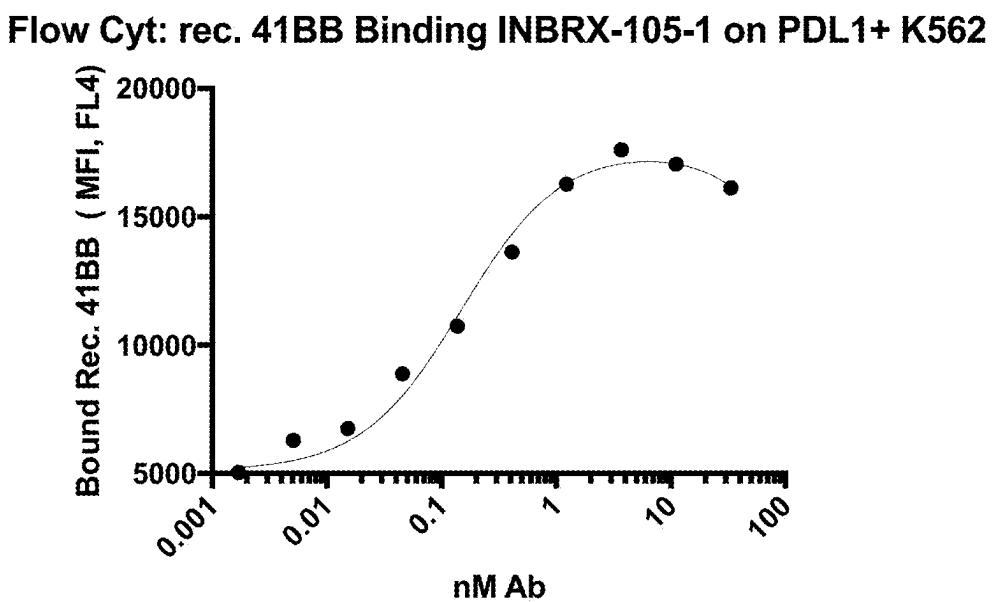


FIG. 20

Bridging ELISA: Coated PDL1 Detect 41BB

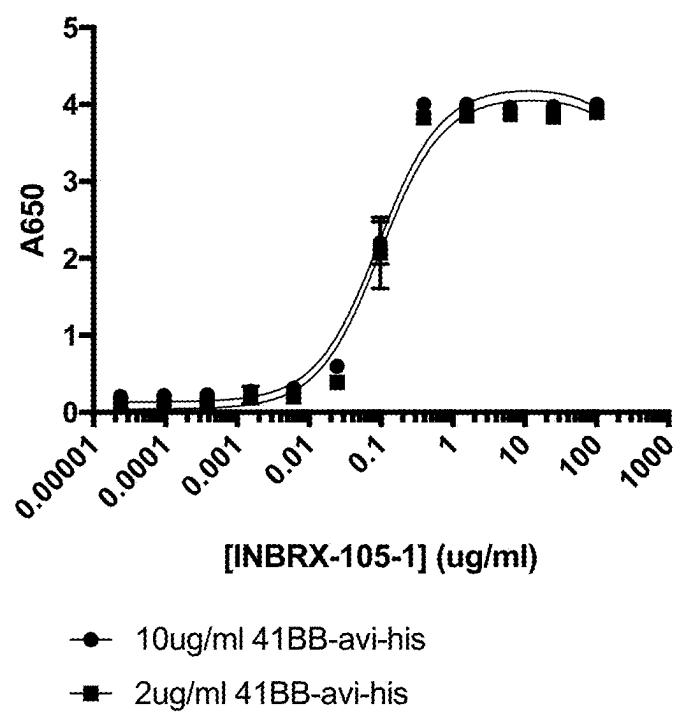


FIG. 21A

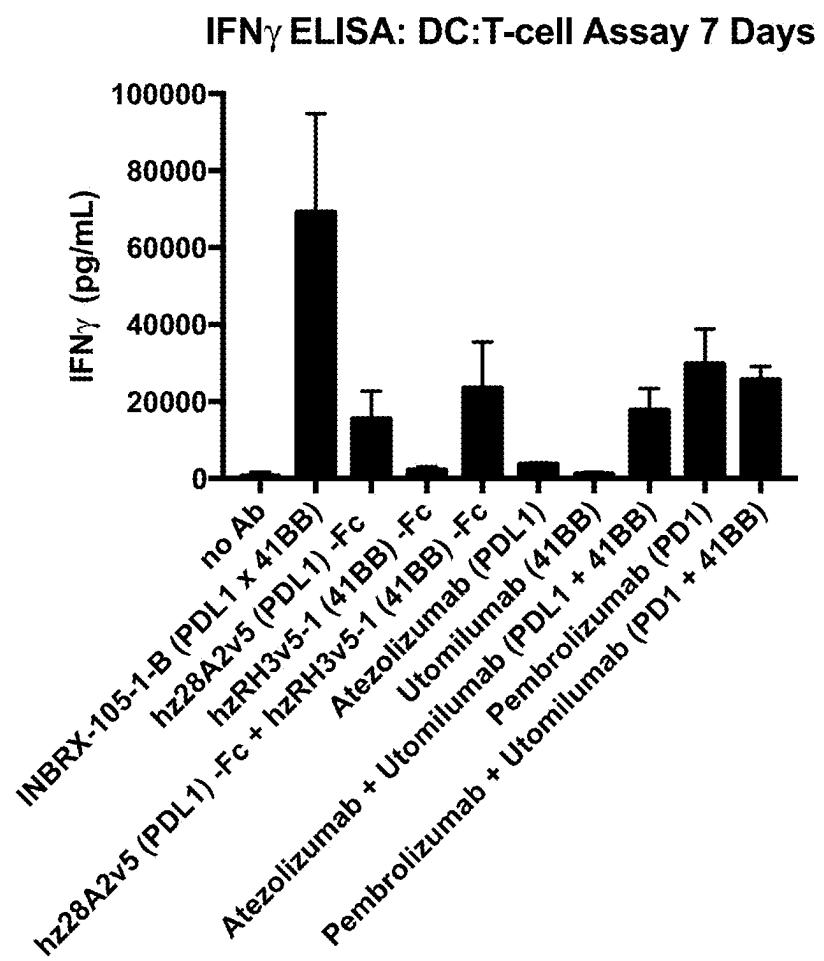


FIG. 21B

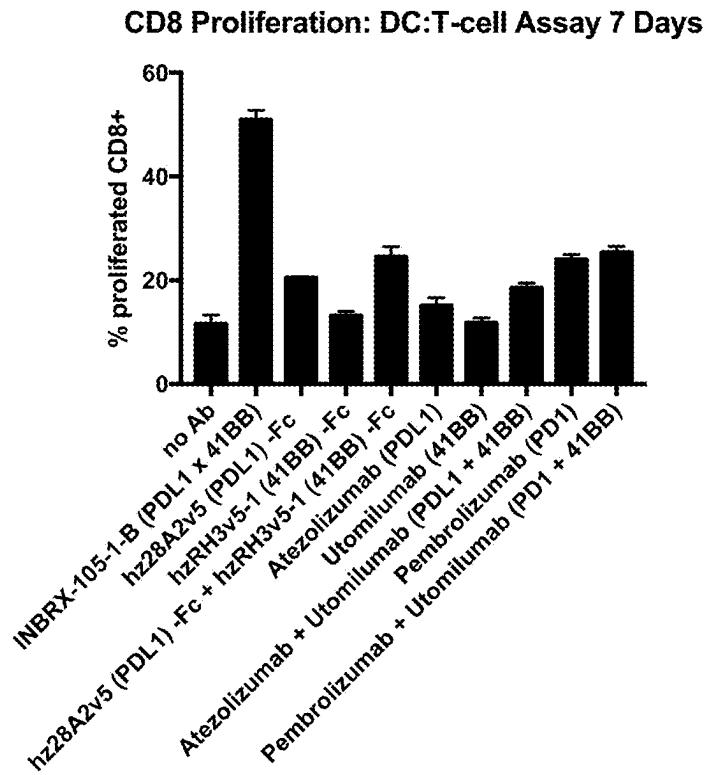


FIG. 21C

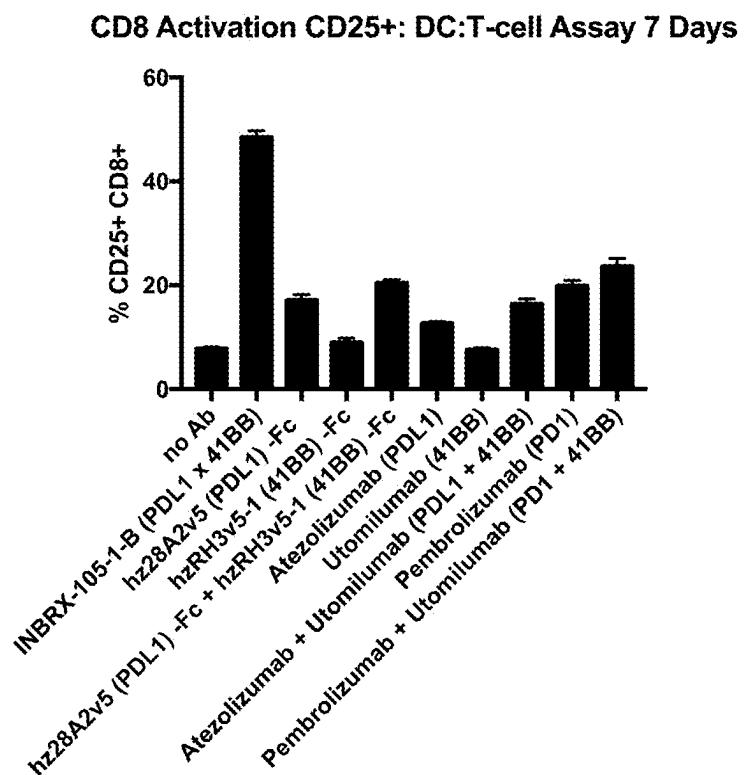


FIG. 22A

CD8 Proliferation: PDL1-Dependent 41BB Agonism

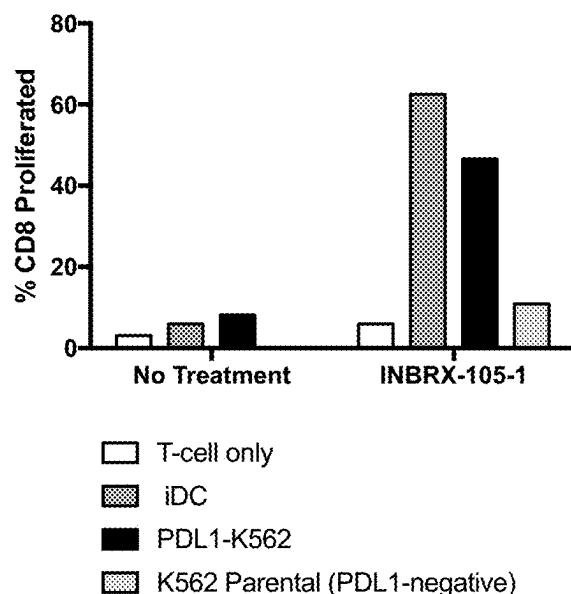


FIG. 22B

INF γ ELISA: PDL1-Dependent 41BB Agonism

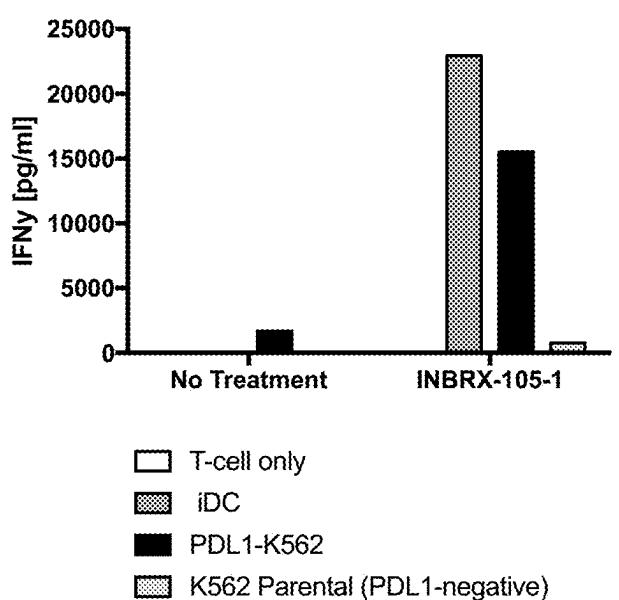


FIG. 23

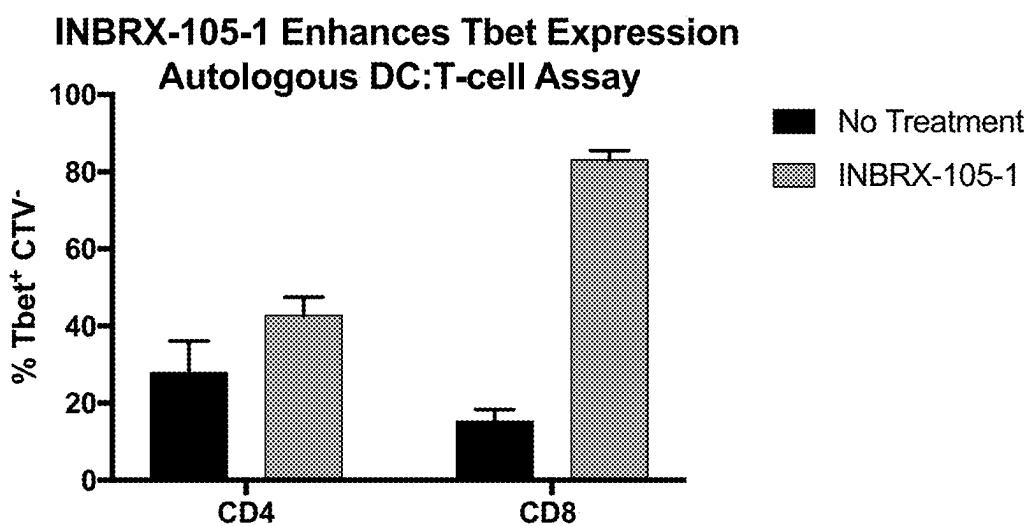


FIG. 24A

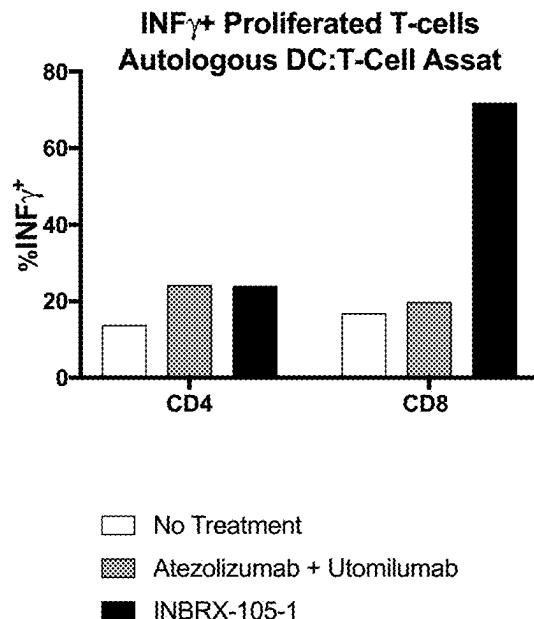


FIG. 24B

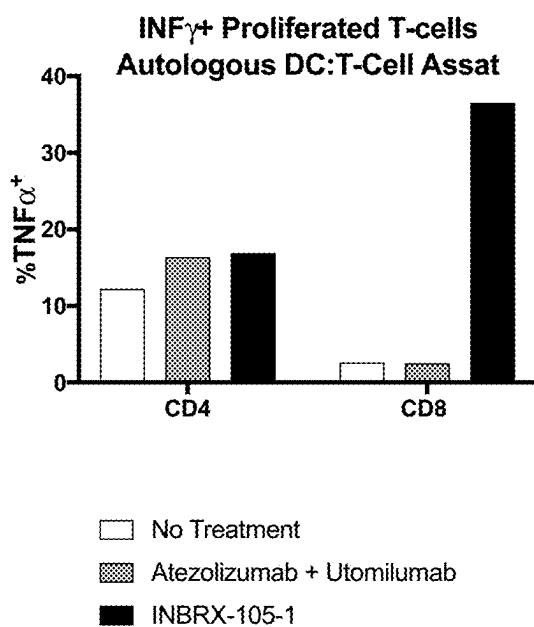


FIG. 25A

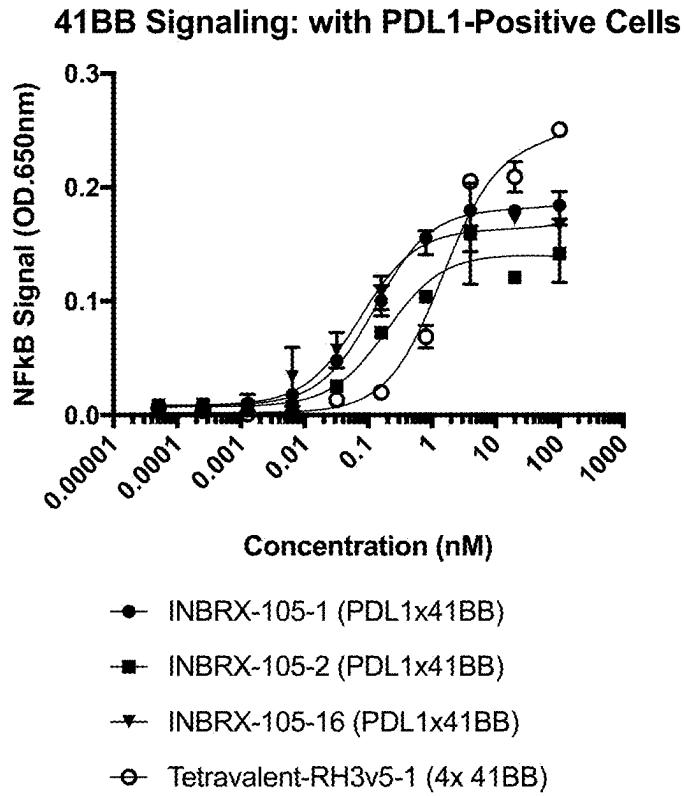
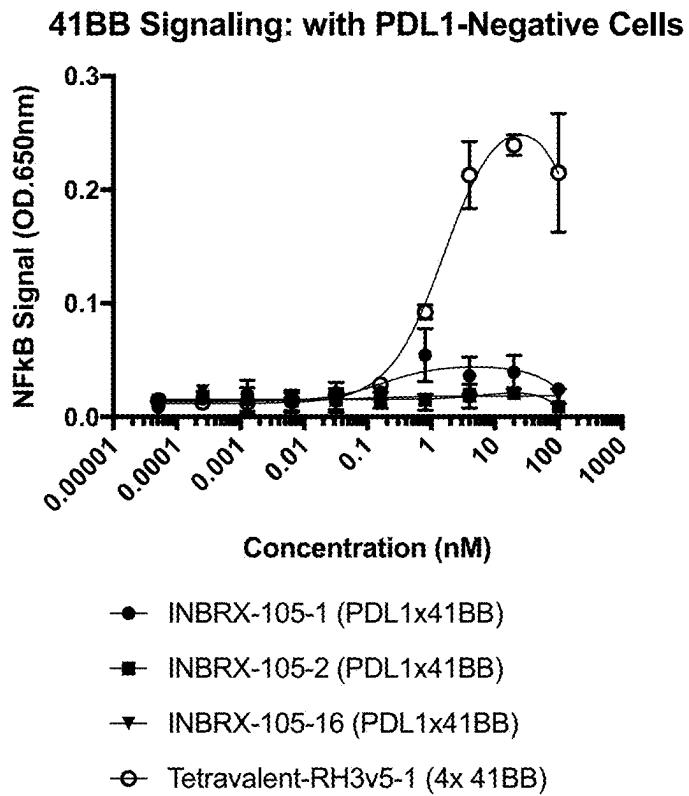


FIG. 25B



USES OF PDL1-BINDING PROTEINS**RELATED APPLICATIONS**

[0001] This application is a divisional of U.S. patent application Ser. No. 18/067,484, filed Dec. 16, 2022, which is a divisional of U.S. patent application Ser. No. 16/601,825, filed Oct. 15, 2019, issued as U.S. Pat. No. 11,566,078, which is a divisional of U.S. patent application Ser. No. 15/404,016, filed Jan. 11, 2017, issued as U.S. Pat. No. 10,501,551, which claims the benefit of U.S. Provisional Application No. 62/277,028, filed Jan. 11, 2016; the contents of each of which are incorporated herein by reference in their entirety.

SEQUENCE LISTING

[0002] The present application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on Dec. 14, 2022, is named “2022-12-14_01202-0005-02US.xml” and is 617,844 bytes in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0003] This invention relates generally to molecules that specifically engage 41BB, a member of the TNF receptor superfamily (TNFRSF). More specifically, this invention relates to multivalent and/or multispecific molecules that bind at least 41BB.

BACKGROUND OF THE INVENTION

[0004] The tumor necrosis factor receptor superfamily consists of several structurally related cell surface receptors. Activation by multimeric ligands is a common feature of many of these receptors. Many members of the TNFRSF have therapeutic utility in numerous pathologies, if activated properly. Agonism of this receptor family often requires higher order clustering, and conventional bivalent antibodies are not ideal for this purpose. Therefore, there exists a therapeutic need for more potent agonist molecules of the TNFRSF.

SUMMARY OF THE INVENTION

[0005] The disclosure provides multivalent and multispecific TNF receptor superfamily (TNFRSF) binding fusion polypeptides that bind at least 41BB (also known as tumor necrosis factor receptor superfamily, member 4 (TNFRSF9) and/or CD137)). The use of the term “41BB” is intended to cover any variation thereof, such as, by way of non-limiting example, 41-BB and/or 4-1BB, and all variations are used herein interchangeably. These molecules that bind at least 41BB are referred to herein as “41BB-targeting molecules” or “41BB-targeting fusions” or “41BB-targeting proteins” or “41BB-targeting fusion polypeptides” or “41BB-targeting fusion proteins.” In some embodiments, the 41BB-targeting molecule is a multivalent molecule, for example, a multivalent 41BB-targeting fusion protein. In some embodiments, the 41BB-targeting molecule is a multispecific molecule, for example, a multispecific 41BB-targeting fusion protein. In some embodiments, the 41BB-targeting molecule is a multivalent and multispecific molecule, for example, a multivalent and multispecific 41BB-targeting fusion protein.

As used herein, the term “fusion protein” or “fusion polypeptide” or “41BB-targeting fusion protein” or “41BB-targeting fusion polypeptide,” unless otherwise specifically denoted, refers to any fusion protein embodiment of the disclosure, including, but not limited to, multivalent fusion proteins, multispecific fusion proteins, or multivalent and multispecific fusion proteins.

[0006] The disclosure also provides multivalent and multispecific fusion polypeptides that bind at least programmed death ligand 1 (PDL1), also known as PD-L1, CD274, B7 homolog 1 and/or B7-H1. The use of the term “PDL1” is intended to cover any variation thereof, such as, by way of non-limiting example, PD-L1 and/or PDL-1, all variations are used herein interchangeably. These molecules that bind at least PDL1 are referred to herein as “PDL1-targeting molecules” or “PDL1-targeting fusions” or “PDL1-targeting proteins” or “PDL1-targeting fusion polypeptides” or “PDL1-targeting fusion proteins.” In some embodiments, the PDL1-targeting molecule is a multivalent molecule, for example, a multivalent PDL1-targeting fusion protein. In some embodiments, the PDL1-targeting molecule is a multispecific molecule, for example, a multispecific PDL1-targeting fusion protein. In some embodiments, the PDL1-targeting molecule is a multivalent and multispecific molecule, for example, a multivalent and multispecific PDL1-targeting fusion protein. As used herein, the term “fusion protein” or “fusion polypeptide” or “PDL1-targeting fusion protein” or “PDL1-targeting fusion polypeptide,” unless otherwise specifically denoted, refers to any fusion protein embodiment of the disclosure, including, but not limited to, multivalent fusion proteins, multispecific fusion proteins, or multivalent and multispecific fusion proteins.

[0007] The disclosure also provides multivalent and multispecific fusion polypeptides that bind at least PDL1 and 41BB. These molecules that bind at least PDL1 are referred to herein as “PDL1×41BB-targeting molecules” or “PDL1×41BB-targeting fusions” or “PDL1×41BB-targeting proteins” or “PDL1×41BB-targeting fusion polypeptides” or “PDL1×41BB-targeting fusion proteins.” In some embodiments, the PDL1×41BB-targeting molecule is a multivalent molecule, for example, a multivalent PDL1×41BB-targeting fusion protein. In some embodiments, the PDL1×41BB-targeting molecule is a multispecific molecule, for example, a multispecific PDL1×41BB-targeting fusion protein. In some embodiments, the PDL1×41BB-targeting molecule is a multivalent and multispecific molecule, for example, a multivalent and multispecific PDL1-targeting fusion protein. As used herein, the term “fusion protein” or “fusion polypeptide” or “PDL1×41BB-targeting fusion protein” or “PDL1×41BB-targeting fusion polypeptide,” unless otherwise specifically denoted, refers to any fusion protein embodiment of the disclosure, including, but not limited to, multivalent fusion proteins, multispecific fusion proteins, or multivalent and multispecific fusion proteins.

[0008] In some embodiments, the multivalent and/or multispecific fusion protein binds at least 41BB. Conventional antibodies targeting members of the TNF receptor superfamily (TNFRSF) have been shown to require exogenous crosslinking to achieve sufficient agonist activity, as evidenced by the necessity for Fc-gamma Receptor (FcγRs) for the activity of antibodies to DR4, DR5, GITR and OX40 (Ichikawa et al 2001 al Nat. Med. 7, 954-960, Li et al 2008 Drug Dev. Res. 69, 69-82; Pukac et al 2005 Br. J. Cancer 92, 1430-1441; Yanda et al 2008 Ann. Oncol. 19, 1060-1067;

Yang et al 2007 Cancer Lett. 251:146-157; Bulliard et al 2013 JEM 210(9): 1685; Bulliard et al 2014 Immunol and Cell Biol 92: 475-480). In addition to crosslinking via Fc γ Rs other exogenous agents including addition of the oligomeric ligand or antibody binding entities (e.g. protein A and secondary antibodies) have been demonstrated to enhance anti-TNFRSF antibody clustering and downstream signaling. For example, the addition of the DR5 ligand TRAIL enhanced the apoptosis inducing ability of an anti-DR5 antibody (Graves et al 2014 Cancer Cell 26: 177-189). These findings suggest the need for clustering of TNFRSFs beyond a dimer.

[0009] The present disclosure provides multivalent TNFRSF binding fusion proteins, which comprise 2 or more TNFRSF binding domains (TBDs) where at least one TBD binds 41BB. In some embodiments, the fusion proteins of the present disclosure have utility in treating neoplasms.

[0010] In some embodiments, the fusion protein contains two or more different TBDs, where each TBD binds 41BB. In some embodiments, the fusion protein contains multiple copies of a TBD that binds 41BB. For example, in some embodiments, the fusion protein contains at least two copies of a TBD that binds 41BB. In some embodiments, the fusion protein contains at least three copies of a TBD that binds 41BB. In some embodiments, the fusion protein contains at least four copies of a TBD that binds 41BB. In some embodiments, the fusion protein contains at least five copies of a TBD that binds 41BB. In some embodiments, the fusion protein contains at least six copies of a TBD that binds 41BB. In some embodiments, the fusion protein contains six or more copies of a TBD that binds 41BB.

[0011] In other embodiments, the fusion proteins of the present disclosure bind 41BB and a second TNFRSF member for example GITR, OX40, CD27, TNFR2 and/or CD40. In these embodiments, the fusion proteins of the present disclosure modulate immune cells leading to enhanced tumor destruction. In other embodiments, the fusion proteins of the present disclosure have utility in treating inflammatory conditions. In these embodiments, the fusion proteins of the present disclosure modulate immune cells leading to dampening of the inflammatory insult. For example, specifically agonizing TNFR2 can enhance Treg proliferation leading to immune suppression.

[0012] The fusion proteins of the present disclosure are capable of enhanced clustering of TNFRSF members compared to non-cross-linked bivalent antibodies. The enhanced clustered of TNFRSF members mediated by the fusion proteins of the present disclosure induce enhanced TNFRSF-dependent signaling compared to non-cross-linked bivalent antibodies. In most embodiments, the fusion protein will incorporate more than 2 TBDs, for example, three, four, five, or six.

[0013] In some embodiments, the fusion proteins are multispecific containing a TBD and a binding domain directed toward a second antigen. In these, embodiments, the binding to the second antigen is capable of providing the additional crosslinking function and TNFRSF activation can be achieved with only one or two TBDs. In these embodiments, the TNFRSF signaling is enhanced and focused by the presence of the second antigen. These multispecific TBD containing fusion proteins are useful means to achieve conditional signaling of a given TNFRSF member.

[0014] In these embodiments, binding to the TNFRSF member by the TBD induces minimal signaling unless the

second antigen is co-engaged. For example, the multispecific fusion proteins of the present disclosure are capable binding 41BB and PD-L1 and 41BB-dependent signaling is greatly enhanced when the fusion protein is bound to a PD-L1 expressing cell. In another example, the multispecific fusion proteins of the present disclosure are capable binding 41BB and Folate Receptor Alpha (FR α) and 41BB-dependent signaling is greatly enhanced when the fusion protein is bound to a FR α expressing cell.

[0015] The present disclosure provides isolated polypeptides that specifically bind 41BB. In some embodiments, the isolated polypeptide is derived from antibodies or antibody fragments including scFv, Fabs, single domain antibodies (sdAb), V_{NAR}, or VHJs. In some embodiments, the isolated polypeptide is human or humanized sdAb. The sdAb fragments can be derived from VHJ, V_{NAR}, engineered VH or VK domains. VHJs can be generated from camelid heavy chain only antibodies. V_{NARS} can be generated from cartilaginous fish heavy chain only antibodies. Various methods have been implemented to generate monomeric sdAbs from conventionally heterodimeric VH and VK domains, including interface engineering and selection of specific germline families. In other embodiments, the isolated polypeptides are derived from non-antibody scaffold proteins for example but not limited to designed ankyrin repeat proteins (darpins), avimers, anticalin/lipocalins, centyrins and fynomers.

[0016] In some embodiments, the isolated polypeptide includes an amino acid sequence selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83. In some embodiments, the isolated polypeptide includes an amino acid sequence selected from the group consisting of SEQ ID NO: 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83.

[0017] In some embodiments, the isolated polypeptide includes an amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83. In some embodiments, the isolated polypeptide includes an amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83.

[0018] In some embodiments, the isolated polypeptide comprises a complementarity determining region 1 (CDR1) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, 21, 26, 30, 50, 65, and 69; a complementarity determining region 2 (CDR2) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, 27, 31, 42, 44, 48, 52, 61, 63, 71, 73, 75, 77, and 79; and a complementarity determining region 3 (CDR3) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 19, 22, 24, 28, 32, 55, and 57.

[0019] The present disclosure provides multivalent fusion proteins, which comprise two or more binding domains

(BDs) where at least one BD binds PDL1. In some embodiments, the fusion proteins of the present disclosure have utility in treating neoplasms.

[0020] In some embodiments, the fusion protein contains two or more different BDs, where each BD binds PDL1. In some embodiments, the fusion protein contains multiple copies of a BD that binds PDL1. For example, in some embodiments, the fusion protein contains at least two copies of a BD that binds PDL1. In some embodiments, the fusion protein contains at least three copies of a BD that binds PDL1. In some embodiments, the fusion protein contains at least four copies of a BD that binds PDL1. In some embodiments, the fusion protein contains at least five copies of a BD that binds PDL1. In some embodiments, the fusion protein contains at least six copies of a BD that binds PDL1. In some embodiments, the fusion protein contains six or more copies of a BD that binds PDL1.

[0021] The present disclosure provides isolated polypeptides that specifically bind 41BB. In some embodiments, the isolated polypeptide is derived from antibodies or antibody fragments including scFv, Fabs, single domain antibodies (sdAb), V_{NAR}, or VHJs. In some embodiments, the isolated polypeptide is human or humanized sdAb. The sdAb fragments can be derived from VHH, V_{NAR}, engineered VH or VK domains. VHJs can be generated from camelid heavy chain only antibodies. V_{NARS} can be generated from cartilaginous fish heavy chain only antibodies. Various methods have been implemented to generate monomeric sdAbs from conventionally heterodimeric VH and VK domains, including interface engineering and selection of specific germline families. In other embodiments, the isolated polypeptides are derived from non-antibody scaffold proteins for example but not limited to designed ankyrin repeat proteins (darpins), avimers, anticalin/lipocalins, cetylryns and fynomers.

[0022] In some embodiments, the isolated polypeptide includes an amino acid sequence selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124. In some embodiments, the isolated polypeptide includes an amino acid sequence selected from the group consisting of SEQ ID NO: 119-124.

[0023] In some embodiments, the isolated polypeptide includes an amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124. In some embodiments, the isolated polypeptide includes an amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 119-124.

[0024] In some embodiments, the isolated polypeptide comprises a complementarity determining region 1 (CDR1) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 101, 105, and 109; a complementarity determining region 2 (CDR2) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 102, 106, 110, and 117; and a complementarity determining region 3 (CDR3) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 103, 107, 111, 113, 115, and 118.

[0025] In some embodiments, the present disclosure provides isolated polypeptides that specifically bind at least 41BB and PDL1. In some embodiments, each binding

domain (BD) in the isolated polypeptide is derived from antibodies or antibody fragments including scFv, Fabs, single domain antibodies (sdAb), V_{NAR}, or VHJs. In some embodiments, each BD is human or humanized sdAb. The sdAb fragments can be derived from VHH, V_{NAR}, engineered VH or VK domains. VHJs can be generated from camelid heavy chain only antibodies. V_{NARS} can be generated from cartilaginous fish heavy chain only antibodies. Various methods have been implemented to generate monomeric sdAbs from conventionally heterodimeric VH and VK domains, including interface engineering and selection of specific germline families. In other embodiments, the isolated polypeptides are derived from non-antibody scaffold proteins for example but not limited to designed ankyrin repeat proteins (darpins), avimers, anticalin/lipocalins, cetylryns and fynomers.

[0026] In some embodiments, the isolated polypeptide includes a first amino acid sequence that binds 4B11 selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, and a second amino acid sequence that binds PDL1 selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124.

[0027] In some embodiments, the isolated polypeptide includes a first amino acid sequence that binds 4B11 selected from the group consisting of SEQ ID NO: 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, and a second amino acid sequence that binds PDL1 selected from the group consisting of SEQ ID NO: 119-124.

[0028] In some embodiments, the isolated polypeptide includes a first amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence that binds 4B11 selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, and a second amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence that binds PDL1 selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124.

[0029] In some embodiments, the isolated polypeptide includes a first amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence that binds 4B11 selected from the group consisting of SEQ ID NO: 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, and a second amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence that binds PDL1 selected from the group consisting of SEQ ID NO: 119-124.

[0030] In some embodiments, the isolated polypeptide includes (i) a first amino acid sequence that binds 4B11 and comprises a complementarity determining region 1 (CDRT) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, 21, 26, 30, 50, 65, and 69; a complementarity determining region 2 (CDR2) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, 27, 31, 42, 44, 48, 52, 61, 63, 71, 73, 75, 77, and 79; and a complementarity determining region 3 (CDR3) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 19, 22, 24, 28, 32, 55,

and 57; and (ii) a second amino acid sequence that binds PDL1 and comprises a CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 101, 105, and 109; a CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 102, 106, 110, and 117; and a CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 103, 107, 111, 113, 115, and 118.

[0031] In some embodiments, the binding domains (BDs) of the present disclosure, e.g., the 41BB-binding domains and/or the PDL1-binding domains, are derived from antibodies or antibody fragments including scFv, Fabs, single domain antibodies (sdAb), V_{NAR} , or VHJs. In some embodiments, the BDs are human or humanized sdAb. The sdAb fragments, can be derived from VHH, V_{NAR} , engineered VH or VK domains. VHHs can be generated from camelid heavy chain only antibodies. V_{NARS} can be generated from cartilaginous fish heavy chain only antibodies. Various methods have been implemented to generate monomeric sdAbs from conventionally heterodimeric VH and VK domains, including interface engineering and selection of specific germline families. In other embodiments, the BDs are derived from non-antibody scaffold proteins for example but not limited to designed ankyrin repeat proteins (darpins), avimer, anticalin/lipocalins, centyrins and fynomers.

[0032] Generally, the fusion proteins of the present disclosure consist of at least two or more BDs operably linked via a linker polypeptide. The utilization of sdAb fragments as the specific BD within the fusion the present disclosure has the benefit of avoiding the heavy chain: light chain mis-pairing problem common to many bi/multispecific antibody approaches. In addition, the fusion proteins of the present disclosure avoid the use of long linkers necessitated by many bispecific antibodies.

[0033] In some embodiments, all of the BDs of the fusion protein are TBDs that recognize the same epitope on the given TNFRSF member. For example, the fusion proteins of present disclosure may incorporate 2, 3, 4, 5, or 6 TBDs with identical specificity to 41BB. In other embodiments, the fusion protein incorporates TBDs that recognize distinct epitopes on the given TNFRSF member. For example, the fusion proteins of present disclosure may incorporate 2, 3, 4, 5, or 6 TBDs with distinct recognition specificities toward various epitopes on 41BB. In these embodiments, the fusion proteins of the present disclosure contain multiple TBDs that target distinct regions of the particular TNFRSF member. In some embodiments, the TBDs may recognize different epitopes on the same TNFRSF member or recognize epitopes on distinct TNFRSF members. For example, the present disclosure provides multispecific fusion proteins incorporating TBDs that bind GITR and 41BB or OX40 and 41BB, or CD27 and 41BB.

[0034] In some embodiments, the multispecific fusion protein is a bispecific molecule that targets 41BB and PDL1. In some embodiments, the bispecific fusion protein includes a 41BB-targeting binding domain selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, operably linked to a second binding domain (BD2) that binds PDL1. In some embodiments, the BD2 comprises an amino acid sequence that specifically binds PDL1. In some embodiments, the BD2 comprises a PDL1-targeting domain selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124. In some embodiments, the BD2 comprises a PDL1-targeting domain selected from the group consisting of SEQ ID NO: 119-124. In some embodiments, the BD2 comprises an amino acid sequence that is selected from the group consisting of SEQ ID NO: 126-408.

[0035] In some embodiments, the multispecific fusion protein is a bispecific molecule that targets 41BB and PDL1. In some embodiments, the bispecific fusion protein includes a 41BB-targeting binding domain selected from the group consisting of SEQ ID NO: 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, operably linked to a second binding domain (BD2) that binds PDL1. In some embodiments, the BD2 comprises an amino acid sequence that specifically binds PDL1. In some embodiments, the BD2 comprises a PDL1-targeting domain selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124. In some embodiments, the BD2 comprises a PDL1-targeting domain selected from the group consisting of SEQ ID NO: 119-124. In some embodiments, the BD2 comprises an amino acid sequence that specifically binds PDL1 and is selected from the group consisting of SEQ ID NO: 126-408.

[0036] In some embodiments, the multispecific fusion protein is a bispecific molecule that targets 41BB and PDL1. In some embodiments, the bispecific fusion protein includes a PDL1-targeting binding domain selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124, operably linked to a second TBD (TBD2) that binds 41BB. In some embodiments, the TBD2 comprises an amino acid sequence that specifically binds 41BB. In some embodiments, the TBD2 comprises a 41BB-targeting domain selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83. In some embodiments, the TBD2 comprises an amino acid sequence that specifically binds 41BB and is selected from the group consisting of SEQ ID NO: 84-99.

[0037] In some embodiments, the multispecific fusion protein is a bispecific molecule that targets 41BB and PDL1. In some embodiments, the bispecific fusion protein includes a PDL1-targeting binding domain selected from the group consisting of SEQ ID NO: 119-124, operably linked to a second TBD (TBD2) that binds 41BB. In some embodiments, the TBD2 comprises an amino acid sequence that specifically binds 41BB. In some embodiments, the TBD2 comprises a 41BB-targeting domain selected from the group consisting of SEQ ID NO: 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83. In some embodiments, the TBD2 comprises an amino acid sequence that specifically binds 41BB and is selected from the group consisting of SEQ ID NO: 84-99.

[0038] In some embodiments, the multispecific fusion protein is a bispecific molecule that targets 41BB and PDL1 and comprises an amino acid sequence that is selected from the group consisting of SEQ ID NO: 448-456.

[0039] In some embodiments, the multispecific fusion protein is a bispecific molecule that targets 41BB and PDL1 and comprises an amino acid sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 448-456.

[0040] In some embodiments, all of the BDs of the fusion protein recognize the same epitope on PDL1. For example, the fusion proteins of present disclosure may incorporate 2, 3, 4, 5, or 6 BDs with identical specificity to PDL1. In other embodiments, the fusion protein incorporates BDs that recognize distinct epitopes on PDL1. For example, the fusion proteins of present disclosure may incorporate 2, 3, 4, 5, or 6 BDs with distinct recognition specificities toward

various epitopes on PDL1. In these embodiments, the fusion proteins of the present disclosure contain multiple BDs that target distinct regions of the PDL1. In some embodiments, the BDs may recognize different epitopes on PDL1.

[0041] In some embodiments, the fusion protein of the present disclosure is composed of a single polypeptide. In other embodiments, the fusion protein of the present disclosure is composed of more than one polypeptide. For example, wherein a heterodimerization domain is incorporated into the fusion protein so as to construct an asymmetric fusion protein. For example, if an immunoglobulin Fc region is incorporated into the fusion protein the CH3 domain can be used as a homodimerization domain, or the CH3 dimer interface region can be mutated so as to enable heterodimerization.

[0042] In some embodiments, the fusion protein contains the BDs opposite ends. For example, the BDs are located on both the amino-terminal (N-terminal) portion of the fusion protein and the carboxy-terminal (C-terminal) portion of the fusion protein. In other embodiments, all the TBDs reside on the same end of the fusion protein. For example, BDs reside on either the amino- or carboxy-terminal portions of the fusion protein.

[0043] In some embodiments, the linker polypeptide contains an immunoglobulin Fc region. In some embodiments, the immunoglobulin Fc region is an IgG isotype selected from the group consisting of IgG1 subclass, IgG2 subclass, IgG3 subclass, and IgG4 subclass.

[0044] In some embodiments, the immunoglobulin Fc region or immunologically active fragment thereof is an IgG isotype. For example, the immunoglobulin Fc region of the fusion protein is of human IgG1 subclass, having an amino acid sequence:

(SEQ ID NO: 1)				
PAPELL E GPS	VFLFPPPKPKD	TLMISRTPEV	TCVVVDVSHE	DPEVKFNWYV
DGVEVHNAKT	KPREEQY N ST	YRVVSVLTVL	HODWLNGKEY	KCKVSNKALP
APIEKTIASKA	KGQPREPQVY	TLPPSRDELT	KNQVSLTCLV	KGFYPSDIAV
EWESNGQOPEN	NYKTTTPPVLD	SDGSFFLYSK	LTVDKSRWQQ	GNVFSCSVMH
EALHNHYTQK	SLSLSPGK			

[0045] In some embodiments, the immunoglobulin Fc region or immunologically active fragment thereof comprises a human IgG1 polypeptide sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1.

[0046] In some embodiments, the human IgG1 Fc region is modified at amino acid Asn297 (Boxed in SEQ ID NOS: 1-4, Kabat Numbering) to prevent to glycosylation of the fusion protein, e.g., Asn297Ala (N297A) or Asn297Asp (N297D). In some embodiments, the Fc region of the fusion protein is modified at amino acid Leu235 (Bold in SEQ ID NO: 1, Kabat Numbering) to alter Fc receptor interactions, e.g., Leu235Glu (L235E) or Leu235Ala (L235A). In some embodiments, the Fc region of the fusion protein is modified at amino acid Leu234 (Bold in SEQ ID NO: 1, Kabat Numbering) to alter Fc receptor interactions, e.g., Leu234Ala (L234A). In some embodiments, the Fc region of the fusion protein is modified at amino acid Leu234 (Boxed, Kabat Numbering) to alter Fc receptor interactions, e.g., Leu235Glu (L235E). In some embodiments, the Fc region of the fusion protein is altered at both amino acid 234 and 235, e.g., Leu234Ala and Leu235Ala (L234A/L235A)

or Leu234Val and Leu235Ala (L234V/L235A). In some embodiments, the Fc region of the fusion protein is lacking an amino acid at one or more of the following positions to reduce Fc receptor binding: Glu233 (E233, Bold in SEQ ID NO: 1), Leu234 (L234), or Leu235 (L235). In some embodiments, the Fc region of the fusion protein is altered at Gly235 to reduce Fc receptor binding. For example, wherein Gly235 is deleted from the fusion protein. In some embodiments, the human IgG1 Fc region is modified at amino acid Gly236 (Boxed in SEQ ID NO: 1) to enhance the interaction with CD32A, e.g., Gly236Ala (G236A). In some embodiments, the human IgG1 Fc region lacks Lys447 (EU index of Kabat et al 1991 Sequences of Proteins of Immunological Interest).

[0047] In some embodiments, the Fc region of the fusion protein is altered at one or more of the following positions to reduce Fc receptor binding: Leu 234 (L234), Leu235 (L235), Asp265 (D265), Asp270 (D270), Ser298 (S298), Asn297 (N297), Asn325 (N325) or Ala327 (A327). For example, Leu 234Ala (L234A), Leu235Ala (L235A), Asp265Asn (D265N), Asp270Asn (D270N), Ser298Asn (S298N), Asn297Ala (N297A), Asn325Glu (N325E) or Ala327Ser (A327S). In preferred embodiments, modifications within the Fc region reduce binding to Fc-receptor-gamma receptors while have minimal impact on binding to the neonatal Fc receptor (FcRn).

[0048] In some embodiments, the Fc region of the fusion protein is lacking an amino acid at one or more of the following positions to reduce Fc receptor binding: Glu233 (E233), Leu234 (L234), or Leu235 (L235). In these embodiments, Fc deletion of these three amino acids reduces the

complement protein C1q binding. These modified Fc region polypeptides are referred to herein as "Fc deletion" polypeptides.

(SEQ ID NO: 2)	
PAPGGPSVFL	FPPPKKD TLM ISRTPEVTCV VVDVSHE DPE
VKFNFYV DGV	EVHNAKTKPR EEQYNSTYRV VS VLTVLHQD
WLNGKEYKCK	VSNKALPAPI EKTISKAKGQ PREPQVYTL
PSRDELTKNQ	VSLTCLVKGF YPSDIAVEWE SNGOPENNYK
TPPPVLDSDG	SFFLYSKLT DKS RWQQGNV FSCS VMHEAL
HNHYTQKSL	S LSPGK

[0049] In some embodiments, the immunoglobulin Fc region or immunologically active fragment thereof comprises a human IgG1 polypeptide sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 2.

[0050] In some embodiments, the immunoglobulin Fc region or immunologically active fragment of the fusion protein is of human IgG2 subclass, having an amino acid sequence:

(SEQ ID NO: 3)				
PAPPVAGPSV	FLFPPPKPKDT	LMISRTPEVT	CVVVVDVSHE	PEVQFNWYVD
GVEVHNAKTK	PREEQFN N STF	RVVSVLTVVH	QDWLNGKEYK	CKVSNKGLPA
PIEKTISKTK	GQPREPQVYT	LPSSREEMTK	NQVSLTCLVK	GFYPSPDISVE
WESNGQPENN	YKTTTPPMLDS	DGSFFFLYSKL	TVDKSRWQQG	NVFSCSVMHE
ALHNHYTQKS	LSSLSPGK			

[0051] In some embodiments, the fusion or immunologically active fragment thereof comprises a human IgG2 polypeptide sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 3.

[0052] In some embodiments, the human IgG2 Fc region is modified at amino acid Asn297 (Boxed in SEQ ID NOS: 1, 3, 4, and 5), to prevent to glycosylation of the antibody, e.g., Asn297Ala (N297A). In some embodiments, the human IgG2 Fc region lacks Lys447, which corresponds to residue 217 of SEQ ID NO: 3 (EU index of Kabat et al 1991 Sequences of Proteins of Immunological Interest).

[0053] In some embodiments, the immunoglobulin Fc region or immunologically active fragment of the fusion protein is of human IgG3 subclass, having an amino acid sequence:

(SEQ ID NO: 4)				
PAPELLGGPS	VFLFPPPKPD	TLMISRTPEV	TCVVVDVSHE	DPEVQFKWYV
DGVEVHNAKT	KPREEQFN N ST	FRVSVLTVL	HQDWLNGKEY	KCKVSNKALP
APIEKTSIKT	KGQPREPQVY	TLPPSREEMT	KNQVSLTCLV	KGFYPSPDIAV
EWESSGQPEN	NYNTTPPMLD	SDGSFFLYSK	LTVDKSRWQQ	GNIFSCSVMH
EALHN R FQTQK	SLSLSPGK			

[0054] In some embodiments, the antibody or immunologically active fragment thereof comprises a human IgG3 polypeptide sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 4.

[0055] In some embodiments, the human IgG3 Fc region is modified at amino acid Asn297 (Boxed in SEQ ID NOS: 1-4, Kabat Numbering) to prevent to glycosylation of the antibody, e.g., Asn297Ala (N297A). In some embodiments,

the human IgG3 Fc region is modified at amino acid 435 to extend the half-life, e.g., Arg435His (R435H, Boxed in SEQ ID NO: 3). In some embodiments, the human IgG3 Fc region lacks Lys447, which corresponds to residue 218 of SEQ ID NO: 4 (EU index of Kabat et al 1991 Sequences of Proteins of Immunological Interest).

[0056] In some embodiments, the immunoglobulin Fc region or immunologically active fragment of the fusion protein is of human IgG4 subclass, having an amino acid sequence:

(SEQ ID NO: 5)				
PAPEF G GGPS	VFLFPPPKPD	TLMISRTPEV	TCVVVDVSQE	DPEVQFNWYV
DGVEVHNAKT	KPREEQFN N ST	YRVSVLTVL	HQDWLNGKEY	KCKVSNKGLP
SSIEKTISKA	KGQPREPQVY	TLPPSQEEMT	KNQVSLTCLV	KGFYPSPDIAV
EWESNGOPEN	NYKTTPPVLQ	SDGSFFLYSR	LTVDKSRWQE	GNVESCSVMH
EALHNHYTQK	SLSLSPGK			

[0057] In some embodiments, the antibody or immunologically active fragment thereof comprises a human IgG4 polypeptide sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 5.

[0058] In other embodiments, the human IgG4 Fc region is modified at amino acid 235 to alter Fc receptor interactions, e.g., Leu235Glu (L235E). In some embodiments, the human IgG4 Fc region is modified at amino acid Asn297 (Boxed in SEQ ID NOs: 1-4, Kabat Numbering) to prevent to glycosylation of the antibody, e.g., Asn297Ala (N297A). In some embodiments, the human IgG4 Fc region lacks Lys447, which corresponds to residue 218 of SEQ ID NO: 5 (EU index of Kabat et al 1991 Sequences of Proteins of Immunological Interest).

[0059] In some embodiments, the immunoglobulin Fc region or immunologically active fragment of the fusion protein is of human IgG4 isotype, having an amino acid sequence:

				(SEQ ID NO: 6)
PAPELLGGPS	VFLFPKKPKD	TLMISRTPEV	TCVVVDVSQE	DPEVQFNWYV
DGVEVHNAKT	KPREEQY N ST	YRVVSVLTVL	HQDWLNGKEY	KCKVSNKGLP
S SIEKTISKA	KGQPREPQVY	TLPPSQEEMT	KNQVSLTCLV	KGFYP PSDIAV
EWESNGQOPEN	NYKTTPPVLD	SDGSFFLYSR	LTVDKSRWQE	GNVFSCSVMH
EALHNHYTQK	SLSLSLGK			

[0060] In some embodiments, the antibody or immunologically active fragment thereof comprises a human IgG4 polypeptide sequence that is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 6.

[0061] In some embodiments, the human IgG Fc region is modified to enhance FcRn binding. Examples of Fc mutations that enhance binding to FcRn are Met252Tyr, Ser254Thr, Thr256Glu (M252Y, S254T, T256E, respectively) (Kabat numbering, Dall'Acqua et al 2006, J. Biol Chem Vol. 281(33) 23514-23524), Met428Leu and Asn434Ser (M428L, N434S) (Zalevsky et al 2010 Nature Biotech, Vol. 28(2) 157-159), or Met252Ile, Thr256Asp, Met428Leu (M252I, T256D, M428L, respectively), (EU index of Kabat et al 1991 Sequences of Proteins of Immunological Interest). Met252 corresponds to residue 23 in SEQ ID NOs: 1, 4, and 5 and residue 22 in SEQ ID NO: 3. Ser254 corresponds to residue 25 in SEQ ID NOs: 1, 4, and 5 and residue 24 in SEQ ID NO: 3. Thr256 corresponds to residue 27 in SEQ ID NOs: 1, 4, and 5 and residue 26 in SEQ ID NO: 3. Met428 corresponds to residue 199 in SEQ ID NOs: 1, 4, and 5 and residue 198 in SEQ ID NO: 3. Asn434 corresponds to residue 205 in SEQ ID NOs: 1, 4, and 5 and residue 204 in SEQ ID NO: 3. In some embodiments where the fusion protein of the disclosure includes an Fc polypeptide, the Fc polypeptide is mutated or modified. In these embodiments, the mutated or modified Fc polypeptide includes the following mutations: Met252Tyr and Met428Leu (M252Y, M428L) using the Kabat numbering system.

[0062] In some embodiments, the human IgG Fc region is modified to alter antibody-dependent cellular cytotoxicity

(ADCC) and/or complement-dependent cytotoxicity (CDC), e.g., the amino acid modifications described in Natsume et al., 2008 Cancer Res, 68(10): 3863-72; Idusogie et al., 2001 J Immunol, 166(4): 2571-5; Moore et al., 2010 mAbs, 2(2): 181-189; Lazar et al., 2006 PNAS, 103(11): 4005-4010, Shields et al., 2001 JBC, 276(9): 6591-6604; Stavenhagen et al., 2007 Cancer Res, 67(18): 8882-8890; Stavenhagen et al., 2008 Advan. Enzyme Regul., 48: 152-164; Alegre et al, 1992 J Immunol, 148: 3461-3468; Reviewed in Kaneko and Niwa, 2011 Biodrugs, 25(1):1-11. Examples of mutations that enhance ADCC include modification at Ser239 and Ile332, for example Ser239Asp and Ile332Glu (S239D, I332E). Examples of mutations that enhance CDC include modifications at Lys326, which corresponds to residue 97 of SEQ ID NOs: 1, 4, and 5 and residue 96 of SEQ ID NO: 2, and Glu333, which corresponds to residue 104 of SEQ ID NOs: 1, 4, and 5 and residue 103 of SEQ ID NO: 3. In some embodiments the Fc region is modified at one or both of these positions, for example Lys326Ala and/or Glu333Ala (K326A and E333A).

[0063] In some embodiments, the human IgG Fc region is modified to induce heterodimerization. For example, having an amino acid modification within the CH3 domain at Thr366, which when replaced with a more bulky amino acid, e.g., Trp (T366W), is able to preferentially pair with a second CH3 domain having amino acid modifications to less bulky amino acids at positions Thr366, which corresponds to residue 137 of SEQ ID NOs: 1, 4, and 5 and residue 136 of SEQ ID NO: 3, Leu368, which corresponds to residue 139 of SEQ ID NOs: 1, 4, and 5 and residue 138 of SEQ ID NO: 2, and Tyr407, which corresponds to residue 178 of SEQ ID NOs: 1, 4, and 5 and residue 177 of SEQ ID NO: 3, e.g., Ser, Ala and Val, respectively (T366S/L368A/Y407V). Heterodimerization via CH3 modifications can be further stabilized by the introduction of a disulfide bond, for example by changing Ser354, which corresponds to residue 125 of SEQ ID NOs: 1, 4, and 5 and residue 124 of SEQ ID NO: 3, to Cys (S354C) and Tyr349, which corresponds to residue 120 of SEQ ID NOs: 1, 4, and 5 and residue 119 of SEQ ID NO: 3, to Cys (Y349C) on opposite CH3 domains (Reviewed in Carter, 2001 Journal of Immunological Methods, 248: 7-15). In some of these embodiments, the Fc region may be modified at the protein-A binding site on one member of the heterodimer so as to prevent protein-A binding and thereby enable more efficient purification of the heterodimeric fusion protein. An exemplary modification within this binding site is Ile253, which corresponds to residue 24 of SEQ ID NOs: 1, 4, and 5 and residue 23 of SEQ ID NO: 3, for example Ile253Arg (1253R). For example, the 1253R modification may be combined with either the T366S/L368A/Y407V modifications or with the T366W modifications. The T366S/L368A/Y407V modified Fc is capable of forming homodimers as there is no steric

occlusion of the dimerization interface as there is in the case of the T336W modified Fc. Therefore, in some embodiments, the I253R modification is combined with the T366S/L368A/Y407V modified Fc to disallow purification any homodimeric Fc that may have formed.

[0064] In some embodiments, the human IgG Fc region is modified to prevent dimerization. In these embodiments, the fusion proteins of the present disclosure are monomeric. For example, modification at residue Thr366 to a charged residue, e.g. Thr366Lys, Thr366Arg, Thr366Asp, or Thr366Glu (T366K, T366R, T366D, or T366E, respectively), prevents CH3-CH3 dimerization.

[0065] In some embodiments, the Fc region of the fusion protein is altered at one or more of the following positions to reduce Fc receptor binding: Leu 234 (L234), Leu235 (L235), Asp265 (D265), Asp270 (D270), Ser298 (S298), Asn297 (N297), Asn325 (N325) or Ala327 (A327). For example, Leu 234Ala (L234A), Leu235Ala (L235A), Asp265Asn (D265N), Asp270Asn (D270N), Ser298Asn (S298N), Asn297Ala (N297A), Asn325Glu (N325E) or Ala327Ser (A327S). In preferred embodiments, modifications within the Fc region reduce binding to Fc-receptor-gamma receptors while have minimal impact on binding to the neonatal Fc receptor (FcRn).

[0066] In some embodiments, the fusion protein contains a polypeptide derived from an immunoglobulin hinge region. The hinge region can be selected from any of the human IgG subclasses. For example, the fusion protein may contain a modified IgG1 hinge having the sequence of EPKSSDKTHCPPC (SEQ ID NO: 7), where in the Cys220 that forms a disulfide with the C-terminal cysteine of the light chain is mutated to serine, e.g., Cys220Ser (C220S). In other embodiments, the fusion protein contains a truncated hinge having a sequence DKTHTCPPC (SEQ ID NO: 8).

[0067] In some embodiments, the fusion protein has a modified hinge from IgG4, which is modified to prevent or reduce strand exchange, e.g., Ser228Pro (S228P), having the sequence ESKYGPPCPPC (SEQ ID NO: 9). In some embodiments, the fusion protein contains one or more linker polypeptides. In other embodiments, the fusion protein contains linker and hinge polypeptides.

[0068] In some embodiments, the fusion proteins of the present disclosure lack or have reduced Fucose attached to the N-linked glycan-chain at N297. There are numerous ways to prevent fucosylation, including but not limited to production in a FUT8 deficient cell line; addition inhibitors to the mammalian cell culture media, for example Castanospermine, 2-deoxy-fucose, 2-fluorofucose; the use of production cell lines with naturally reduced fucosylation pathways and metabolic engineering of the production cell line.

[0069] In some embodiments, the single domain antibody, VH_H, or humanized single domain antibody, or human single domain antibody is engineered to eliminate recognition by pre-existing antibodies found in humans. In some embodiments, single domain antibodies of the present disclosure are modified by mutation of position Leu1, for example Leu1Glu (L11E) or Leu1Lys (L 11K). In other embodiments, single domain antibodies of the present disclosure are modified by changes in carboxy-terminal region, for example the terminal sequence consists of GQGTLVTVKPGG (SEQ ID NO: 14) or GQGTLVTVE-PGG (SEQ ID NO: 15) or modification thereof. In some embodiments, the single domain antibodies of the present

disclosure are modified by mutation of position 11 and by changes in carboxy-terminal region.

[0070] In some embodiments, the BDs of the fusion proteins of the present disclosure are operably linked via amino acid linkers. In some embodiments, these linkers are composed predominately of the amino acids Glycine and Serine, denoted as GS-linkers herein. The GS-linkers of the fusion proteins of the present disclosure can be of various lengths, for example 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 amino acids in length.

[0071] In some embodiments, the GS-linker comprises an amino acid sequence selected from the group consisting of GGSGGS, i.e., (GGS)₂ (SEQ ID NO: 10); GGSGGGSGGS, i.e., (GGS)₃ (SEQ ID NO: 11); GGSGGGSGGS, i.e., (GGS)₄ (SEQ ID NO: 12); and GGSGGGSGGS, i.e., (GGS)₅ (SEQ ID NO: 13).

[0072] In some embodiments, the multivalent binding fusion protein is tetravalent. In some embodiments, the tetravalent fusion protein has the following structure: BD-Linker-BD-Linker-Hinge-Fc. In some embodiments, the tetravalent fusion protein has the following structure: BD-Linker-Hinge-Fc-Linker-BD.

[0073] In some embodiments, the BD of the tetravalent fusion protein is a single domain antibody or VH_H. In some embodiments, each BD of the tetravalent fusion protein is a single domain antibody or VH_H. In some embodiments, the tetravalent fusion protein has the following structure: VH_H-Linker-VH_H-Linker-Hinge-Fc, where the VH_H is a humanized or fully human VH_H sequence. In some embodiments, the tetravalent fusion protein has the following structure: VH_H-Linker-Hinge-Fc-Linker-VH_H, where the VH_H is a humanized or fully human VH_H sequence.

[0074] In some embodiments, the multivalent TNFRSF binding fusion protein is tetravalent. In some embodiments, the tetravalent TNFRSF binding fusion protein has the following structure: TBD-Linker-TBD-Linker-Hinge-Fc. In some embodiments, the tetravalent TNFRSF binding fusion protein has the following structure: TBD-Linker-Hinge-Fc-Linker-TBD.

[0075] In some embodiments, the TBD of the tetravalent TNFRSF binding fusion protein is a single domain antibody or VH_H. In some embodiments, each TBD of the multivalent TNFRSF binding fusion protein is single domain antibody or VH_H. In some embodiments, the tetravalent TNFRSF binding fusion protein has the following structure: VH_H-Linker-VH_H-Linker-Hinge-Fc, where the VH_H is a humanized or fully human VH_H sequence. In some embodiments, the tetravalent TNFRSF binding fusion protein has the following structure: VH_H-Linker-Hinge-Fc-Linker-VH_H, where the VH_H is a humanized or fully human VH_H sequence.

[0076] In some embodiments, the GS-linker comprises an amino acid sequence selected from the group consisting of GGSGGS, i.e., (GGS)₂ (SEQ ID NO: 10); GGSGGGSGGS, i.e., (GGS)₃ (SEQ ID NO: 11); GGSGGGSGGS, i.e., (GGS)₄ (SEQ ID NO: 12); and GGSGGGSGGS, i.e., (GGS)₅ (SEQ ID NO: 13).

[0077] In some embodiments, the multivalent fusion protein is hexavalent. In some embodiments, the hexavalent fusion protein has the following structure: BD-Linker-TBD-Linker-BD-Linker-Hinge-Fc. In some embodiments, the hexavalent fusion protein has the following structure: BD-Linker-BD-Linker-Hinge-Fc-Linker-BD, or BD-Linker-Hinge-Fc-Linker-BD-Linker-BD.

[0078] In some embodiments, the BD of the hexavalent fusion protein is a single domain antibody or VHH. In some embodiments, each BD of the hexavalent fusion protein is a single domain antibody or VHH. In some embodiments, the hexavalent fusion protein has the following structure: VHH-Linker-VHH-Linker-VHH-Linker-Hinge-Fc, where the VHH is a humanized or fully human VHH sequence. In some embodiments, the hexavalent fusion protein has the following structure: VHH-Linker-VHH-Linker-Hinge-Fc-Linker-VHH, or VHH-Linker-Hinge-Fc-Linker-VHH-Linker-VHH where the VHH is a humanized or fully human VHH sequence.

[0079] In some embodiments, the multivalent TNFRSF binding fusion protein is hexavalent. In some embodiments, the hexavalent TNFRSF binding fusion protein has the following structure: TBD-Linker-TBD-Linker-TBD-Linker-Hinge-Fc. In some embodiments, the hexavalent TNFRSF binding fusion protein has the following structure: TBD-Linker-TBD-Linker-Hinge-Fc-Linker-TBD, or TBD-Linker-Hinge-Fc-Linker-TBD-Linker-TBD.

[0080] In some embodiments, the TBD of the hexavalent TNFRSF binding fusion protein is a single domain antibody or VHH. In some embodiments, each TBD of the hexavalent TNFRSF binding fusion protein is a single domain antibody or VHH. In some embodiments, the hexavalent TNFRSF binding fusion protein has the following structure: VHH-Linker-VHH-Linker-VHH-Linker-Hinge-Fc, where the VHH is a humanized or fully human VHH sequence. In some embodiments, the hexavalent TNFRSF binding fusion protein has the following structure: VHH-Linker-VHH-Linker-Hinge-Fc-Linker-VHH, or VHH-Linker-Hinge-Fc-Linker-VHH-Linker-VHH where the VHH is a humanized or fully human VHH sequence.

[0081] In some embodiments, the multivalent fusion protein lacks an Fc region. In some of these embodiments, the fusion protein is tetravalent and has the following structure BD-Linker-BD-Linker-BD-Linker-BD-Linker. In some of these embodiments, the fusion protein is pentavalent and has the following structure BD-Linker-BD-Linker-BD-Linker-BD-Linker-BD. In some of these embodiments, the fusion protein is hexavalent and has the following structure BD-Linker-BD-Linker-BD-Linker-BD-Linker-BD.

[0082] In some embodiments, the multivalent TNFRSF binding fusion protein lacks an Fc region. In some of these embodiments, the TNFRSF binding fusion protein is tetravalent and has the following structure TBD-Linker-TBD-Linker-TBD-Linker-TBD. In some of these embodiments, the TNFRSF binding fusion protein is pentavalent and has the following structure TBD-Linker-TBD-Linker-TBD-Linker-TBD. In some of these embodiments, the TNFRSF binding fusion protein is hexavalent and has the following structure TBD-Linker-TBD-Linker-TBD-Linker-TBD-Linker-TBD.

[0083] In some embodiments, the BD of a multivalent fusion protein is a single domain antibody or VHH. In some embodiments, the multivalent fusion protein lacks an Fc region. In some of these embodiments, the fusion protein is tetravalent and has the following structure VHH-Linker-VHH-Linker-VHH-Linker-VHH-Linker-VHH. In some of these embodiments, the fusion protein is hexavalent and has the following structure VHH-Linker-VHH-Linker-VHH-Linker-VHH-

Linker-VHH-Linker-VHH. In any of these embodiments, the VHH is a humanized or fully human VHH sequence.

[0084] In some embodiments, the TBD of the a multivalent TNFRSF binding fusion protein is a single domain antibody or VHH. In some embodiments, the multivalent TNFRSF binding fusion protein lacks an Fc region. In some of these embodiments, the TNFRSF binding fusion protein is tetravalent and has the following structure VHH-Linker-VHH-Linker-VHH-Linker-VHH-Linker. In some of these embodiments, the TNFRSF binding fusion protein is pentavalent and has the following structure VHH-Linker-VHH-Linker-VHH-Linker-VHH-Linker-VHH. In some of these embodiments, the TNFRSF binding fusion protein is hexavalent and has the following structure VHH-Linker-VHH-Linker-VHH-Linker-VHH-Linker-VHH. In any of these embodiments, the VHH is a humanized or fully human VHH sequence.

[0085] In some embodiments, the GS-linker comprises an amino acid sequence selected from the group consisting of GGSGGS, i.e., (GGS)₂ (SEQ ID NO: 10); GGSGGGSGGS, i.e., (GGS)₃ (SEQ ID NO: 11); GGSGGGSGGS, i.e., (GGS)₄ (SEQ ID NO: 12); and GGSGGGSGGS, i.e., (GGS)₅ (SEQ ID NO: 13).

[0086] In some embodiments, the fusion proteins are multispecific containing a TBD and a binding domain directed toward a second antigen. In these embodiments, the second antigen binding domain can be positioned at numerous positions within the molecule relative to the TBD. In some embodiments, the second antigen binding domain is located N-terminal TBD. In other embodiments, the second antigen binding domain is located C-terminal to the TBD. In other embodiments, the second antigen binding domain is located on a distinct polypeptide that associates with a first polypeptide containing the TBD.

[0087] In some embodiments, the fusion proteins are multispecific containing an anti-41BB binding domain and a binding domain directed toward a second antigen. In these embodiments, the second antigen binding domain can be positioned at numerous positions within the molecule relative to the an anti-41BB binding domain. In some embodiments, the second antigen binding domain is located N-terminal an anti-41BB binding domain. In other embodiments, the second antigen binding domain is located to C-terminal to the an anti-41BB binding domain. In other embodiments, the second antigen binding domain is located on a distinct polypeptide that associates with a first polypeptide containing the an anti-41BB binding domain.

[0088] In some embodiments, the fusion proteins are multispecific containing an anti-PDL1 binding domain and a binding domain directed toward a second antigen. In these embodiments, the second antigen binding domain can be positioned at numerous positions within the molecule relative to the an anti-PDL1 binding domain. In some embodiments, the second antigen binding domain is located N-terminal an anti-PDL1 binding domain. In other embodiments, the second antigen binding domain is located to C-terminal to the an anti-PDL1 binding domain. In other embodiments, the second antigen binding domain is located on a distinct polypeptide that associates with a first polypeptide containing the an anti-PDL1 binding domain.

[0089] In some embodiments, the TBD within the multispecific TNFRSF binding fusion protein is a single domain antibody or VHH. In some embodiments, the TBD within the multispecific TNFRSF binding fusion protein is a com-

posed of antibody variable heavy (VH) chain and variable light (VL) chain region. In some embodiments, the VH and VL of the TBD are formatted as a single chain variable fragment (scFv) connected via a linker region. In some embodiments, the VH and VL of the TBD are formatted as a Fab fragment that associates via a constant heavy 1 (CH1) domain and a constant light chain (CL) domain. In some embodiments, non-antibody heterodimerization domains are utilized to enable the proper association of the VH and VL of the TBD. In some embodiments, the TBD within the multispecific TNFRSF binding fusion protein is derived from non-antibody scaffold proteins for example but not limited to designed ankyrin repeat proteins (darpins), avimer, anticalin/lipocalins, centyrins and fynomers.

[0090] In some embodiments, the TBD within the multispecific TNFRSF binding fusion protein is a single domain antibody or VHH that binds 41BB. In some embodiments, the anti-41BB binding domain within the multispecific TNFRSF binding fusion protein is a composed of antibody variable heavy (VH) chain and variable light (VL) chain region. In some embodiments, the VH and VL of the anti-41BB binding domain are formatted as a single chain variable fragment (scFv) connected via a linker region. In some embodiments, the VH and VL of the anti-41BB binding domain are formatted as a Fab fragment that associates via a constant heavy 1 (CH1) domain and a constant light chain (CL) domain. In some embodiments, non-antibody heterodimerization domains are utilized to enable the proper association of the VH and VL of the anti-41BB binding domain. In some embodiments, the anti-41BB binding domain within the multispecific TNFRSF binding fusion protein is derived from non-antibody scaffold proteins for example but not limited to designed ankyrin repeat proteins (darpins), avimer, anticalin/lipocalins, centyrins and fynomers.

[0091] In some embodiments, the binding domain within the multispecific fusion protein is a single domain antibody or VHH that binds PDL1. In some embodiments, the anti-PDL1 binding domain within the multispecific TNFRSF binding fusion protein is a composed of antibody variable heavy (VH) chain and variable light (VL) chain region. In some embodiments, the VH and VL of the anti-PDL1 binding domain are formatted as a single chain variable fragment (scFv) connected via a linker region. In some embodiments, the VH and VL of the anti-PDL1 binding domain are formatted as a Fab fragment that associates via a constant heavy 1 (CH1) domain and a constant light chain (CL) domain. In some embodiments, non-antibody heterodimerization domains are utilized to enable the proper association of the VH and VL of the anti-PDL1 binding domain. In some embodiments, the anti-PDL1 binding domain within the multispecific fusion protein is derived from non-antibody scaffold proteins for example but not limited to designed ankyrin repeat proteins (darpins), avimer, anticalin/lipocalins, centyrins and fynomers.

[0092] In some embodiments, the anti-41BB binding domain of the multispecific TNFRSF binding fusion protein is a bispecific antibody or antigen-binding fragment thereof.

[0093] In some embodiments, the anti-PDL1 binding domain of the multispecific fusion protein is a bispecific antibody or antigen-binding fragment thereof.

[0094] In any of these embodiments, the bispecific antibody or antigen-fragment thereof can be any suitable bispecific format known in the art, including, by way of

non-limiting example, formats based on antibody fragments such as, e.g., X-Link Fab, cross-linked Fab fragments; tascFv/BiTE, tandem-scFv/Bispecific T cell Engager; Db, diabody; taDb, tandem diabody; formats based on Fc-fusions such as, e.g., Db-Fc, diabody-Fc fusion; taDb-Fc fusion, tandem diabody-Fc fusion; taDb-CH3, tandem diabody-CH3 fusion; (scFv)₄-Fc, tetra scFv-Fc fusion; DVD-Ig, dual variable domain immunoglobulin; IgG formats such as, e.g., knob-hole and SEED, strand exchange engineered domain; CrossMab, knob-hole combined with heavy and light chain domain exchange; bsAb, quadroma derived bispecific antibody; sdAb, single domain based antibody; and kappa-lambda bodies such as those described in PCT Publication No. WO 2012/023053.

[0095] In any of the above embodiments, at least one TBD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83.

[0096] In any of the above embodiments, at least one TBD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83.

[0097] In any of the above embodiments, at least one TBD comprises a complementarity determining region 1 (CDR1) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, 21, 26, 30, 50, 65, and 69; a complementarity determining region 2 (CDR2) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, 27, 31, 42, 44, 48, 52, 61, 63, 71, 73, 75, 77, and 79; and a complementarity determining region 3 (CDR3) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 19, 22, 24, 28, 32, 55, and 57.

[0098] In any of the above embodiments, at least one BD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124.

[0099] In any of the above embodiments, at least one BD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 119-124.

[0100] In any of the above embodiments, at least one BD comprises a CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 101, 105, and 109; a CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 102, 106, 110, and 117; and a CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 103, 107, 111, 113, 115, and 118.

[0101] In any of the above embodiments, at least one TBD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 16, 20, 23, 25, 29, 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, and at least one BD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 100, 104, 108, 112, 114, 116, and 119-124.

[0102] In any of the above embodiments, at least one TBD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 33, 39, 33-41, 43, 45-47, 49, 51, 53, 54, 56, 58-60, 62, 65, 66, 68, 70, 72, 74, 76, 78, and 80-83, and at least one BD comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 119-124.

[0103] In any of the above embodiments, at least one TBD comprises a complementarity determining region 1 (CDR1) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, 21, 26, 30, 50, 65, and 69; a complementarity determining region 2 (CDR2) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, 27, 31, 42, 44, 48, 52, 61, 63, 71, 73, 75, 77, and 79; and a complementarity determining region 3 (CDR3) comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 19, 22, 24, 28, 32, 55, and 57, and at least one BD comprises a CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 101, 105, and 109; a CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 102, 106, 110, and 117; and a CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 103, 107, 111, 113, 115, and 118.

BRIEF DESCRIPTION OF THE DRAWINGS

[0104] FIG. 1 is schematic of exemplary multivalent and multispecific fusion proteins of the present disclosure.

[0105] FIGS. 2A and 2B are a pair of graphs demonstrating the ability of 41BB single domain antibodies (sdAbs) to bind recombinant human 41BB (FIG. 2A) or cyno 41BB (FIG. 2B). Binding was assessed by ELISA wherein recombinant 41BB-mFc protein was immobilized on a Medisorp 96 well plate.

[0106] FIG. 3 is a graph demonstrating the ability of 41BB single domain antibodies (sdAbs) to bind cell surface 41BB. Binding was assessed by flow cytometry using 41BB expressing CHO cells and data is presented as median fluorescence intensity.

[0107] FIG. 4 is a graph demonstrating the ability of 41BB single domain antibodies, RH3 and 4H04 to bind cynomolgus monkey 41BB. Binding was assessed by ELISA wherein recombinant 41BB-mFc protein was immobilized on a Medisorp 96 well plate.

[0108] FIG. 5 is a graph demonstrating the capacity of 41BB single domain antibodies (VHJs) to block the interaction between 41BB and 41BBL. All single domain antibodies tested, with the exception of RH3 blocks the interaction between 41BB and 41BBL. Blocking was assessed by flow cytometry using a recombinant 41BB fusion protein and 41BB expressing CHO cells, data is presented as median fluorescence intensity.

[0109] FIG. 6 is a graph demonstrating the inability of a conventional bivalent anti-41BB antibody PF-05082566 to induce 41BB signaling unless further clustered with an exogenous crosslinking anti-human IgG antibody. 41BB signaling was monitored using a NF- κ B reporter 293 cell line expressing 41BB.

[0110] FIGS. 7A and 7B are a pair of graphs demonstrating the capacity of an exemplary PDL1 single domain antibody (28A10) to bind cell surface PDL1 and to block the interaction with PD1. Binding (FIG. 7A) was assessed by flow cytometry on PDL1 expressing CHO cells. Blocking (FIG. 7B) was assessed by flow cytometry using a recombinant PD1 fusion protein and PDL1 expressing CHO cells, data is presented as median fluorescence intensity.

[0111] FIGS. 8A, 8B, and 8C are a series of illustrations and a graph depicting PDL1-dependent 41BB agonism mediated by bispecific PDL1-41BB targeting fusion proteins of the present disclosure. FIGS. 8A and 8B are conceptual schematics, wherein the bispecific fusion proteins

have minimal 41BB agonistic properties (FIG. 8A) unless bound by a PD-L1 expressing cell (FIG. 8B). FIG. 8C is a graph demonstrating the ability of a PDL1-positive cell (here PDL1 transfected CHO cells) to mediate 41BB signaling and the inability of PDL1-negative cell (here untransfected CHO cells) to mediate 41BB signaling. 41BB signaling was monitored using a NF- κ B reporter 293 cell line expressing 41BB.

[0112] FIGS. 9A, 9B, 9C, 9D, and 9E are a series of graphs demonstrating the binding to human (FIG. 9A and FIG. 9C) or cynomolgus monkey (FIG. 9B and FIG. 9D) 41BB of humanized RH3 variants. Binding was assessed by flow cytometry on 41BB expressing 293freestyle cells. FIG. 9E is a graph demonstrating that the humanized variants hzRH3v5-1 and hzRH3v9 do not block binding of 41BBL to cell surface 41BB. Herein a recombinant fusion protein 41BBL-mFc, containing a mouse Fc region was used and bound 41BBL was detected using an anti-mouse IgG-Fc specific secondary antibody.

[0113] FIG. 10 is a graph demonstrating the specific binding of hzRH3v5-1 (40 nM) to 41BB compared to other TNFRSF members OX40 and GITR. Binding was assessed by flow cytometry using CHO cells expressing the given TNFRSF member.

[0114] FIGS. 11A, 11B, 11C, and 11D are a series of graphs demonstrating the binding to human (FIG. 11A and FIG. 11C) or cynomolgus monkey (FIG. 11B) 41BB of humanized 4E01 variants. Binding was assessed by flow cytometry on 41BB expressing 293freestyle cells. FIG. 11D is a graph demonstrating that the humanized variants hz4E01v16, hz4E01v18, hz4E01v21, hz4E01v22 and hz4E01v23 block binding of 41BBL to cell surface 41BB. In these studies, a recombinant fusion protein 41BBL-mFc, containing a mouse Fc region was used and bound 41BBL was detected using an anti-mouse IgG-Fc specific secondary antibody.

[0115] FIG. 12 is a graph demonstrating binding of humanized single domain antibodies targeting PDL1. Binding was assessed by flow cytometry on PDL1-expressing CHO cells.

[0116] FIG. 13 is a schematic of two exemplary formats of a PDL1 \times 41BB bispecific, INBRX-105-1. INBRX-105-1-A (left) has the PDL1 and 41BB binding domains, located at opposing terminal positions with a central Fc region, whereas INBRX-105-1-B (right) has the PDL1 and 41BB binding domains positioned in tandem, N-terminal to an Fc region.

[0117] FIGS. 14A, 14B, and 14C are a series of graphs demonstrating the equivalent binding to human (FIG. 14A) or cynomolgus monkey (FIG. 14B) 41BB by the two distinct formats of a bispecific fusion protein targeting PDL1 and 41BB referred to herein as INBRX-105-1-A and INBRX-105-1-B. Binding was assessed by flow cytometry on 41BB expressing 293freestyle cells. FIG. 14C is a graph that demonstrates that the bispecific fusion protein containing hzRh3v5-1 does not block 41BBL binding to cell surface 41BB. Herein a recombinant fusion protein of 41BBL and mouse Fc region was used and bound 41BBL was detected using an anti-mouse IgG-Fc specific secondary antibody.

[0118] FIGS. 15A, 15B, 15C, and 15D are a series of graphs demonstrating the equivalent binding (FIG. 15A and FIG. 15C) and PD1 blocking (FIG. 15B and FIG. 15D) by the two distinct formats of a bispecific fusion protein targeting PDL1 and 41BB referred to herein as INBRX-105-

1-A and INBRX-105-1-B. Binding was assessed by flow cytometry on human (FIG. 15A) or cynomolgus monkey (FIG. 15C) PDL1 expressing 293freestyle cells. Blocking was assessed by flow cytometry using on human (FIG. 15B) or cynomolgus monkey (FIG. 15D) PDL1 expressing 293freestyle cells with either recombinant human (FIG. 15B) or cynomolgus monkey (FIG. 15D) PD1-mFc fusion protein. Bound PD1 was detected using an anti-mouse IgG-Fc specific secondary antibody.

[0119] FIG. 16 is a graph demonstrating the ability of humanized versions of a PDL1×41BB bispecific fusion protein (INBRX-105-1) to induce PDL1-dependent 41BB agonism. A 41BB-expressing HEK293 NF-kB reporter cell line was used to assess 41BB signaling and a PDL1-expressing CHO cell line was used as the source of PDL1.

[0120] FIGS. 17A and 17B are a pair of graphs demonstrating the 41BB-specific binding by the 41BB-binding portion of a PDL1×41BB bispecific fusion protein (INBRX-105-1) of the present disclosure. Binding was assessed on 41BB (FIG. 17A) or the closest homolog, TNFRSF21/DR6 (FIG. 17B), expressing 293freestyle cells by flow cytometry. An anti-DR6 antibody (Invitrogen) was used to as positive control for DR6 expression.

[0121] FIGS. 18A, 18B, and 18C are a series of graphs demonstrating the PDL1-specific binding by the PDL1-binding portion of a PDL1×41BB bispecific fusion protein (INBRX-105-1) of the present disclosure. Binding was assessed on PDL1 (FIG. 18A), and its closest homologs PDL2 (FIG. 18B) or VISTA/PDL3 (FIG. 18C), expressing 293freestyle cells by flow cytometry. Anti-PDL2 and anti-VISTA antibodies were used to as positive controls for PDL2 and PDL3 expression respectively.

[0122] FIGS. 19A and 19B are a pair of graphs demonstrating the ability of a PDL1×41BB bispecific fusion protein to simultaneously bind PDL1 and 41BB. Bound 41BB was detected using an anti-mouse IgG-Fc specific secondary antibody. FIG. 19A. is a graph showing the binding of INBRX-105-1 to the PDL1 expressing K562 cells. FIG. 19B is a graph showing the binding of recombinant 41BB to INBRX-105-1 on the PDL1 expressing cells.

[0123] FIG. 20 is a graph demonstrating the ability of a PDL1×41BB bispecific fusion protein to simultaneously bind recombinant PDL1 and recombinant 41BB in an ELISA. Bound recombinant 41BB was detected via streptavidin-HRP.

[0124] FIGS. 21A, 21B, and 21C are a series of graphs demonstrating the effect of a PDL1×41BB bispecific fusion protein (INBRX-105-1) of the present disclosure on T-cell activation and proliferation. INF γ production in the cell supernatant was monitored using an ELISA and normalized to the standard curve. T-cell proliferation was monitored by flow cytometry using CTV labeling of T-cells. T-cell activation was assessed by the presence of the activation marker CD25 monitored by flow cytometry. Antibodies were used at 10 nM.

[0125] FIGS. 22A and 22B are a pair of graphs demonstrating PDL1-dependent 41BB agonism mediated by a PDL1×41BB bispecific fusion protein (INBRX-105-1) of the present disclosure. CD8 $^{+}$ T-cell proliferation (FIG. 22A) was monitored using CTV labeling and INF γ production (FIG. 22B) in the cell supernatant was monitored using an ELISA and normalized to the standard curve.

[0126] FIG. 23 is a graph demonstrating the capacity of a PDL1×41BB bispecific fusion protein (INBRX-105-1) of

the present disclosure to enhance the Th1 lineage defining transcription factor, T-bet, expression in T-cell populations. T-bet expression was assessed on CD4 $^{+}$ and CD8 $^{+}$ T-cell population by flow cytometry via intracellular staining following fixation and permeabilization.

[0127] FIGS. 24A and 24B are a pair graphs contrasting the capacity of a PDL1×41BB bispecific fusion protein (INBRX-105-1) of the present disclosure and the combination of monospecific antibodies Atezolizumab (anti-PDL1) and Utomilumab (anti-41BB) to induce INF γ (FIG. 24A) or TNF α (FIG. 24B) production from CD4 $^{+}$ or CD8 $^{+}$ T-cells. Cytokine expression was assessed on CD4 $^{+}$ and CD8 $^{+}$ T-cell population by flow cytometry via intracellular staining following fixation and permeabilization.

[0128] FIGS. 25A and 25B are a pair of graphs demonstrating the agonistic capacity of a tetravalent 41BB-binding fusion protein and PDL1×41BB bispecific fusion proteins of the present disclosure in the presence of an additional PDL1 positive (FIG. 25A) or negative (FIG. 25B) cell line. Herein a 41BB-expressing HEK293 NF-kB reporter cell was used and co-incubated with either the PDL1-negative K562 cell line (FIG. 25B) or a stably transfected, PDL1-expressing K562 cell line (FIG. 25A).

DETAILED DESCRIPTION OF THE INVENTION

[0129] All patents and publications mentioned in this specification are herein incorporated by reference to the same extent as if each independent patent and publication was specifically and individually indicated to be incorporated by reference.

Definitions

[0130] Unless otherwise defined, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Generally, nomenclatures utilized in connection with, and techniques of, cell and tissue culture, molecular biology, and protein and oligo- or polynucleotide chemistry and hybridization described herein are those well-known and commonly used in the art. Standard techniques are used for recombinant DNA, oligonucleotide synthesis, and tissue culture and transformation (e.g., electroporation, lipofection). Enzymatic reactions and purification techniques are performed according to manufacturer's specifications or as commonly accomplished in the art or as described herein. The foregoing techniques and procedures are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification. See e.g., Sambrook et al. Molecular Cloning: A Laboratory Manual (2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)). The nomenclatures 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. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

[0131] As utilized in accordance with the present disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

[0132] As used herein, the terms "dual-targeting fusion protein" and "antibody" can be synonyms. As used herein, the term "antibody" refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, i.e., molecules that contain an antigen binding site that specifically binds (immunoreacts with) an antigen. By "specifically bind" or "immunoreacts with" "or directed against" is meant that the antibody reacts with one or more antigenic determinants of the desired antigen and does not react with other polypeptides or binds at much lower affinity ($K_d > 10^{-6}$). Antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, dAb (domain antibody), single chain, Fab, Fab' and F(ab')₂ fragments, Fv, scFvs, a Fab expression library, and single domain antibody (sdAb) fragments, for example V_HH, V_{NAR}, engineered V_H or V_K.

[0133] The basic antibody structural unit is known to comprise a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kDa) and one "heavy" chain (about 50-70 kDa). The amino-terminal portion of each chain includes a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector function. In general, antibody molecules obtained from humans relate to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses (also known as isotypes) as well, such as IgG₁, IgG₂, and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain.

[0134] The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs contain an antigen binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

[0135] The term "antigen-binding site" or "binding portion" refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains, referred to as "hypervariable regions," are interposed between more conserved flanking stretches known as "framework regions," or "FRs". Thus, the term "FR" refers to amino acid sequences which are naturally found between, and adjacent to, hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three-dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and

light chains are referred to as "complementarity-determining regions," or "CDRs." The assignment of amino acids to each domain is in accordance with the definitions of Kabat Sequences of Proteins of Immunological Interest (National Institutes of Health, Bethesda, Md. (1987 and 1991)), or Chothia & Lesk J. Mol. Biol. 196:901-917 (1987), Chothia et al. Nature 342:878-883 (1989).

[0136] The single domain antibody (sdAb) fragments portions of the fusion proteins of the present disclosure are referred to interchangeably herein as targeting polypeptides herein.

[0137] As used herein, the term "epitope" includes any protein determinant capable of specific binding to/by an immunoglobulin or fragment thereof, or a T-cell receptor. The term "epitope" includes any protein determinant capable of specific binding to/by an immunoglobulin or T-cell receptor. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. An antibody is said to specifically bind an antigen when the dissociation constant is ≤ 1 mM, for example, $\leq 1 \mu\text{M}$; e.g., $\leq 100 \text{nM}$, for example, $\leq 10 \text{nM}$ and for example, $\leq 1 \text{nM}$.

[0138] As used herein, the terms "immunological binding," and "immunological binding properties" refer to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant (K_d) of the interaction, wherein a smaller K_d represents a greater affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and geometric parameters that equally influence the rate in both directions. Thus, both the "on rate constant" (k_{on}) and the "off rate constant" (k_{off}) can be determined by calculation of the concentrations and the actual rates of association and dissociation. (See Nature 361:186-87 (1993)). The ratio of k_{off}/k_{on} enables the cancellation of all parameters not related to affinity, and is equal to the dissociation constant K_d . (See, generally, Davies et al. (1990) Annual Rev Biochem 59:439-473). An antibody of the present disclosure is said to specifically bind to an antigen, when the equilibrium binding constant (K_d) is 1 M, for example, $\leq 100 \text{nM}$, for example, 10 nM, and for example, 100 μM to about 1 μM , as measured by assays such as radioligand binding assays, surface plasmon resonance (SPR), flow cytometry binding assay, or similar assays known to those skilled in the art.

[0139] The term "isolated polynucleotide" as used herein shall mean a polynucleotide of genomic, cDNA, or synthetic origin or some combination thereof, which by virtue of its origin the "isolated polynucleotide" (1) is not associated with all or a portion of a polynucleotide in which the "isolated polynucleotide" is found in nature, (2) is operably linked to a polynucleotide which it is not linked to in nature, or (3) does not occur in nature as part of a larger sequence.

[0140] The term "isolated protein" referred to herein means a protein of cDNA, recombinant RNA, or synthetic origin or some combination thereof, which by virtue of its

origin, or source of derivation, the “isolated protein” (1) is not associated with proteins found in nature, (2) is free of other proteins from the same source, e.g., free of marine proteins, (3) is expressed by a cell from a different species, or (4) does not occur in nature.

[0141] The term “polypeptide” is used herein as a generic term to refer to native protein, fragments, or analogs of a polypeptide sequence. Hence, native protein fragments, and analogs are species of the polypeptide genus.

[0142] The term “naturally-occurring” as used herein as applied to an object refers to the fact that an object can be found in nature. For example, a polypeptide or polynucleotide sequence that is present in an organism (including viruses) that can be isolated from a source in nature and which has not been intentionally modified by man in the laboratory or otherwise is naturally-occurring.

[0143] The term “operably linked” as used herein refers to positions of components so described are in a relationship permitting them to function in their intended manner. A control sequence “operably linked” to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences.

[0144] The term “control sequence” as used herein refers to polynucleotide sequences which are necessary to effect the expression and processing of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism in prokaryotes, such control sequences generally include promoter, ribosomal binding site, and transcription termination sequence in eukaryotes, generally, such control sequences include promoters and transcription termination sequence. The term “control sequences” is intended to include, at a minimum, all components whose presence is essential for expression and processing, and can also include additional components whose presence is advantageous, for example, leader sequences and fusion partner sequences. The term “polynucleotide,” as referred to herein, refers to a polymeric boron of nucleotides of at least 10 bases in length, either ribonucleotides or deoxynucleotides or a modified form of either type of nucleotide. The term includes single and double stranded forms of DNA.

[0145] The term “oligonucleotide” referred to herein includes naturally occurring, and modified nucleotides linked together by naturally occurring, and non-naturally occurring oligonucleotide linkages. Oligonucleotides are a polynucleotide subset generally comprising a length of 200 bases or fewer. In some embodiments, oligonucleotides are 10 to 60 bases in length and for example, 12, 13, 14, 15, 16, 17, 18, 19, or 20 to 40 bases in length. Oligonucleotides are usually single stranded, e.g., for probes, although oligonucleotides may be double stranded, e.g., for use in the construction of a gene mutant. Oligonucleotides of the disclosure are either sense or antisense oligonucleotides.

[0146] The term “naturally occurring nucleotides” referred to herein includes deoxyribonucleotides and ribonucleotides. The term “modified nucleotides” referred to herein includes nucleotides with modified or substituted sugar groups and the like. The term “oligonucleotide linkages” referred to herein includes oligonucleotides linkages such as phosphorothioate, phosphorodithioate, phosphoroselenoate, phosphorodiselenoate, phosphoroanilothioate, phosphoranylilate, phosphoromimidate, and the like. See e.g., LaPlanche et al. *Nucl. Acids Res.* 14:9081 (1986); Stec et al. *J. Am. Chem. Soc.* 106:6077 (1984); Stein et al. *Nucl. Acids Res.* 16:3209 (1988); Zon et al. *Anti Cancer Drug Design* 6:539 (1991); Zon et al. *Oligonucleotides and Analogs: A*

Practical Approach, pp. 87-108 (F. Eckstein, Ed., Oxford University Press, Oxford England (1991)); Stec et al. U.S. Pat. No. 5,151,510; Uhlmann and Peyman *Chemical Reviews* 90:543 (1990). An oligonucleotide can include a label for detection, if desired.

[0147] The term “selectively hybridize” referred to herein means to detectably and specifically bind. Polynucleotides, oligonucleotides and fragments thereof in accordance with the disclosure selectively hybridize to nucleic acid strands under hybridization and wash conditions that minimize appreciable amounts of detectable binding to nonspecific nucleic acids. High stringency conditions can be used to achieve selective hybridization conditions as known in the art and discussed herein. Generally, the nucleic acid sequence homology between the polynucleotides, oligonucleotides, and fragments of the disclosure and a nucleic acid sequence of interest will be at least 80%, and more typically with increasing homologies of at least 85%, 90%, 95%, 99%, and 100%. Two amino acid sequences are homologous if there is a partial or complete identity between their sequences. For example, 85% homology means that 85% of the amino acids are identical when the two sequences are aligned for maximum matching. Gaps (in either of the two sequences being matched) are allowed in maximizing matching gap lengths of 5 or less are preferred with 2 or less being more preferred. Alternatively, two protein sequences (or polypeptide sequences derived from them of at least 30 amino acids in length) are homologous, as this term is used herein, if they have an alignment score of at more than 5 (in standard deviation units) using the program ALIGN with the mutation data matrix and a gap penalty of 6 or greater. See Dayhoff, M. O., in *Atlas of Protein Sequence and Structure*, pp. 101-110 (Volume 5, National Biomedical Research Foundation (1972)) and Supplement 2 to this volume, pp. 1-10. The two sequences or parts thereof are more preferably homologous if their amino acids are greater than or equal to 50% identical when optimally aligned using the ALIGN program. The term “corresponds to” is used herein to mean that a polynucleotide sequence is homologous (i.e., is identical, not strictly evolutionarily related) to all or a portion of a reference polynucleotide sequence, or that a polypeptide sequence is identical to a reference polypeptide sequence. In contradistinction, the term “complementary to” is used herein to mean that the complementary sequence is homologous to all or a portion of a reference polynucleotide sequence. For illustration, the nucleotide sequence “TATAC” corresponds to a reference sequence “TATAC” and is complementary to a reference sequence “GTATA”.

[0148] The following terms are used to describe the sequence relationships between two or more polynucleotide or amino acid sequences: “reference sequence”, “comparison window”, “sequence identity”, “percentage of sequence identity”, and “substantial identity”. A “reference sequence” is a defined sequence used as a basis for a sequence comparison a reference sequence may be a subset of a larger sequence, for example, as a segment of a full-length cDNA or gene sequence given in a sequence listing or may comprise a complete cDNA or gene sequence. Generally, a reference sequence is at least 18 nucleotides or 6 amino acids in length, frequently at least 24 nucleotides or 8 amino acids in length, and often at least 48 nucleotides or 16 amino acids in length. Since two polynucleotides or amino acid sequences may each (1) comprise a sequence (i.e., a portion of the complete polynucleotide or amino acid sequence) that is similar between the two molecules, and (2) may further comprise a sequence that is divergent between the two

polynucleotides or amino acid sequences, sequence comparisons between two (or more) molecules are typically performed by comparing sequences of the two molecules over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window", as used herein, refers to a conceptual segment of at least 18 contiguous nucleotide positions or 6 amino acids wherein a polynucleotide sequence or amino acid sequence may be compared to a reference sequence of at least 18 contiguous nucleotides or 6 amino acid sequences and wherein the portion of the polynucleotide sequence in the comparison window may comprise additions, deletions, substitutions, and the like (i.e., gaps) of 20 percent or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith and Waterman Adv. Appl. Math. 2:482 (1981), by the homology alignment algorithm of Needleman and Wunsch J. Mol. Biol. 48:443 (1970), by the search for similarity method of Pearson and Lipman Proc. Natl. Acad. Sci. (U.S.A.) 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, (Genetics Computer Group, 575 Science Dr., Madison, Wis.), Geneworks, or MacVector software packages), or by inspection, and the best alignment (i.e., resulting in the highest percentage of homology over the comparison window) generated by the various methods is selected.

[0149] The term "sequence identity" means that two polynucleotide or amino acid sequences are identical (i.e., on a nucleotide-by-nucleotide or residue-by-residue basis) over the comparison window. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, U or I) or residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the comparison window (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The terms "substantial identity" as used herein denotes a characteristic of a polynucleotide or amino acid sequence, wherein the polynucleotide or amino acid comprises a sequence that has at least 85 percent sequence identity, preferably at least 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison window of at least 18 nucleotide (6 amino acid) positions, frequently over a window of at least 24-48 nucleotide (8-16 amino acid) positions, wherein the percentage of sequence identity is calculated by comparing the reference sequence to the sequence which may include deletions or additions which total 20 percent or less of the reference sequence over the comparison window. The reference sequence may be a subset of a larger sequence.

[0150] As used herein, the twenty conventional amino acids and their abbreviations follow conventional usage. See Immunology—A Synthesis (2nd Edition, E. S. Golub and D. R. Gren, Eds., Sinauer Associates, Sunderland Mass. (1991)). Stereoisomers (e.g., D-amino acids) of the twenty conventional amino acids, unnatural amino acids such as α - α -disubstituted amino acids, N-alkyl amino acids, lactic acid, and other unconventional amino acids may also be suitable components for polypeptides of the present disclosure. Examples of unconventional amino acids include: 4-hydroxyproline, γ -carboxyglutamate, ϵ -N,N,N,N-trimethyllysine,

sine, ϵ -N-acetyllysine, σ -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 carboxy-terminal direction, in accordance with standard usage and convention.

[0151] Similarly, unless specified otherwise, the left-hand end of single-stranded polynucleotide sequences is the 5' end the left-hand direction of double-stranded polynucleotide sequences is referred to as the 5' direction. The direction of 5' to 3' addition of nascent RNA transcripts is referred to as the transcription direction sequence regions on the DNA strand having the same sequence as the RNA and which are 5' to the 5' end of the RNA transcript are referred to as "upstream sequences", sequence regions on the DNA strand having the same sequence as the RNA and which are 3' to the 3' end of the RNA transcript are referred to as "downstream sequences".

[0152] As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, for example, at least 90 percent sequence identity, for example, at least 95 percent sequence identity, and for example, at least 99 percent sequence identity.

[0153] In some embodiments, residue positions which are not identical differ by conservative amino acid substitutions.

[0154] Conservative amino acid substitutions refer to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine; a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulfur-containing side chains is cysteine and methionine. Suitable conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine valine, glutamic-aspartic, and asparagine-glutamine.

[0155] As discussed herein, minor variations in the amino acid sequences of antibodies or immunoglobulin molecules are contemplated as being encompassed by the present disclosure, providing that the variations in the amino acid sequence maintain at least 75%, for example, at least 80%, 90%, 95%, and for example, 99%. In particular, conservative amino acid replacements are contemplated. Conservative replacements are those that take place within a family of amino acids that are related in their side chains. Genetically encoded amino acids are generally divided into families: (1) acidic amino acids are aspartate, glutamate; (2) basic amino acids are lysine, arginine, histidine; (3) non-polar amino acids are alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan, and (4) uncharged polar amino acids are glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. The hydrophilic amino acids include arginine, asparagine, aspartate, glutamine, glutamate, histidine, lysine, serine, and threonine. The hydrophobic amino acids include alanine, cysteine, isoleucine, leucine, methionine, phenylalanine, proline, tryptophan, tyrosine and valine. Other families of amino acids include (i) serine and threonine, which are the aliphatic-hydroxy family; (ii) asparagine and glutamine, which are the amide

containing family; (iii) alanine, valine, leucine and isoleucine, which are the aliphatic family; and (iv) phenylalanine, tryptophan, and tyrosine, which are the aromatic family. For example, it is reasonable to expect that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid will not have a major effect on the binding or properties of the resulting molecule, especially if the replacement does not involve an amino acid within a framework site. Whether an amino acid change results in a functional peptide can readily be determined by assaying the specific activity of the polypeptide derivative. Assays are described in detail herein. Fragments or analogs of antibodies or immunoglobulin molecules can be readily prepared by those of ordinary skill in the art. Suitable amino- and carboxy-termini of fragments or analogs occur near boundaries of functional domains. Structural and functional domains can be identified by comparison of the nucleotide and/or amino acid sequence data to public or proprietary sequence databases. In some embodiments, computerized comparison methods are used to identify sequence motifs or predicted protein conformation domains that occur in other proteins of known structure and/or function. Methods to identify protein sequences that fold into a known three-dimensional structure are known. Bowie et al. Science 253:164 (1991). Thus, the foregoing examples demonstrate that those of skill in the art can recognize sequence motifs and structural conformations that may be used to define structural and functional domains in accordance with the disclosure.

[0156] Suitable amino acid substitutions are those which: (1) reduce susceptibility to proteolysis, (2) reduce susceptibility to oxidation, (3) alter binding affinity for forming protein complexes, (4) alter binding affinities, and (4) confer or modify other physicochemical or functional properties of such analogs. Analogs can include various mutants of a sequence other than the naturally-occurring peptide sequence. For example, single or multiple amino acid substitutions (for example, conservative amino acid substitutions) may be made in the naturally-occurring sequence (for example, in the portion of the polypeptide outside the domain(s) forming intermolecular contacts. A conservative amino acid substitution should not substantially change the structural characteristics of the parent sequence (e.g., a replacement amino acid should not tend to break a helix that occurs in the parent sequence, or disrupt other types of secondary structure that characterizes the parent sequence). Examples of art-recognized polypeptide secondary and tertiary structures are described in Proteins, Structures and Molecular Principles (Creighton, Ed., W. H. Freeman and Company, New York (1984)); Introduction to Protein Structure (C. Branden and J. Tooze, eds., Garland Publishing, New York, N.Y. (1991)); and Thornton et al. Nature 354:105 (1991).

[0157] The term "polypeptide fragment" as used herein refers to a polypeptide that has an amino terminal and/or carboxy-terminal deletion, but where the remaining amino acid sequence is identical to the corresponding positions in the naturally-occurring sequence deduced, for example, from a full length cDNA sequence. Fragments typically are at least 5, 6, 8 or 10 amino acids long, for example, at least 14 amino acids long, for example, at least 20 amino acids long, usually at least 50 amino acids long, and for example, at least 70 amino acids long. The term "analog" as used herein refers to polypeptides which are comprised of a segment of at least 25 amino acids that has substantial

identity to a portion of a deduced amino acid sequence and which has specific binding to CD47, under suitable binding conditions. Typically, polypeptide analogs comprise a conservative amino acid substitution (or addition or deletion) with respect to the naturally-occurring sequence. Analogs typically are at least 20 amino acids long, for example, at least 50 amino acids long or longer, and can often be as long as a full-length naturally-occurring polypeptide.

[0158] Peptide analogs are commonly used in the pharmaceutical industry as non-peptide drugs with properties analogous to those of the template peptide. These types of non-peptide compound are termed "peptide mimetics" or "peptidomimetics". Fauchere, J. Adv. Drug Res. 15:29 (1986), Veber and Freidinger TINS p.392 (1985); and Evans et al. J. Med. Chem. 30:1229 (1987). Such compounds are often developed with the aid of computerized molecular modeling. Peptide mimetics that are structurally similar to therapeutically useful peptides may be used to produce an equivalent therapeutic or prophylactic effect. Generally, peptidomimetics are structurally similar to a paradigm polypeptide (i.e., a polypeptide that has a biochemical property or pharmacological activity), such as human antibody, but have one or more peptide linkages optionally replaced by a linkage selected from the group consisting of: —CH₂NH—, —CH₂S—, —CH₂—CH₂—, —CH=CH—(cis and trans), —COCH₂—, CH(OH)CH₂—, and —CH₂SO—, by methods well known in the art. Systematic substitution of one or more amino acids of a consensus sequence with a D-amino acid of the same type (e.g., D-lysine in place of L-lysine) may be used to generate more stable peptides. In addition, constrained peptides comprising a consensus sequence or a substantially identical consensus sequence variation may be generated by methods known in the art (Rizo and Giersch Ann. Rev. Biochem. 61:387 (1992)); for example, by adding internal cysteine residues capable of forming intramolecular disulfide bridges which cyclize the peptide.

[0159] The term "agent" is used herein to denote a chemical compound, a mixture of chemical compounds, a biological macromolecule, and/or an extract made from biological materials.

[0160] As used herein, the terms "label" or "labeled" refers to incorporation of a detectable marker, e.g., by incorporation of a radiolabeled amino acid or attachment to a polypeptide of biotinyl moieties that can be detected by marked avidin (e.g., streptavidin containing a fluorescent marker or enzymatic activity that can be detected by optical or calorimetric methods). In certain situations, the label or marker can also be therapeutic. Various methods of labeling polypeptides and glycoproteins are known in the art and may be used. Examples of labels for polypeptides include, but are not limited to, the following: radioisotopes or radionuclides (e.g., ³H, ¹⁴C, ¹⁵N, ³⁵S, ⁹⁰Y/⁹⁹Tc, ¹¹¹In, ¹²⁵I, ¹³¹I), fluorescent labels (e.g., FITC, rhodamine, lanthanide phosphors), enzymatic labels (e.g., horseradish peroxidase, O-galactosidase, luciferase, alkaline phosphatase), chemiluminescent, biotinyl groups, predetermined polypeptide epitopes recognized by a secondary reporter (e.g., leucine zipper pair sequences, binding sites for secondary antibodies, metal binding domains, epitope tags). In some embodiments, labels are attached by spacer arms of various lengths to reduce potential steric hindrance. The term "pharmaceutical agent or drug" as used herein refers to a chemical compound or composition capable of inducing a desired therapeutic effect when properly administered to a patient.

[0161] The term "antineoplastic agent" is used herein to refer to agents that have the functional property of inhibiting a development or progression of a neoplasm in a human,

particularly a malignant (cancerous) lesion, such as a carcinoma, sarcoma, lymphoma, or leukemia. Inhibition of metastasis is frequently a property of antineoplastic agents.

[0162] As used herein, the terms "treat," "treating," "treatment," and the like refer to reducing and/or ameliorating a disorder and/or symptoms associated therewith. By "alleviate" and/or "alleviating" is meant decrease, suppress, attenuate, diminish, arrest, and/or stabilize the development or progression of a disease such as, for example, a cancer. It will be appreciated that, although not precluded, treating a disorder or condition does not require that the disorder, condition or symptoms associated therewith be completely eliminated.

[0163] Other chemistry terms herein are used according to conventional usage in the art, as exemplified by The McGraw-Hill Dictionary of Chemical Terms (Parker, S., Ed., McGraw-Hill, San Francisco (1985)).

[0164] As used herein, "substantially pure" means an object species is the predominant species present (i.e., on a molar basis it is more abundant than any other individual species in the composition), and a substantially purified fraction is a composition wherein the object species comprises at least about 50 percent (on a molar basis) of all macromolecular species present.

[0165] Generally, a substantially pure composition will comprise more than about 80 percent of all macromolecular species present in the composition, for example, more than about 85%, 90%, 95%, and 99%. In some embodiments, the object 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.

[0166] In this disclosure, "comprises," "comprising," "containing," "having," and the like can have the meaning ascribed to them in U.S. Patent law and can mean "includes," "including," and the like; the terms "consisting essentially of" or "consists essentially" likewise have the meaning ascribed in U.S. Patent law and these terms are open-ended, allowing for the presence of more than that which is recited so long as basic or novel characteristics of that which is recited are not changed by the presence of more than that which is recited, but excludes prior art embodiments.

[0167] By "effective amount" is meant the amount required to ameliorate the symptoms of a disease relative to an untreated patient. The effective amount of active compound(s) used to practice the present disclosure for therapeutic treatment of a disease varies depending upon the manner of administration, the age, body weight, and general health of the subject. Ultimately, the attending physician or veterinarian will decide the appropriate amount and dosage regimen. Such amount is referred to as an "effective" amount.

[0168] By "subject" is meant a mammal, including, but not limited to, a human or non-human mammal, such as a bovine, equine, canine, rodent, ovine, primate, camelid, or feline.

[0169] The term "administering," as used herein, refers to any mode of transferring, delivering, introducing, or transporting a therapeutic agent to a subject in need of treatment with such an agent. Such modes include, but are not limited to, oral, topical, intravenous, intraperitoneal, intramuscular, intradermal, intranasal, and subcutaneous administration.

[0170] By "fragment" is meant a portion of a polypeptide or nucleic acid molecule. This portion contains, for example, at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of the entire length of the reference nucleic acid

molecule or polypeptide. A fragment may contain 10, 20, 30, 40, 50, 60, 70, 80, 90, or 100, 200, 300, 400, 500, 600, 700, 800, 900, or 1000 nucleotides or amino acids.

[0171] Ranges provided herein are understood to be shorthand for all of the values within the range. For example, a range of 1 to 50 is understood to include any number, combination of numbers, or sub-range from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50.

[0172] Unless specifically stated or obvious from context, as used herein, the terms "a," "an," and "the" are understood to be singular or plural. Unless specifically stated or obvious from context, as used herein, the term "or" is understood to be inclusive.

[0173] Unless specifically stated or obvious from context, as used herein, the term "about" is understood as within a range of normal tolerance in the art, for example within 2 standard deviations of the mean. About can be understood as within 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.1%, 0.05%, or 0.01% of the stated value. Unless otherwise clear from the context, all numerical values provided herein are modified by the term "about." 41BB (CD137, TNFRSF9) Targeting

[0174] 41BB is a member of the TNF receptor superfamily that is predominately expressed on activated T-cells and NK cells and serves as a co-stimulatory molecule. Agonizing 41BB enhances T cell proliferation and survival, cytolytic activity and cytokine secretion (e.g., IL-2, TNF α and INF γ). In mice, 41BB engagement has been shown to enhance anti-tumor immunity (Croft, 2009, Nat Rev Immunol 9:271-285; Lynch, 2008, Immunol Rev. 22: 277-286). Importantly, tumor infiltrating cytotoxic T-cells (CTLs), have been shown to be express 41BB and it is these 41BB positive CTLs that have the highest anti-tumor cytotoxic activity (Ye et al Clin Cancer Res; 20(1): 44-55). The ligand for 41BB, 41BBL, naturally forms a homotrimer and thereby suggests that signaling is mediated by higher order clustering of 41BB. This activation mechanism is shared with many members of the TNFRSF. Interest in exploiting 41BB signaling for anti-tumor immunotherapy has prompted the development of therapeutic 41BB antibodies. However, the capacity of bivalent 41BB antibodies to induce signaling is weak in absence of an exogenous clustering event. This can be achieved to some degree through the interaction with Fc γ -receptors (Fc γ Rs), yet this can also lead to depletion of the 41BB-expressing cell through effector mechanisms (e.g. ADCC and ADCP). Furthermore, competition with the high concentration of IgG in serum attenuates efficient Fc γ R interactions. Therefore, current bivalent antibodies targeting 41BB are either ineffective agonists or have the liability of depleting the very cells wherein 41BB signaling is desired. It has previously been shown that the therapeutic 41BB antibody, PF-05082566 is only capable of mediated 41BB signaling with cross-linked with anti-human secondary antibody (Fisher et al Cancer Immunol Immunother (2012) 61:1721-1733). Therefore, there exists a need for optimized 41BB agonist capable of mediating signaling in the absence of an exogenous crosslinking agent or Fc γ R interaction. The fusion proteins of the present disclosure are capable of mediating potent 41BB signaling 1) without any additional interactions when formatted as a multivalent fusion protein or 2) conditionally when engaged with at least a second antigen interaction when formatted as a multispecific fusion protein. The fusion proteins of the present disclosure are

capable of standalone (multivalent) or conditional (multi-specific) co-stimulatory activity on T-cell and NK cells.

[0175] Exemplary amino acid sequences of 41BB binding single domain antibodies are shown below:

4H04 :

(SEQ ID NO: 16)

QVQLQESGGGLVQAGDSLRLSCAASGWAFDNYGMAWFHQAPGKEREFIGRLAWNGGSTDYADSV

KGRFTISRDNPKNTLYLQMNNLKPEDTAVYYCARQRSYSGYGIRTPQTYDYWGQGTQVT

(SEQ ID NO: 17)

CDR1 : GWAFDNYG

(SEQ ID NO: 18)

CDR2 : LAWNGGST

(SEQ ID NO: 19)

CDR3 : ARQRSYSGYGIRTPQTYDY

4E1 :

(SEQ ID NO: 20)

QVQLQQSGGGLVQAGDSLRLSCAASGWAFGNYGMAWFRRAPGKEREFIGRLAWNGGSTDYVDSV

KGRFTISRDNPKNTLYLQMNNLKPDDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTQVT

(SEQ ID NO: 21)

CDR1 : GWAFGNYG

(SEQ ID NO: 18)

CDR2 : LAWNGGST

(SEQ ID NO: 22)

CDR3 : ARQRSYSRYDIRTPQTYDY

4F5 :

(SEQ ID NO: 23)

QVQLVQSGGGLVQPQGGSLRLSCAASGWAFDNYGMAWFHQAPGKEREFIGRLAWNGGSTDYADSV

KGRFTISRDNPKNTLYLQMNSLKPEDTAVYYCARQRSYSRYGIRAPQTYDYWGQGTQVT

(SEQ ID NO: 17)

CDR1 : GWAFDNYG

(SEQ ID NO: 18)

CDR2 : LAWNGGST

(SEQ ID NO: 24)

CDR3 : ARQRSYSRYGIRAPQTYDY

RH3 :

(SEQ ID NO: 25)

QVQLQESGGGLVQPQGGSLRLSCAVSGFSFSINAMGWYRQAPGKRREFLAIDSGRNTVYAVSVK

GRFTISRDNAKNTVYLQMNSLKPEDTAIYYCCLLKGNRVSPSVAYWGQGTQVT

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CDR1: GFSFSINA (SEQ ID NO: 26)
 CDR2: IDSGRNT (SEQ ID NO: 27)
 CDR3: GLLKGNRVVSPSVAY (SEQ ID NO: 28)
 D1: (SEQ ID NO: 29)
 EVQPVQSGGLVQAGESRLSCAASATIFSNNAMGWYRQAPGKORELVATITGGFTNYRDSVK
 GRFDISRDNAKNTVYLQMNNLKPEDTAVYYCMVLRYSRDYSYTTVKEYWGQGTQV
 CDR1: ATIFSNNA (SEQ ID NO: 30)
 CDR2: ITTGGFT (SEQ ID NO: 31)
 CDR3: NVVLRYSRDYSYTTVKEY (SEQ ID NO: 32)
 1G3: (SEQ ID NO: 432)
 QVQLVQSGGLVQPGGSLRLSCAASGTFSSYMSWVRQAPGKGLEWVSIPAGDGSTKYADSV
 KGRFTISRDNAKNTVYLQMDSLKPEDTAVYFQAKSRGWSTVDDMDYNGKGTQV
 CDR1: GTFSSYA (SEQ ID NO: 433)
 CDR2: IPAGDGST (SEQ ID NO: 434)
 CDR3: AKSRGWSTVDDMDY (SEQ ID NO: 435)
 1H4: (SEQ ID NO: 436)
 QVQLVQSGGLVQPGGSLRLSCVVSGFTFRSYMSWVRQAPGKGLEWVSINSGESSTKYADSV
 KGRFTISRDDAKNTLYLQMSDLKPEDTAVYFQAKHRGWSTVDDINYNGKGTQV
 CDR1: GFTERSYA (SEQ ID NO: 437)
 CDR2: INSGESST (SEQ ID NO: 438)
 CDR3: AKHRGWSTVDDINY (SEQ ID NO: 439)
 1H1: (SEQ ID NO: 440)
 QVQLVQSGGLVQPGGSLRLSCAASGTFDDHAMSWVRQAPGKGLEWVSISWNGHYTYYAESM
 KGRFAISRDNAKNTLYLQMNSLKSEDTAVYYCVKGWRGSYTRDRPFAWGQGTQV
 CDR1: GTFDDHA (SEQ ID NO: 441)
 CDR2: ISWNGHYT (SEQ ID NO: 442)
 CDR3: VKGWRGSYTRDRPFA (SEQ ID NO: 443)

-continued

1H8:

(SEQ ID NO: 444)

EVQLVQSGGLVQPGGSLRLSCAASGFTFSSYYMSWVRQAPGKGLEWVSTILSTNTGGSTIYYAY

ADSVVKGRFTISRDNAKNTLYLEMNSLKPEDTAQYYCVRTRWEGVYDYWGLGTQV

(SEQ ID NO: 445)

CDR1: GFTFSSYY

(SEQ ID NO: 446)

CDR2: ISTMNTGGST

(SEQ ID NO: 447)

CDR3: VRTRWEGVYDY

H24E1-v1:

(SEQ ID NO: 33)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKGLEWVARILAWNGGSTIDYAESV

KGRFTISRDNAKNTLYLOMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLVTVK

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

H24E1-v3:

(SEQ ID NO: 34)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKGREFVARILAWNGGSTIDYAESV

KGRFTISRDNAKNTLYLOMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLVTVK

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v7-1:

(SEQ ID NO: 35)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFSRLAWNGGSTIDYVAES

VKGRFTISRDNAKNTLYLOMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLVTVK

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v8:

(SEQ ID NO: 36)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTIDYVESV

KGRFTISRDNPKNTLYLOMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLVTVK

(SEQ ID NO: 21)

CDR1: GWAFGNYG

-continued

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v9:

(SEQ ID NO: 37)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v10:

(SEQ ID NO: 38)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTDYVESV

KGRFTISRDNPKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v11:

(SEQ ID NO: 39)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTDYVESV

KGRFTISRDNAKNTLYLOMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v12:

(SEQ ID NO: 40)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 18)

CDR2: LAWNGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

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hz4E01v13:
(SEQ ID NO: 41)
EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTIDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

CDR1: GWAFGNYG
(SEQ ID NO: 21)

CDR2: LAWQGGST
(SEQ ID NO: 42)

CDR3: ARQRSYSRYDIRTPQTYDY
(SEQ ID NO: 22)

hz4E01v14:
(SEQ ID NO: 43)
EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTIDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

CDR1: GWAFGNYG
(SEQ ID NO: 21)

CDR2: LAWNAGST
(SEQ ID NO: 44)

CDR3: ARQRSYSRYDIRTPQTYDY
(SEQ ID NO: 22)

hz4E01v16:
(SEQ ID NO: 43)
EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTIDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

CDR1: GWAFGNYG
(SEQ ID NO: 21)

CDR2: LAQGGST
(SEQ ID NO: 42)

CDR3: ARQRSYSRYDIRTPQTYDY
(SEQ ID NO: 22)

hz4E01v17:
(SEQ ID NO: 46)
EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTIDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

CDR1: GWAFGNYG
(SEQ ID NO: 21)

CDR2: LAWNAGST
(SEQ ID NO: 44)

CDR3: ARQRSYSRYDIRTPQTYDY
(SEQ ID NO: 22)

hz4E01v18:
(SEQ ID NO: 47)
EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFIGRLAWNGGSTIDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

CDR1: GWAFGNYG
(SEQ ID NO: 21)

-continued

(SEQ ID NO: 48)

CDR2: LAWGGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v21:

(SEQ ID NO: 49)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFVSPLAWNGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 50)

CDR1: GWAFSNYG

(SEQ ID NO: 48)

CDR2: LAWGGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v22:

(SEQ ID NO: 47)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFVSPLAWNGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 52)

CDR2: LAWGGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v23:

(SEQ ID NO: 53)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFVSPLAWGGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 50)

CDR1: GWAFSNYG

(SEQ ID NO: 52)

CDR2: LAWGGGST

(SEQ ID NO: 22)

CDR3: ARQRSYSRYDIRTPQTYDY

hz4E01v24:

(SEQ ID NO: 47)

EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFVSPLAWGGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSGYDIRTPQTYDYWGQGTLTVKP

(SEQ ID NO: 21)

CDR1: GWAFGNYG

(SEQ ID NO: 48)

CDR2: LAWGGGST

(SEQ ID NO: 55)

CDR3: ARQRSYSGYDIRTPQTYDY

-continued

hz4E01v25:
 (SEQ ID NO: 56)
 EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFVSRLAWGGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRYSRYSRGIRTPQTYDYNGQGTLTVKP

(SEQ ID NO: 21)
 CDR1: GWAFGNYG

(SEQ ID NO: 48)
 CDR2: LAWGGGST

(SEQ ID NO: 57)
 CDR3: ARQRYSRYSRGIRTPQTYDY

hz4E01v26:
 (SEQ ID NO: 56)
 EVQLLESGGGEVQPGGSLRLSCAASGWAFGNYGMAWFRQAPGKEREFVSRLAWGGGSTDYVESV

KGRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRYSRYSGYGIRTPQTYDYNGQGTLTVKP

(SEQ ID NO: 21)
 CDR1: GWAFGNYG

(SEQ ID NO: 48)
 CDR2: LAWGGGST

(SEQ ID NO: 19)
 CDR3: ARQRYSRYSGYGIRTPQTYDY

hzRH3-v1:
 (SEQ ID NO: 59)
 EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMAWFRQAPGKGLEWVAATIDSGRNTVYAESVK

GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 26)
 CDR1: GFSFSINA

(SEQ ID NO: 27)
 CDR2: IDSGRNT

(SEQ ID NO: 28)
 CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-1:
 (SEQ ID NO: 60)
 EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESGRNTVYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 26)
 CDR1: GFSFSINA

(SEQ ID NO: 61)
 CDR2: IESGRNT

(SEQ ID NO: 28)
 CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-2:
 (SEQ ID NO: 62)
 EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIYSGRNTVYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 26)
 CDR1: GFSFSINA

-continued

(SEQ ID NO: 63)

CDR2: IYSGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-3

(SEQ ID NO: 64)

EVQLLESGGGEVQPGGSLRLSCAASGFTFSINAMGWYRQAPGKRREFVAAIESGRNTIYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 65)

CDR1: GFTFSINA

(SEQ ID NO: 61)

CDR2: IESGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-6

(SEQ ID NO: 66)

EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMSWYRQAPGKRREFVAAIESGRNTVYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 67)

CDR1: GFSFSINA

(SEQ ID NO: 61)

CDR2: IESGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-8

(SEQ ID NO: 68)

EVQLLESGGGEVQPGGSLRLSCAASGFTFSSNAMGWYRQAPGKRREFVAAIESGRNTIYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 69)

CDR1: GFTFSINA

(SEQ ID NO: 61)

CDR2: IESGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-10

(SEQ ID NO: 70)

EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESSRNTIYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 71)

CDR2: IESSIONT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

-continued

hzRH3v5-12

(SEQ ID NO: 72)

EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESTGSNTIVAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYWGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 73)

CDR2: IESTGSNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-14

(SEQ ID NO: 74)

EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESTGRNTIVAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYWGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 75)

CDR2: IESTGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-15

(SEQ ID NO: 74)

EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESTGRNTIVAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYWGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 75)

CDR2: IESTGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v5-16

(SEQ ID NO: 78)

EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIYSGSNTIVAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYWGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 79)

CDR2: IYSGSNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v7

(SEQ ID NO: 80)

EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESTGRNTIVAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVRVSPSVAYWGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

-continued

(SEQ ID NO: 61)

CDR2: IESGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v8

(SEQ ID NO: 81)

EVQLLESGGVEQPGGSLRLSCAVSGFSFSINAMGWYRQAPGKRREFVAIESGRNTIVYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 61)

CDR2: IESGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v9

(SEQ ID NO: 82)

EVQLLESGGVEQPGGSLRLSCAVSGFSFSINAMGWYRQAPGKRREFVAIESGRNTIVYAVSVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 61)

CDR2: IESGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

hzRH3v13

(SEQ ID NO: 83)

EVQLLESGGVEQPGGSLRLSCAVSGFSFSINAMGWYRQAPGKRREFLAIESGRNTIVYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYGLLKGNRVRVSPSVAYNGQGTLTVKP

(SEQ ID NO: 26)

CDR1: GFSFSINA

(SEQ ID NO: 61)

CDR2: IESGRNT

(SEQ ID NO: 28)

CDR3: GLLKGNRVRVSPSVAY

[0176] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a variable heavy chain (VH) sequence and a variable light chain (VL) sequence selected from the group consisting of:

-continued

(SEQ ID NO: 85)

QVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMHWRQAPGKGLEWVSV
ISGSGSNNTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLY
AQPEGDFWGQGTLTVSS

VH Sequences:

(SEQ ID NO: 84)

QVQLVQSGAEVKPGSSVKVSCKASGGTFNSYAISSWVRQAPGQGLEWMGG

IIPGFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARKN

EEDGGFDHWGQGTLTVSS

(SEQ ID NO: 86)

QVQLVQSGAEVKPGESLKISCKGSGYSFSTYWIWVWRQMPGKGLEWMGG
IYPGDSYTNYSPLSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGY
GIFDYWGQGTLTVSS

- continued

(SEQ ID NO: 87)

EVQLVQSGAEVKPGESLRISCKGSGYSFSTYWIWVVRQMPGKGLEWMGK

IYPGDSYTNYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGY

GIFDYWGQGTLTVSS

VL Sequences:

(SEQ ID NO: 88)

DIELTQPPSVSVPQQTARISCGDNLDYYASWYQQKPGQAPVLIYDD

SERPSGIPERFSGSNSGNTATLTISGTQAEDeadYYCQTDGTLHVFVGG

GTKLTVL

(SEQ ID NO: 89)

DIELTQPPSVSVPQQTARISCGDNIGSKYVWSYQQKPGQAPVLIYSD

SERPSGIPERFSGSNSGNTATLTISGTQAEDeadYYCQSWDGSISRVFGG

GTKLTVL

(SEQ ID NO: 90)

DIELTQPPSVSVPQQTARISCGDNIGDQYAHWYQQKPGQAPVVIYQD

KNRPSGIPERFSGSNSGNTATLTISGTQAEDeadYYCATYTGFGLAVFG

GGTKLTVL

(SEQ ID NO: 91)

SYELTQPPSVSVPQQTASITCGDNIGDQYAHWYQQKPGQSPVLIYQD

KNRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCATYTGFGLAVFG

GGTKLTVL

(SEQ ID NO: 92)

SYELTQPPSVSVPQQTASITCGDNIGDQYAHWYQQKPGQSPVVIYQD

KNRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCATYTGFGLAVFG

GGTKLTVL

(SEQ ID NO: 93)

DIELTQPPSVSVPQQTARISCGDNIGDQYAHWYQQKPGQAPVVIYQD

KNRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCSTYTFVGFTTVFG

GGTKLTVL

(SEQ ID NO: 94)

SYELTQPPSVSVPQQTASITCGDNIGDQYAHWYQQKPGQSPVLIYQD

KNRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCSTYTFVGFTTVFG

GGTKLTVL

(SEQ ID NO: 95)

SYELTQPPSVSVPQQTASITCGDNIGDQYAHWYQQKPGQSPVVIYQD

KNRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCSTYTFVGFTTVFG

GGTKLTVL

[0177] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a heavy chain (HC) sequence and a light chain (LC) sequence selected from the group consisting of.

HC Sequences:

(SEQ ID NO: 96)

QVQLQQWGAGLLKPSLTLTCAVYGGSFSGYWSWIRQSPEKGLEWIGE

INHGGYVTYNPSLESRTISVDTSKNQFSKLSSVTAADTAVYYCARDYG

- continued

PGNYDWYPDLWGRGTLTVSSASTKGPSVPLAPCSRSTSESTAALGCLV

KDYFPEPVTSWNNGALTSVGHTFPAVLQSSGLYSLSSVTPSSSLGKT

TYTCNVDHKPSNTKVDKRVESKYGPPCPCCPAPEFLGGPSVFLFPPKPD

TLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNNAKTKPREEQNST

YRVSVSLTVLHQDWLNKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVY

TLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGOPENNYKTPVLD

SDGSFFLYSRLTVDKSRWQEGNVFSCSVHEALHNHYTQKSLSLSGK

(SEQ ID NO: 97)

QVQLQQWGAGLLKPSLTLTCAVYGGSFSGYWSWIRQSPEKGLEWIGE

INHGGYVTYNPSLESRTISVDTSKNQFSKLSSVTAADTAVYYCARDYG

PGNYDWYPDLWGRGTLTVSSASTKGPSVPLAPSSKSTSGGTAALGCLV

KDYFPEPVTSWNNGALTSVGHTFPAVLQSSGLYSLSSVTPSSSLGTO

TYICNVNHKPSNTKVDKRVEPKSCDKTHTCPCPAPELLGGPSVFLFPPK

PKDTLMISRTPEVTCVVVDVSHEDEVKENWYVDGVEVHNNAKTKPREEQY

NSTYRVSVSLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPREP

QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGOPENNYKTPP

VLDSDGSFFLYSKLTVDKSRWQOGNVFSCSVHEALHNHYTQKSLSLSPG

K

LC Sequences:

(SEQ ID NO: 98)

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYD

ASNRATGIPARFSGSGSGTDFLTISLEPEDFAVYYCQQRSNWPPALTF

GGGTKVEIKRTVAAPSFIGFPPSDEQLKSGTASVVCVLLNNFYPREAKVQW

KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTSKADYEKHKVYACEVTH

QGLSSPVTKSENRGEC

[0178] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof selected from the antibody sequences described in US Patent Application Publication No. 20160244528, the contents of which are hereby incorporated by reference in their entirety.

[0179] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof selected from the antibody sequences described in U.S. Pat. No. 8,337,850, the contents of which are hereby incorporated by reference in their entirety.

[0180] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof selected from the antibody sequences described in PCT Publication No. WO 2005/035584, the contents of which are hereby incorporated by reference in their entirety.

[0181] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof selected from the antibody sequences described in EP Patent No. EP 1670828 B1, the contents of which are hereby incorporated by reference in their entirety.

[0182] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof selected from the antibody sequences described in PCT Publication No. WO 2006/088447, the contents of which are hereby incorporated by reference in their entirety.

[0183] In some embodiments, the 41BB binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof selected from the antibody sequences described in US Patent Application Publication No. 20080166336, the contents of which are hereby incorporated by reference in their entirety.

[0184] In some embodiments, the 41BB binding domain comprises or is derived from an anti-cancer fusion protein sequence or antigen-binding fragment thereof selected from the sequences described in PCT Publication No. WO 2016/177802, the contents of which are hereby incorporated by reference in their entirety. In some embodiments, the 41BB binding domain comprises or is derived from an amino acid sequence comprising:

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(SEQ ID NO: 99)
QDSTS DLI PAPPLSKVPLQQNFQDNQFHGKWWYVGQAGNIRLREDKDPIK
MMATI YEL KED KSY DVT MVFKDDKKCMYDIWTFVPGS QPGEFTL GKIKSF
PGHTSSLVRVVSTNYNQHAMVFFKFVFQNREEFYITLYGRTKELTSELKE
NFIRFSKSLGLPENHIVFPVPIDQCIDG
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[0185] In some embodiments, the 41BB binding domain comprises or is derived from an 41BB-targeting polypeptide sequence or antigen-binding fragment thereof selected from the sequences described in PCT Publication No. WO 2016/177762, the contents of which are hereby incorporated by reference in their entirety. In some embodiments, the 41BB binding domain comprises or is derived from an amino acid sequence comprising: PDL1 Targeting

[0186] In some embodiments, the fusion proteins are multispecific containing at least a first binding domain, e.g., a TBD, and a second binding domain directed toward Program Death Ligand 1 (PD-L1). In these, embodiments, the binding to PD-L1 is capable of providing the additional crosslinking function and TNFRSF activation is achieved with only one or two TBDs. In these embodiments, the TNFRSF signaling is enhanced and focused by the presence of a PD-L1 expressing cell.

[0187] PDL1 is a 40 kDa type I transmembrane protein that forms a complex with its receptor programmed cell death protein 1 (PD1), also known as CD279. Engagement of PDL1 with its receptor PD1 on T cells delivers a signal that inhibits TCR-mediated activation of IL-2 production and T cell proliferation. Aberrant expression and/or activity of PDL1 and PDL1-related signaling has been implicated in the pathogenesis of many diseases and disorders, such as cancer, inflammation, and autoimmunity.

[0188] In some embodiments, the PD-L1 binding portion is single domain antibody. In some embodiments, the PDL1 binding portion of the fusion blocks or dampens the interaction of PDL1 and PD-1. Exemplary PDL1-targeting single domain sequences are shown below:

28A10 :	<pre>(SEQ ID NO: 100) QVQLQESGGGLVQAGGS LRLACTTS<u>GGIFNIRP</u>I SWYRQPPGMQREWVAT<u>IAFGGAT</u>NYANSIK</pre>
	(SEQ ID NO: 101)
CDR1 : GGIFNIRP	
	(SEQ ID NO: 102)
CDR2 : IAFGGAT	
	(SEQ ID NO: 103)
CDR3 : NAEFI	
	(SEQ ID NO: 104)
28A2 :	<pre>QLQLQESGGGLV RAGGS LRLACTTS<u>GGIFAIKP</u>I SWYRQPPGQEREWVTT<u>TTSSGAT</u>NYANSIK</pre>
	(SEQ ID NO: 105)
CDR1 : GGIFAIKP	
	(SEQ ID NO: 106)
CDR2 : TTSSGAT	
	(SEQ ID NO: 107)
CDR3 : NVF EY	
	(SEQ ID NO: 108)
B03 :	<pre>QVQLQESGGDLVQAGSS LRLACATS<u>GGVENIRP</u>I SWYRQPPGKOREWVAT<u>TASGGAT</u>NYANSIK</pre>
	(SEQ ID NO: 109)
GRFTASRDNAKNTVYLQMNGLKPEDTAVYYC <u>NAFEV</u> WGQGTQTV	

-continued

(SEQ ID NO: 109)

CDR1: GGVENIRP

(SEQ ID NO: 110)

CDR2: IASGGAT

(SEQ ID NO: 111)

CDR3: NAFEV

B10:

(SEQ ID NO: 112)

QVQLQQSGGGLVQAGGSLRLACTTSGGIFNIRPI SWYROP~~PGM~~REWVATIASGGATNYANSIK

GRFTASRDNAKNTVYLOMNGLKPEDTAVYYCNTLNFWGQGTQVT

(SEQ ID NO: 101)

CDR1: GGIFNIRP

(SEQ ID NO: 110)

CDR2: IASGGAT

(SEQ ID NO: 113)

CDR3: NTLNF

D02:

(SEQ ID NO: 114)

QVQLQESGGGLVQAGGSLRLACTTSGGIFNIRPI SWYROP~~PGM~~REWVATIASGGATNYANSIK

GRFTASRDNAKNTVYLQMNGLKPEDTAVYYCNVFEIWGQGTQVT

(SEQ ID NO: 101)

CDR1: GGIFNIRP

(SEQ ID NO: 110)

CDR2: IASGGAT

(SEQ ID NO: 115)

CDR3: NVFEI

A03:

(SEQ ID NO: 116)

QVQLQQSGGGLVQAGGSLRLACITGGIFNIRPI SWYRQPPGKQREWVATIASGGANYANSIK

GRFTASRDNAKNTVYLQMNGLKPEDTAVYYCNAFENWGQGTQVT

(SEQ ID NO: 101)

CDR1: GGIFNIRP

(SEQ ID NO: 117)

CDR2: IASGGAA

(SEQ ID NO: 118)

CDR3: NAFEN

hz28A2v1

(SEQ ID NO: 119)

QVQLQESGGGEVQP~~GG~~SLRLSCAASGGIFAIKPI SWYROAPGKQREWVSTTTSSGATNYAESVK

GRFTISRDNAKNTLYLOMSSLRAEDTAVYYCNVFEYWGQGTLTVKP

(SEQ ID NO: 105)

CDR1: GGIFAIKP

(SEQ ID NO: 106)

CDR2: TTSSGAT

(SEQ ID NO: 107)

CDR3: NVFEY

-continued

hz28A2v1-1

(SEQ ID NO: 120)
EVQLQESGGEVQPGGSLRLSCAASGGIFAIKPI SWYRQAPGKOREWVSTTTSSGATNYAESVK

GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFEYWGQGTLVTVKP

(SEQ ID NO: 105)
CDR1: GGIFAIKP

(SEQ ID NO: 106)
CDR2: TTSSGAT

(SEQ ID NO: 107)
CDR3: NVF

hz28A2v2

(SEQ ID NO: 121)
EVQLLESGGEVQPGGSLRLSCAASGGIFAIKPI SWYRQAPGKOREWVSTTTSSGATNYAESVK

GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFEYWGQGTLVTVKP

(SEQ ID NO: 105)
CDR1: GGIFAIKP

(SEQ ID NO: 106)
CDR2: TTSSGAT

(SEQ ID NO: 107)
CDR3: NVF

hz28A2v3

(SEQ ID NO: 122)
EVQLLESGGEVQPGGSLRLSCAASGGIFAIKPI SWYRQAPGKOREWVSTTTSSGATNYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCNVFEYWGQGTLVTVKP

(SEQ ID NO: 105)
CDR1: GGIFAIKP

(SEQ ID NO: 106)
CDR2: TTSSGAT

(SEQ ID NO: 107)
CDR3: NVF

hz28A2v4:

(SEQ ID NO: 123)
EVQLLESGGEVQPGGSLRLSCAASGGIFAIKPI SWYRQAPGKOREWVSTTTSSGATNYAESVK

GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCNVFEYWGQGTLVTVKP

(SEQ ID NO: 105)
CDR1: GGIFAIKP

(SEQ ID NO: 106)
CDR2: TTSSGAT

(SEQ ID NO: 107)
CDR3: NVF

hz28A2v5:

(SEQ ID NO: 124)
EVQLLESGGEVQPGGSLRLSCAASGGIFAIKPI SWYRQAPGKOREWVSTTTSSGATNYAESVK

GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFEYWGQGTLVTVKP

(SEQ ID NO: 105)
CDR1: GGIFAIKP

-continued

(SEQ ID NO: 106)

CDR2: TTSSGAT

(SEQ ID NO: 107)

CDR3: NVFEY

[0189] In other embodiments, the PD-L1 binding portion is derived from the extracellular domain of PD-1 containing at least the IgV domain as shown below:

(SEQ ID NO: 125)

PTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPFE

DRSQPGQDCRFRVTQLPNGRDFHMSVVRARRNDSTYLCGAISLAPKAQI

KESLRRAELRVT

[0190] In some embodiments, the PDL1 binding domain comprises or is derived from a known anti-PDL1 antibody sequence or antigen-binding fragment thereof. In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence disclosed in PCT Publication No. WO 2016/149201, the contents of which are hereby incorporated by reference in their entirety.

[0191] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a variable heavy chain (VH) sequence and a variable light chain (VL) sequence selected from the group consisting of:

VH Sequences :

(SEQ ID NO: 126)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYGFSWVRQAPGQGLEWMGW

ITAYNGNTNYAQKLQGRVTMTTDTSTSTVYMELRSLSRSDDTAVYYCARDY

FYGMDVWGQGTTVTVSS

(SEQ ID NO: 127)

QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTYAIWVRQAPGQGLEWMGG

IIPIFGKAHYAQKFQGRVTITADESTSTAYMELSLRSEDTAVYFCARKF

HFVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 128)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDVHWRQAPGQRLEWMW

LHADTGITKFSQKFQGRVTITRDTSASTAYMELSLRSEDTAVYYCARER

IQLWFDFYWGQGT

(SEQ ID NO: 129)

QVQLVQSGAEVKKPGSSVKVSCKVSGGIFSTYAINWVRQAPGQGLEWMGG

IIPIFGTANHAQKFQGRVTITADESTSTAYMELSLRSEDTAVYYCARDQ

GIAAALFDYWGQGTLTVSS

(SEQ ID NO: 130)

EVQLVESGGGLVQPGRLSRLSCAVSGTFDDYVVHWRQAPGKGLEWMVG

NSGNIGYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCAVPFDYW

GQGTLTVSS

-continued

(SEQ ID NO: 131)

QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSSYAIWVRQAPGQGLEWMGG

IIPIFGRAHYAQKFQGRVTITADESTSTAYMELSLRSEDTAVYFCARKF

HFVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 132)

QVQLVQSGAEVKKPGSSVKVSCKTSGGTFSYAIWVRQAPGQGLEWMGG

IIPIFGKAHYAQKFQGRVTITADESTTAYMELSLRSEDTAVYYCARKY

DYVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 133)

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAINWVRQAPGQGLEWMGG

IIPIFGSANYAQKFQDRVTITADESTSAAYMELSLRSEDTAVYYCARDS

SGWSRYYMDVWGQGTTVTVSS

(SEQ ID NO: 134)

QVQLVQSGAEVKEPGSSVKVSCKASGTFNSYAIWVRQAPGQGLEWMGG

IIPLEGIAHYAQKFQGRVTITADESTNTAYMDLSSLRSEDTAVYYCARKY

SYVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 135)

EVQLVESGGGLVQPGRLSRLSCAASGFTEDDYGMHWVRQAPGKGLEWMVG

ISWNRGRIEYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCAKGR

FRYFDWFLDYWGQGTLTVSS

(SEQ ID NO: 136)

QMLQVQSGGLVQPGGLSRLSCAASGFTFSSYWMWSVRQAPGKGLEWMVAN

IKQDGSEKYYVDSDKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDY

FWSGFSAFDIWGKGTLTVSS

VL Sequences :

(SEQ ID NO: 137)

EIVLTQSPATLSLSPGERATLSCRASQS VSSYLVWYQQKPGQAPRLLIYD

ASN RATGIPARFSGSGSGTDFLTISLLEPEDFAVYYCQQRSNWPTFGQ

GTKVEIK

(SEQ ID NO: 138)

EIVLTQSPATLSLSPGERATLSCRASQS VSSYLA WYQQKPGQAPRLLIYD

ASN RATGIPARFSGSGSGTDFLTISLLEPEDFAVYYCQQRSNWPTFGQ

TKVEIK

(SEQ ID NO: 139)

DIQMTQSPSSLSASVGDRTITCRASQGISSWLA WYQQKPEKAPKSLIYA

ASSLQSGVPSRFSGSGSGTDFLTISLQPEDFATYYCQQYNSYPYTFGQ

GTKLEIK

-continued

(SEQ ID NO: 140)
 EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIY
 GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFG
 QGTKEIK

(SEQ ID NO: 141)
 EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIY
 GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPFGGG
 TKVEIK

(SEQ ID NO: 142)
 EIVLTQSPATLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYD
 ASN RATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPTFGQG
 TRLEIK

(SEQ ID NO: 143)
 AIQLTQSPSSLSASVGDRVITTCRASQGISSWALAWYQQKPGKAPKLLIYD
 ASSLEGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQFNNSYPFTFGP
 GTKVDIK

(SEQ ID NO: 144)
 DIVMTQSPSTLSSLASVGDRVITTCRASQGISSWALAWYQQKPGRAPKVLIIYK
 ASTLEGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPWTFGQ
 GTKLEIK

[0192] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequence:
 (SEQ ID NO: 145)
 EVQLVESGGGLVQPGGSLRLSCAASGFTFSRYWMSWVRQAPGKLEWVAN
 IKQDGSEKYYDSVKGRTISRDNAKNSLYLQMNSLRAEDTAVYYCAREG
 GWFGELAFDYWGQGTIVTSS

VL Sequence:
 (SEQ ID NO: 146)
 EIVLTQSPGTLSSLSPGERATLSCRASQRVSSSYLAWYQQKPGQAPRLLIY
 DASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSLPWTFG
 QGTKEIK

[0193] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:
 (SEQ ID NO: 147)
 EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWVRQAPGKLEWVAN
 ISPYGGSTYYADSVKGRTISADTSKNTAYLQMNSLRAEDTAVYYCARRH
 WPGGFDYWGQGTIVTSS

-continued

(SEQ ID NO: 148)
 EVQLVESGGGLVQPGGSLRLSCAASGFTFSGSWIHWVRQAPGKLEWVAN
 ILPYGGSSYYADSVKGRTISADTSKNTAYLQMNSLRAEDTAVYYCARRH
 WPGGFDYWGQGTIVTSS

VL Sequences:
 (SEQ ID NO: 149)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 150)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 151)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 152)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 153)
 DIQMTQSPSSLSASVGDRVITTCRASQINTFLAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 154)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 155)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 156)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 157)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

(SEQ ID NO: 158)
 DIQMTQSPSSLSASVGDRVITTCRASQDVSTAVAWYQQKPGKAPKLLIYS
 ASFLYSGVPSRFSRGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQ
 GTKVEIKR

-continued

(SEQ ID NO: 159)
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYS

ASFLYSGVPSRSGSGSGTDFTLTISLQPEDFATYYCQQSLFTPPTFGQ
GTKVEIKR

(SEQ ID NO: 160)
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYS

ASFLYSGVPSRSGSGSGTDFTLTISLQPEDFATYYCQQSLFTPPTFGQ
GTKVEIKR

(SEQ ID NO: 161)
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYS

ASFLYSGVPSRSGSGSGTDFTLTISLQPEDFATYYCQQSWYHPPTFGQ
GTKVEIKR

(SEQ ID NO: 162)
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYS

ASFLYSGVPSRSGSGSGTDFTLTISLQPEDFATYYCQQYFYIPPTFGQ
GTKVEIKR

(SEQ ID NO: 163)
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYS

ASFLYSGVPSRSGSGSGTDFTLTISLQPEDFATYYCQQYWYTPPTFGQ
GTKVEIKR

(SEQ ID NO: 164)
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYS

ASFLYSGVPSRSGSGSGTDFTLTISLQPEDFATYYCQQSYFIPPTFGQ
GTKVEIKR

[0194] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of.

VH Sequences:

(SEQ ID NO: 165)
METGLRWLLLAVLKGVOQLSVEESGGRLVTPGTLTLCCTASGFTITNY
HMFWRVRQAPGKGGLEWIGVITSSGIGSSTTYYAWAKGRFTISKTTVN
LRITSPTTEDTATYFCARDYFTNTYYALDIWGPGLTVTVSS

(SEQ ID NO: 166)
QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTYAIWVRQAPGQGLEWMGG
IIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKF
HFVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 167)
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDVHWRQAPGQRLEWMGW
LHADTGITKFSQKFQGRVTITRDTSASTAYMELSSLRSEDTAVYCARER
IQLWFDFYWGQGTLTVSS

-continued

(SEQ ID NO: 168)
QVQLVQSGAEVKKPGSSVKVSCKVSGGIFTSTYAINWVRQAPGQGLEWMGG

IIPIFGTAHQAKFQGRVTITADESTSTAYMELSSLRSEDTAVYCCARDQ
GIAAALFDYWGQGTLTVSS

(SEQ ID NO: 169)
EVOLVESGGGLVQPGRLRLSCAVSGFTFDDYVVHWRQAPGKGLEWMGG
ISGNNSNIGNYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCAVPF
DYWGQGTLTVSS

(SEQ ID NO: 170)
QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSSYAIWVRQAPGQGLEWMGG
IIPIFGRAHYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKF
HFVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 171)
QVQLVQSGAEVKKPGSSVKVSCKTSGGTFSYAIWVRQAPGQGLEWMGG
IIPIFGKAHYAQKFQGRVTITADESTTAYMELSSLRSEDTAVYCCARKY
DYVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 172)
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAINWVRQAPGQGLEWMGG
IIPIFGSANYAQKFQDRVTITADESTAAYMELSSLRSEDTAVYCCARDS
SGWSRYMDVWGQGTTVTVSS

(SEQ ID NO: 173)
QVQLVQSGAEVKEPGSSVKVSCKASGGTFNSYAIWVRQAPGQGLEWMGG
IIPIFGIAHYAQKFQGRVTITADESTNTAYMDLSSLRSEDTAVYCCARKY
SYVSGSPFGMDVWGQGTTVTVSS

(SEQ ID NO: 174)
EVOLVESGGGLVQPGRLRLSCAASGITEDDYGMHWVRQAPGKGLEWMGG
ISWNRGRIEYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCAKGR
FRYFDWFLDYWGQGTLTVSS

VL Sequences:

(SEQ ID NO: 175)
MDTRAPTQLLGLLLWLPGARCALVMTQTPSSTSTAVGGTVTIKCQASQS
ISVYLAWYQQKPGQPKLIIYSASTLASGVPSRFKGSRSGTEYTLISGV
QREDAATYYCLGSAGS

(SEQ ID NO: 176)
EIVLTQSPATLSLSPGERATLSCRASQSVSSYLVWYQQKPGQAPRLLIYD
ASN RAT GIPARFSGSGSGTDFTLTISLEPEDFAVYYCQQRSNWPTFGQ
GTKVEIK

(SEQ ID NO: 177)
EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAZYQQKPGQAPRLLIYD
ASN RAT GIPARFSGSGSGTDFTLTISLEPEDFAVYYCQQRSNWPTFGQ
TKVEIK

(SEQ ID NO: 178)
DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAZYQQKPEKAPKSLIYA
ASSLQSGVPSRSGSGSGTDFTLTISLQPEDFATYYCQQYNSYPYTFGQ
GTKLEIK

-continued

(SEQ ID NO: 179)
 EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIY
 GASSRATGIPDRFSGSGSGTDETLTISRLEPEDFAVYYCQQYGSSPWTFG
 QGTTKVEIK

(SEQ ID NO: 180)
 EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIY
 GASSRATGIPDRFSGSGSGTDETLTISRLEPEDFAVYYCQQYGSSPFGGG
 TKVEIK

(SEQ ID NO: 181)
 EIVLTQSPATLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYD
 ASN RATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPTFGQG
 TRLEIK

(SEQ ID NO: 182)
 AIQLTQSPSSLSASVGDRVITCRASQGISSALAWYQQKPGKAPKLLIYD
 ASSLESGVPSRPGSGSGSGTDFTLTISSLQPEDFATYYCQQFNNSYPFTFG
 PGTKVDIK

[0195] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:
 (SEQ ID NO: 183)
 EVQLLESGGGLVQPGGSLRLSCAASGTFSSYIMMWVRQAPGKGLEWVSS
 IYPSGGITFYADTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARIK
 LGTVTTVDYWGQGTLVTVSS

VL Sequences:
 (SEQ ID NO: 184)
 QSALTQPASVSGSPGQSITISCTGTSSDVGGYNVSWYQQHPGKAPKLMI
 YDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDAEADYYCSSYTSSSTRV
 FGTGTVTVL

[0196] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:
 (SEQ ID NO: 185)
 EVKLQESGPSPLVKPSQTLSSLTCVTGYSITSODYWNWIRKFPGNKLEYVGYISYTGSTYYNPSLK
 SRISITRDTSKNQYYLQLNSVTSEDTATYYCARYGGWLSPFDYWQGTTLVSS
 (SEQ ID NO: 186)
 EVQLQESGPGLVAPSQSLSITCTVSGFSLTTYSINWIRQPPGKGLEWLGVMWAGGGTNNSNVLK
 SRLII SKDNSKSQVFLKMNSLQTDDTARYYCARYGGWLSPFDYWQGTTLVSS

(SEQ ID NO: 187)
 EVKLQESGPSPLVKPGASVKLCKASGYTFTSYDINWVKQRPGQGLEWIGWIPPRDNNTKYNEF
 SRISITRDTSKNQYYLQLNSVTTEDTATYYCARRGGWLLPPDYWGQGTTLVSS

(SEQ ID NO: 188)
 EVKLQESGPSPLVKPGASVKLCKASGYTFTSYDINWVKQRPGQGLEWIGWIPPRDNNTKYNEF
 KGKATLTVDTSSTAYMELHSLTSEDSAVYFCTKENWVGDFDYWGQGTTLVSS
 (SEQ ID NO: 189)
 EVOLOQSGPDLVTPGASVRISCOASGYTFPDYMMNWWVQSHGKSLEWIGIDDPNYGGTTYNQKF
 KGKAILTVDRSSSTAYMELRSLTSEDSAVYYCARGALTDWGQGTSLTVSS

(SEQ ID NO: 190)
 EIVLTQSPATLSSLSPGERATLSCRASSSVSYIYWFQQKPGQSPRPLIYAAFNRATGIPARFSGS
 GSGTDYTLTISSLEPEDFAVYYCQQWSNNPLTFQGQTKVEIK

(SEQ ID NO: 191)
 QVQLVQSGAEVKKPGASVKVSCKASGYTFPDYMMNWWVQAPGQGLEWMGDIDPNYGGTNYAQKF
 QGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARGALTDWGQGTMVTVSS

(SEQ ID NO: 192)
 QVQLVQSGAEVKKPGASVKVSCKASGYTFPDYMMNWWVQAPGQGLEWMGDIDPNYGGTNYAQKF
 QGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARGALTDWGQGTMVTVSS

(SEQ ID NO: 193)
 EVOQLVQSGAEVKKPGASVKVSCKASGYTFPDYMMNWWVQAPGQGLEWMGDIDPNYGGTNYAQKF
 QGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARGALTDWGQGTMVTVSS

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(SEQ ID NO: 194)

EVQLVESGGGLVQPGRLSCTASGYTFPDYMMWVRQAPGKGLEWVGIDPNYGGTTYAASV

KGRFTISVDRSKSIAYLQMSSLKTEDTAVYYCTRGALTDWGQGTMVTVSS

(SEQ ID NO: 195)

EVQLVESGGGLVQPGRLSCTASGYTFPDYMMWVRQAPGKGLEWVGIDPNYGGTTYNASV

KGRFTISVDRSKSIAYLQMSSLKTEDTAVYYCARGALTDWGQGTMVTVSS

VH Sequences:

(SEQ ID NO: 196)

DIVMTQSHKLMSTSVGDRVSITCKASQDVGTAVAWYQQKPGQSPKLLIYWASTRHTGVPDFRTG

SGSGTDFTLTISNVQSEDLADYFCQQDSSYPLTFGAGTKVELK

(SEQ ID NO: 197)

DIVTTQSHKLMSTSVGDRVSITCKASQDVGTAVAWYQQKPGQSPKLLIYWASTRHTGVPDFRTG

SGSGTDFTLTISNVQSEDLADYFCQQDSSYPLTFGAGTKVELK

(SEQ ID NO: 198)

DIVMTQSPSSLAVSVEKVMGCKSSQSLLYSSNQKNSLAWYQQKPGQSPKLLIYWASTRHTGVPDFRTG

PDRFTGSGSGTDFTLTISSVKAEDLAVYYCQQYYGYPLTFGAGTKLELK

(SEQ ID NO: 199)

DIVMTQSPAAMSASPGEKVMTCSASSSIRYMWYQQKPGTSPKRWISDTSKLTSGVPARFSGS

GSGTSYALTISMEAEDAATYYCHQRSSYPWTFGGGTKEIK

(SEQ ID NO: 200)

QIVLSQSPAILSSASPGEKVMTCRASSSVSYIYWFFQQKPGSSPKPWIYATENLASGVPARFSGS

GSGTSYSLTISRVEDEAATYYCQQWSNNPLTFGAGTKLELK

(SEQ ID NO: 201)

EIVLTQSPATLSPGERATLSCRASSSVSYIYWFFQQKPGQAPRLLIYAAFN RATGIPARFSGS

GSGTDYTLTISSLEPEDFAVYYCQQWSNNPLTFGQGKVEIK

(SEQ ID NO: 202)

QIVLTQSPATLSPGERATLSCRASSSVSYIYWFFQQKPGQSPRPLIYATENLASGVPARFSGS

GSGTSYTLTISRLEPEDFAVYYCQQWSNNPLTFGQGKVEIK

(SEQ ID NO: 203)

DIQLTQSPSSLASVGDRVTITCRASSGVSYIYWFFQQKPGKAPKLLIYAAFN LASGVPSRFSGS

GSGTEYTLTISSLQPEDFATYYCQQWSNNPLTFGQGKVEIK

(SEQ ID NO: 204)

DIQLTQSPSSLASVGDRVTITCRASSGVSYIYWFFQQKPGKAPKPLIYAAFN LASGVPSRFSGS

GSGTEYTLTISSLQPEDFATYYCQQWSNNPLTFGQGKVEIK

(SEQ ID NO: 205)

DIQLTQSPSILSASVGDRVTITCRASSSVSYIYWFFQQKPGKAPKPLIYATE NLASGVPSRFSGS

GSGTSYTLTISRLEPEDFATYYCQQWSNNPLTFGQGKVEIK

[0197] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:

(SEQ ID NO: 206)

QVQLVQSGAEVKPGASVKVKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNYAQKL

QGRVTMTTDTSTSTAYMELRSLSDDTAVYYCARALPSGTILVGGWEDPWGQGTLVTVSS

- continued

(SEQ ID NO: 207)
EVQLVQSGGGVVQPGRSRLSCAASGFTFSSYALSWVRQAPGKLEWVSAISGGGSTYYADSV

KGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDVFPETFSMNYGMDVWGQGTLVTVSS

(SEQ ID NO: 208)
QVQLVQSGGGVVQPGGSRLSCAASGFTEDDYAMHWVRQAPGKGLEWVSLISGDGGSTYYADSV

KGRFTISRDNSKNSLYLQMNSLRTEDTALYYCAKVLPCSSTSCYGSVGAFDIWGQGTTVTVSS

(SEQ ID NO: 209)
QVQLVQSGGSVVRPGESLRLSCVASGFIFDNYDMWSVRQVPGKGLEWVSRVNNGGSTTYADAV

KGRFTISRDNTKNSLYLQMNNLRAEDTAVYYCVERFVGAYDLWGQGTTVTVSS

(SEQ ID NO: 210)
QVQLVQSGAEVKPGATVKVSKVFGDTFRGLYIHWRQAPGQGLEWMGGIIPIFGTANYAQKF

QGRVTITTDESTSTAYMELSSLRSEDTAVYYCASGLRWGIWGWFDPWGQGTLVTVSS

(SEQ ID NO: 211)
EVQLVQSGAELKKPGSSVKVSKAFGGTFSDNAISWVRQAPGQGLEWMGGIIPIFGKPNYAQKF

QGRVTITADESTSTAYMLVLSLRSEDTAVYYCARTMVRGFLGVMDVWGQGTTVTVSS

(SEQ ID NO: 212)
QVQLVQSGGLVQPGGSRLSCAASGFTFSSYAMSWSVRQAPGKGLEWVSAISGGGSTYYADSV

KGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDOFVTIPGVPRYGMVDVWGQGTTVTVSS

(SEQ ID NO: 213)
QVQLVQSGAEVKPGSSVKVSKASGGTFSSYAIWVRQAPGQGLEWMGGIIPIFGTANYAQKF

QGRVTITADKSTSTAYMELSSLRSEDTAVYYCARGRQMFAGIDFWGPGLTVTVSS

(SEQ ID NO: 214)
EVQLVESGAEVKKPGSSVKVSKVSGGTFGTYALNWVRQAPGQGLEWMGRIVPLIGLVNYAHNF

EGRISITADKSTGTAYMELSNLRSDDTAVYYCAREVYGGNSDYWGQGTLVTVSS

(SEQ ID NO: 215)
QVQLVQSGGEVKPGASVKVSKASGYTLSSHGIFTWVRQAPGQGLEWMGWISAHNGHASNAQKV

EDRVMTTDTSTNTAYMELRSLTADDTAVYYCARVHAALYYGMDVWGQGTLVTVSS

(SEQ ID NO: 216)
QVQLQESGGVVQPGRSRLSCASGFTFSRHMHWVRQAPGKGLEWVAVISHDSVKYYADSM

KGRESISRDNSNNTLYLQMDSLRADDTAVYYCARGLSYQVSGWFDPWGQGTLVTVSS

(SEQ ID NO: 217)
NEMLTQPHSVSESPGKTVTISCTRSGSIASNYVQWYQQRPGSSPTTVIYEDNQRPSGVPDFRS

GSIDTSSNSASLTISGLKTDEADYYCQSYDITVIFGGGKLTVL

(SEQ ID NO: 218)
NEMLTQPHSVSGSPGKTVTLPCTRSGSIASHYVQWYQQRPGSAPTTVIYEDNKRPSGVPDFRS

GSIDSSNSASLSISGLKTEDEADYYCQSYDSNRWVFGGGKLTVL

(SEQ ID NO: 219)
LPVLTQPASLSASPGASASLTCTLRSGLNVGSYRIYWYQQKPGSRPQYLLNYKSDSNKQQASGV

PSRFSGSKDASANAGILLISGLQSEDEADYYCMIWYSSAVVFGGGKLTVL

VL Sequences:
(SEQ ID NO: 220)

NEMLTQPHSVSESPGKTVTISCTRSGNIASNYVQWYQQRPGSAPTTVIYEDNQRPSGVPDFRS

GSIDSSNSASLTISGLKTEDEADYYCQSYDSNLWVFGGGKLTVL

(SEQ ID NO: 221)
SSELTDQPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLIYGKNRPSGIPDRFSGS

SSGNTASLTITGAQAEDAYYCNSRDSSGNHYVPGTGTKTVL

- continued

(SEQ ID NO: 222)
LPVLTQAPSJVAPGKTARITCGGSDIGRKSVHWYQQKPGQAPALVIYSDRDRPSGISERFSGS

NSGNTATLTISRVEAGDEADYYCQVWDNNSDHYVFGAGTELIVL

(SEQ ID NO: 223)
QSALTQPAVGSPGQSICTGTSSDVGYYNYVSWYQQHPGKAPKLMYDVSNRPSGVSNRF

SGSKSGNTASLTISGLQAEDADYYCSSYTSTLPPGGTQLTVL

(SEQ ID NO: 224)
EIVLTQSPATLSLSPGERATLSCRASQSIGNSLAWYQQKPGQAPRLLMYGASSRATGIPDRFSG

SGAGTDFTLTISLEPEDFATYYCQQHTIPTFSFGPGTKVEVK

(SEQ ID NO: 225)
DIVMTQTPSFLSASIGDRVVTICRASQGIGSYLAWYQQRPGEAPEKLLIYAASTLQSGVPSRFSG

SGSGTDFTLTISNLQPEDFATYYCQQLNNYPITFGQGTRLEIK

(SEQ ID NO: 226)
QSALTQPPSVSPGQTANIPCGDKLGKAYWYQQKPGQSPVLLIYQDIKRPSRIPERFSGS

NSADTATLTISGTQAMDEADYYCQTWDNSVVFGGGTQLTVL

(SEQ ID NO: 227)
NFMLTQPHSVSESPGKTVTISCTRSGSIDSNVQWYQQRPGSAPTTVIYEDNQRPSGVPDFRS

GSIDSSNSASLTISGLKTEDADYYCQSYDSNNRHVIFGGGTQLTVL

(SEQ ID NO: 228)
NEMLTQPHSVSESPGKTVTISCTRSGNIGTNVQWYQQRPGSAPVALIYEDYRRPSGVPDFRS

GSIDSSNSASLIISGLKPEDADYYCQSYHSSGWFFGGTQLTVL

(SEQ ID NO: 229)
QSVLTQPPSVAPGQTARITCGNNIGSKGVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGS

NSGNTATLTISRVEAGDEADYYCQVWDSSDHVVEGGGTQLTVL

(SEQ ID NO: 230)
NEMLTQPHSVSESPGKTVTISCTRSGSIASNYVQWYQQRPGSAPTTVIYEDNQRPSGVPDFRS

GSIDSSNSASLTISGLKTEDADYYCQSYDSTTPSVFGGGTQLTVL

(SEQ ID NO: 231)
QVQLVQSGAEVKPGASVKVSKASGYTFTSYGISWVRQAPGQGLEWMGWTSPHNGLTAFQIL

EGRVTMTDTSTNTAYMELRNLTDDTAVYFCAKVHPVFSYALDVWGQGTLTVSS

(SEQ ID NO: 232)
EVQLVESGAEVMPNGSSVRVSCRGSGDFSTYAFSWVRQAPGQGLEWMGRIIPILGIANYAQKF

QGRVTITADKSTSTAYMELSSLRSDDTAVYYCARDGYGSDPVLWGQGTLTVSS

(SEQ ID NO: 233)
EVQLVQSGAEVKPGASVKVSKASGYTFTNYGISWVRQAPGQGLEWMGWISAYNGNTNYAQKV

QGRVTMTDTSTGYMELRSDDTAVYYCARGDFRKPPDYWGQGTLTVSS

[0198] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:

(SEQ ID NO: 234)
EVQLVQSGPELKPGASVKMSCKASGYTFTSYVMHWVKQAPGQRLEWIGY

VNPENDGTKYNEMFKGRTLSDKSTSTAYMELSSLRSEDAVYYCARQA

WGYPWGQGTLTVSS

- continued

(SEQ ID NO: 235)
EVQLVOSGAEVKKPGASVKMSCKASGYTFTSYVMHWVKQAPGQRLEWIGY

VNPENDGTKYNEMFKGRTLSDKSTSTAYMELSSLRSEDTAVYYCARQA

WGYPWGQGTLTVSS

(SEQ ID NO: 236)
EVQLVQSGAEVKPGASVKMSCKASGYTFTSYVMHWVKQAPGQRLEWIGY

VNPENDGTKYNEMFKGRTLSDKSTSTAYMELSSLRSEDTAVYYCARQA

WGYPWGQGTLTVSS

-continued

(SEQ ID NO: 237)

EVQLVQSGAEVKPGASVKVSCKASGYTFTSYVMHWRQAPGQRLEWIGY
VNPNEDGTKYNEFMKGRATLSDKSTSTAYMELSSLRSEDTAVYYCARQA
WGYPWGQGTLVTVSS

(SEQ ID NO: 238)

EVQLVQSGAEVKPGASVKVSCKASGYTFTSYVMHWRQAPGQRLEWIGY
VNPNEDGTKYNEFMKGRATLSDKSTSTAYMELSSLRSEDTAVYYCARQA
WGYPWGQGTLVTVSS

VL Sequences:

(SEQ ID NO: 239)

DIVLTQSPASLALSPGERATLSCRATESVEYYGTSLVQWYQQKPGQPPKL
LIYAASSVDSGVPSRFSGSGSGTDFTLTINSLEEDAAMYPCQQSRRVY
TFGQGTTKLEIK

(SEQ ID NO: 240)

DIVLTQSPATLSLSPGERATLSCRATESVEYYGTSLVQWYQQKPGQPPKL
LIYAASSVDSGVPSRFSGSGSGTDFTLTINSLEEDAAMYPCQQSRRVY
TFGQGTTKLEIK

(SEQ ID NO: 241)

EIVLTQSPATLSLSPGERATLSCRATESVEYYGTSLVQWYQQKPGQPPKL
LIYAASSVDSGVPSRFSGSGSGTDFTLTINSLEEDAAMYPCQQSRRVY
TFGQGTTKLEIK

(SEQ ID NO: 242)

DIVLTQSPATLSLSPGERATLSCRATESVEYYGTSLVQWYQQKPGQPPKL
LIYAASSVDSGVPSRFSGSGSGTDFTLTINSLEEDAATYPCQQSRRVY
TFGQGTTKLEIK

[0199] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of.

VH Sequences:

(SEQ ID NO: 243)

EVQLVQSGAEVKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGL
EWMGGIIPIFGTANYAQKFQGRVTITADKSTSTAYMELSSLRSED
TAVYYCAREGTIYDSSGYSFDYWQGTLVTVSS

(SEQ ID NO: 244)

EVQLVQSGAEVKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGL
EWMGGIINPSGGSTSYAQKFQGRVSMTRDTSTSTVYMELSSLTSED
TAVYYCARDLFPHIYGNYYGMDIWQGTTTVSS

(SEQ ID NO: 245)

EVQLVQSGAEVKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGL
EWMGGIIPIFGTANYAQKFQGRVTITADKSTSTAYMELSSLRSED
TAVYYCARLAVPGAFDIWGQGTMVTVSS

-continued

(SEQ ID NO: 246)

EVQLVESGGVVQPGRLRLSCAASGFTFSSYAMHWVRQAPGKG
AVISYDGSNKYYADSVKGRFTISRDNKNTLYLQMNSLRaedTAV
YYCARGQWLVTTELWDYWGQGTLVTVSS

(SEQ ID NO: 247)

EVQLVESGSEVEKPGSSVKVSCKASGGTFSDSGISWVRQAPGQGL
EWMGGIIPMFATPYYAQKEQDRVTITADESTSTVYMELSGLRSD
TAVFYCARDRGRGHLPWYFDLWGRGTLVTVSS

(SEQ ID NO: 248)

EVQLVESGAEVKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGL
EWMGGIIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSED
TAVYYCARAPYYYYYMDVWQGTTTVSS

(SEQ ID NO: 249)

EVQLLESGAEVKPGSSVKVSCKASGGTLSRYALSWVRQAPGQGP
EWVGAIPIIFGTPHYSKKFQDRVITITVDTSTNTAFMELSSLRFED
TALYFCARGHDEYD1SGYHRLDYWGQGTLVTVSS

(SEQ ID NO: 250)

QVQLVQSGSELKKPGSSVKVSCKASGGTSFGYYIHWRQAPGQGL
EWMGWIDPNSGVTNVRRFQGRVTITMRTDSLSTAYMELSGLTADD
TAVYYCARDENLWQFGYLDYWQGTLVTVSS

(SEQ ID NO: 251)

QVQLVQSGAEVKPGSSVKVSCKASGGTSRYGVHWVRQAPGQGL
EWMGRLIPIVSMNTNYAQKFQDRVSITTDKSTGTAYMELRSLTSED
TALYCCASVGQQLPWVFFAWQGTLVTVSS

(SEQ ID NO: 252)

QVQLVESGGVVQPGRLRLSCAASGFTFSSYAMHWVRQAPGKG
EWVAVIDESGSNKYYADSVKGRFTISRDNKNTLYLQMNSLRTED
TAVYYCARGWLDRDIDYWQGTLVTVSS

(SEQ ID NO: 253)

EVQLVESGGVVQPGRLRLSCAASGFTFSSYAMHWVRQAPGKG
EWAVAVIDESGSNKYYADSVKGRFTISRDNKNTLYLQMNSLRTED
TAVYYCARGWLDRDIDYWQGTLVTVSS

(SEQ ID NO: 254)

EVQLVQSGGGLVQPGSLRLSCAASGFTFSYDGMHWVRQAPGKG
EWLAVISYDGSYKIHADSVQGRFTISRDNAKNSVPLQMNLSKTED
TAVYYCTTDRKWLAHGMDDVWQGTTTVSS

(SEQ ID NO: 255)

EVQLVQSGAEVKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGL
EWMGGIIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSED
TAVYYCARDGIVADFQHWGQGTLVTVSS

(SEQ ID NO: 256)

EVQLVESGAEVKPGASVKVSCKASGDTFSRYGITWVRQAPGRGL
EWMGNIPFFGATNYAQKEQGRLTITADKSSYTSMYLSSLRSD
TAVYYCARDHFYGSGGYFDYWQGTLVTVSS

- continued

(SEQ ID NO: 257)

EVQLLESGAEVKKPGASVKVSKASGYTFMSYDINWVRQAPGQGL
 EWMGGIIPVFGTANYAESFOGRVTMTADHSTSTAYMELNNLRSED
 TAVYYCARDRWHYESRPMDVWGQGTTVTVSS

(SEQ ID NO: 258)

EVQLVESGGGLVRPGGSLRLACAASGESFSYDYYMTWIRQAPGRGL
 EWIAYISDSGQTVHYADSVKGRFTISRDNKNSLFLQVNTLRAED
 TAVYYCAREDLLGYYLQSWGQGTLTVSS

(SEQ ID NO: 259)

QVQLQQSGPGLVKPSQTLSLTCIAISGDSVSSNSAAWNWIRQSPSR
 GLEWLGRRTYYRSKWNDYAVSVKSRSITINPDTSKNQFSLQLNSVT
 PEDTAVYYCARDEPRAVAGSQAYYYYGMDVWGQGTTVTVSS

(SEQ ID NO: 260)

EVQLVQSGAEVKKPGASVKVSKASGYTFTSYMMHWVRQAPGQGL
 EWMGIINPSDGSTSAYQKFQGRVTMTRDTSTVHMELESSLRSED
 TAVYYCARDLFPHIYGNYYGMDIWGQGTTVTVSS

(SEQ ID NO: 261)

QMQLVQSGGGVVQPGRSRRLSCAASGFTFSSYAMHWVRQAPGKGL
 EWVAVISEDGSNKYYADSVRGRFTISRDN SKNTLYLQMNSLRTED
 TAVYYCARGWLDRDIDYWQGQGTLTVSS

(SEQ ID NO: 262)

QVQLVQSGGGVVQPGRSRRLSCAASGFTFSSYAMHWVRQAPGKGL
 EWVAVISEDGSNKYYADSVRGRFTISRDN SKNTLYLQMNSLRTED
 TAVYYCARGWLDRDIDYWQGQGTLTVSS

VL Sequences:

(SEQ ID NO: 263)

QSVLTQPPSVSAAPGQKVТИCSGNNSNIANNYVSWYQQLPGTAP
 KLLIYDNNYRPSGIPDRESGSKSGTSATLDITGLQTGDEADYYCG
 VWDGSLTTGVFGGGTKLTVL

(SEQ ID NO: 264)

AIQMTQSPSSL SASVGDRVТИCRASQGISNYLAWYQQPGKVKP
 LLIYAASL ESGVPSRESGSGSGTDFTLTISSLQPEDLATYYCQQ
 LHTFPPLTFGGGKVEIK

(SEQ ID NO: 265)

QPVLTQPPSASGSPGQSVTISCTGTSSDVGAYNFVSWYRQHPGKA
 PKLMYEVNKRPSGVPDFRSGSKSGNTASLT VSGLQAEDEADYYC
 SSYAGTNSLGIFGTTKLT

(SEQ ID NO: 266)

QSVVTQPPSVSAAPGQKVТИCSGSSSDIGNHYVSWYQQLPGTAP
 KLLIYDNNQRPSGIPDRESGSKSGTSATLAITGLQTGDEADYYCG
 TWDNSLSPHLLFGGGTKLTVL

(SEQ ID NO: 267)

QSVLTQPPSVSAAPGQKVТИCSGSSSNMGNNYVSWYKQVPGTAP
 KLLIYENDKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYCG
 TWDNSLSGFVFASGTTKLT

- continued

(SEQ ID NO: 268)

QSALTQPPASVSGSGQSVTISCTGTSSDVGSYNLVSWYQQHPGKA
 PNLMYDVSKRSGVSNRESGSKSGNTASLTISGLQAEDEADYYC
 SYTGISTVVFGGGTKLTVL

(SEQ ID NO: 269)

QSVLTQPPASVSGSPGQSVTISCTGTSSDVGSYNLVSWYQQHPGKA
 PKLMYEVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYC
 SSYGGENNLLFGGGTKLTVL

(SEQ ID NO: 270)

DIVMTQSPSSL SASIGDRVТИCRASQRI SAYVNWYQQPGKAP
 VLIYAASSLRSRGVPSRESGSGSGTDFTLTISSLQPEDFATYYCQQ
 TYSSPWTFGQGKVEIK

(SEQ ID NO: 271)

QSVLTQPPSASGSPGQSVTISCTGTSSDVGSYNLVSWYQQHPGKA
 PKLMYDVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYC
 SSYTSSSIFFYVFGTGT

(SEQ ID NO: 272)

LPVLTQPPASVSGSPGQSVTISCTGTSSDVGSYNLVSWYQQHPGKA
 PKLMYDVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYC
 SSYTSSSTHVFGTGT

(SEQ ID NO: 273)

QSALTQPPASVSGSPGQSVTISCTGTSSDVGSYNLVSWYQQHPGKA
 PKLMYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYC
 SSYRSSSTLGPVFGGGTKLTVL

(SEQ ID NO: 274)

QAGLTQPPSVSEAPRQRVТИCSGSSSNIGNNAVNWYQQLPGTAP
 KLLIYDDLLPSGVSDRESGSKSGTSASLAISGLQSEDEADYYC
 AWDDSLNGYVFGTGT

(SEQ ID NO: 275)

QSALTQPRSVSGSPGQSVTISCTGTSSDVGSYNLVSWYQQHPGKA
 PKLMYDVSKRPSGVPDFRSGSKSGNTASLTISGLQAEDEADYYC
 SSYTSSTTHVFGTGT

(SEQ ID NO: 276)

QSVVTQPPSVSAAPGQKVТИCSGSSSNIGNNYVSWYQQLPGTAP
 KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYCG
 TWDSSLSVWVFGGGT

(SEQ ID NO: 277)

QSVLTQPPASVSGSPGQSVTISCTGTSSDVGSYNLVSWYQQHPGKA
 PRLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEGDYYC
 SSYTSGGTLGPVFGGGTKLTVL

(SEQ ID NO: 278)

QAGLTQPPSASGTPQGRVTICSGSSSNIGSNTNVNWYQQLPGTAP
 KLLIYNNQRPSGVPDFRSGSKSGTSASLAISGLQSEDEADYYC
 AWDDSLNGWVFGGGTKLTVL

-continued

(SEQ ID NO: 279)

AIRMTQSPSSLSASVGDRVITICRASQSIISNYLNWYQQRPGKAPN
LLIYAASSLQSGVPSRESGSGSGTDFTLTISSLQPEDFATYYCQQ
TYSTPYTFGGTKLEIK

(SEQ ID NO: 280)

QSVLTQPASVGSPGQSIITISCTGTSSDVGGYNVSWYRQHPGKA
PKLMIYDVSYRPGSVSNRFSGSKSGNTASLTISGLQAEDEADYYC
SSYTDSSTRYVFVFGTGTKLTVL

(SEQ ID NO: 281)

QPVLTQPPSASGTPGQRVIAISCGSRNSIEINSVNWYQQLPGTAP
KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYCG
SWDSSLADVEGTGTKLTVL

(SEQ ID NO: 282)

QSVLTQPPSVAAAPGKKVTISCGSSSNIGNNYVSWYQQLPGTAP
KLLIYRNNQRPSGVDPRESGSKSGTSASLAIISGLQSEDEADYYCA
TWDDSLNGWVFGGGTKLTVL

(SEQ ID NO: 283)

QSVVTQPPSVSGAPGQRTVISCTGSSSNIGAGYDVHWYQQLPGT
PKLLIYGNNNRHSGVPDRESGSKSGTSASLAIITGLQAEDEAEFFC
GTWDSRLTTVFGSGTKLTVL

(SEQ ID NO: 284)

QSVVTQPPSVAAAPGQKVITISCGSSSNIGNNYVSWYQQLPGTAP
KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYCG
TWDSLSSAVVFGGGTKLTVL

(SEQ ID NO: 285)

VIWMTQSPSSLSASVGDRVITICAASSLQSWYQQKPGKAPKLLIY
EASTLESGVPSRFSGSGSGTEFTLTISLQPEDFATYYCQQSYST
PYTFGGTGTLEIK

(SEQ ID NO: 286)

QSVVTQPPSVAAAPGQKVITISCGSSSNIGNNYVSWYQQVPGTAP
KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYCG
TWDSLSSAVVFGGGTKLTVL

(SEQ ID NO: 287)

QSVVTQPPSVAAAPGQKVITISCGSSSNIGNNYVSWYQQLPGTAP
KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYCG
TWDSLSSAGSVVFGGGTKLTVL

(SEQ ID NO: 288)

SYELMQPPSVVAPGKTATIACGGENIGRKTVHWYQQKPGQAPVL
VIYYDSDRPSGIPERFSGNSGNATLTISRVEAGDEADYYCLVW
DSSSDHRIFFGGTKLTVL

(SEQ ID NO: 289)

SYELMQPPSVVAPGKTATIACGGENIGRKTVHWYQQKPGQAPVL
VIYYDSDRPSGIPERFSGNSGNATLTISRVEAGDEADYYCQWV
DSSSDHRIFFGGTKLTVL

-continued

(SEQ ID NO: 290)

SYELMQPPSVVAPGKTATIACGGENIGRKTVHWYQQKPGQAPVL
VIYYDSDRPSGIPERFSGNSGNATLTISRVEAGDEADYYCQWV
DSSSDHRIFFGGTKLTVL

(SEQ ID NO: 291)

SYELMQPPSVVAPGKTATIACGGENIGRKTVHWYQQKPGQAPVL
VIYYDSDRPSGIPERFSGNSGNATLTISRVEAGDEADYYCQWV
DSSSDHRIFFGGTKLTVL

[0200] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a heavy chain (HC) and a light chain sequence (LC) selected from the group consisting of:

HC Sequences:

(SEQ ID NO: 292)

QVQLVQSGVEVKPGASVKVSCKASGYTFTNYYMWVRQAPGQGL
EWMMGGINPSNGGTNFNEKFKNRVTLLTDSTTAYMELKSLQFDD

TAVYYCARRDYRFDMGFDYWGQGTTVSSASTKGPSVFPALCPS

RSTSESTAALGCLVKDYLFPPEPVTVSWNSGALTSGVHTFPAVLQSS

GLYSLSSVTVPSLGLTAKTTCNVNDHKPSNTKVDKRVESKYGPP

CPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQED

PEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLWN

GKEYKCKVSNKGLPSSIEKTISKAKGQPREPVYTLPPSQEEMTK

NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFF

LYSRLTVDKSRWQEGNVFSCSVMEHALHNHYTQKSLSLSGK

(SEQ ID NO: 293)

QVQLVESGGVVQPGRLRLDKASGITFNSGMHWVRQAPGKGL

EWAVAVIYDGSKRYYADSVKGRFTISRDNSKNTLFLQMNSLRAED

TAVYYCATNDDYWQGTLTVVSSASTKGPSVFPALPCSRSTSEST

AALGCLVKDYLFPPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS

VVTPVSSSLGKTYTCNVNDHKPSNTKVDKRVESKYGPPCP

EFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW

YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK

VSNKGLPSSIEKTISKAKGQPREPVYTLPPSQEEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLTV

DKSRWQEGNVFSCSVMEHALHNHYTQKSLSLSGK

LC Sequences:

(SEQ ID NO: 294)

EIVLTQSPATLSLSPGERATLSCRASKGVSTSGSYLHWYQQKPG

QAPRLLIYLASYLESQVPARFSGSGSGTDFTLTISSLEPEDFAVY

YCQHSRDLPLTFGGTKEIKRTVAAPSFIGPPSDEQLKSGTAS

VVCLLNNFYPREAKVQWKVDNALQSGNSQEVTEQDSKDSTYSLS

STLTLSKADYEKHKVYACEVTHQGLSSPVTKSENRCGEC

- continued

(SEQ ID NO: 295)

```
EIVLTQSPATLSLSPGERATLSCRASQS VSSYLA WYQQKPGQAPR  
LLIYDASNRATGIPARESGSGSGTDFLTISLEPEDFAVYYCQO  
SSNPWRTFGQGTKVEIKRTVAAPS FIFPPSDEQLKSGTASVVCL  
LNNFYFPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT  
LSKADYEKHKVYACEVTHQGLSPVTKSEN RGE C
```

[0201] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:

(SEQ ID NO: 296)

```
EVQLVESGGLVQPGGSLRLSCAASGFTFSDSWIH WVRQAPGKGL  
EWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAED  
TAVYYCARRHWPGGF DYWGQGTLTVSSASTK
```

(SEQ ID NO: 297)

```
EVQLVESGGLVQPGGSLRLSCAASGFTFSDSWIH WVRQAPGKGL  
EWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAED  
TAVYYCARRHWPGGF DYWGQGTLTVSS
```

HC Sequences:

(SEQ ID NO: 298)

```
EVQLVESGGLVQPGGSLRLSCAASGFTFSDSWIH WVRQAPGKGL  
EWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAED  
TAVYYCARRHWPGGF DYWGQGTLTVSSASTKGP SVEPLAPSSKS  
TSGGTAALGCLVKD YFPEPPTVWSN GALTSGVHTFP AVLQSSGL  
YSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVKD KVEPKSCDKTH  
TCPPCPAPELLGGPSVFLFPPKP KDTLMISRTP ETCVV DV SHE  
DPEVKFNWY WDGV EHVNAKTKP REEQYASTYRVV SVLTVLHQDWL  
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMT  
KNQVSLTCLVKGFYPS DIAV EWE SNGQ PENNYK TTPPVLD SDGSF  
FLYSKLTVDKSRWQQGNVFCS VMHEALHNHYTQKSLSLSPG
```

VL Sequences:

(SEQ ID NO: 299)

```
DIQMTQSPSSLSASVGDRVTITCRASQDV STAVAWYQQKPGKAPK  
LLIYSASFLYSGVPSRFSGSGSGTDFLTISSLQPEDFATYYCQO  
YLYHPATFGQGTKVEIKR
```

LC Sequences:

(SEQ ID NO: 300)

```
DIQMTQSPSSLSASVGDRVTITCRASQDV STAVAWYQQKPGKAPK  
LLIYSASFLYSGVPSRESGSGSGTDFLTISSLQPEDFATYYCQO  
YLYHPATFGQGTKVEIKRTVAAPS FIFPPSDEQLKSGTASVVCL  
LNNFYFPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT  
LSKADYEKHKVYACEVTHQGLSPVTKSEN RGE C
```

[0202] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or

antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:

(SEQ ID NO: 301)

```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSRFMSWVRQAPGKGL  
EWVANIQDGTEKYYDSVKG RTFTISRDNAKNSLYLQMNSL RAGD  
TAVYYCANTYYDFWSGHFDYWGQGTLTVSS
```

(SEQ ID NO: 302)

```
QEHLVESGGGVVQPGRSRLSCAASGFTFSNFGMHWVRQAPGKGL  
EWVAALWSDGSNSKYYADSVKGRFTISRDNSKNTLYLQMNSL RAE  
TAVYYCARGRGAPGIPIFGYWGQGTLTVSS
```

(SEQ ID NO: 303)

```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSNAWMSWVRQAPGKGL  
EWVGRIKRKT DGGTTDYAAPVKG RTFTISRDNSKNTLHLQMNSL K  
EDTAVYYCTTDDIVVVPAVMREYYFGMDVWGQGTTVSS
```

(SEQ ID NO: 304)

```
QVQLVQSGAEVKKPGASVQVSCKASGYSFTGYYIH WVRQAPGQGL  
EWMGWINPNSGT KKYAHKFQGRVTMTRDT SISD TAYMILSSLISDD  
TAVYYCARDEDWNFGSWFDSWQGTLTVSS
```

(SEQ ID NO: 305)

```
QVHLVQSGAEVKKPGASVKSCKASGYTFGTGYYIH WVRQAPG HGL  
EWMGWLNPNTGTTKYIQN FQGRVTMTRDTSS STAYMELTRLR SDD  
TAVYYCARDEDWNFGSWFDTWGQGTLTVSS
```

(SEQ ID NO: 306)

```
EVQLVESGGGVVRPGGSLRLSCAASGFTFDDYGM ITWVRQAPGR GL  
EWVSGIHW HGKRTG YADSVKGRFTISRDNAKSLY LQMNSL KGED  
TALYHCVRGGMSTGDWEDPWGQGTLVIVSS
```

(SEQ ID NO: 307)

```
EVQLVESGGGVVRPGGSLRLSCAASGFTTEDDYGM ITWVRQAPV PGKGL  
EWVSGIHW SGRTG YADSVKGRFTISRDNAKNSLYLQMNSL RAE  
TALYCCARGGMSTGDWEDPWGQGTLVIVSS
```

(SEQ ID NO: 308)

```
EVQLVESGGGLVQPGGSLRLSCAASGFTVGS NYMNWVRQAPGKGL  
EWVSVIYSGGSTYYADSVKGRFTISRLTSKNTLYLQMSSLR PEDT  
AVYYCARGIRGLD VWGQGTTVSS
```

(SEQ ID NO: 309)

```
EE RLVESGGDLVQPGGSLRLSCAASGFTVGTNYMNWVRQAPGKGL  
EWVSVIYSGGNT HYADSVKGRFIMS QTSKNTLYLQMNSL ETE DT  
AVYYCARGIRGLD VWGQGTTVSS
```

(SEQ ID NO: 310)

```
QVQLVQSGAEVKKMPGSSVRVSKASGGIFSS STISWVRQAPGQGL  
EWMGEIIPVFGTVNYAQKFQDRVIFTADESTTTAYMELSSLK SGD  
TAVYFCARNWGLGSFYIWGQGTMVTVSS
```

- continued

(SEQ ID NO: 311)

EVQLVESGGDLVHPGRSLRLSCAASGFPFDEYAMHWVRQPGKGL
EWVSGISWSNNNIGYADSVKGRFTISRDNAKNSLYLQMNSLRPED
TAFYYCAKSGIFDSDWGQGTLTVSS

(SEQ ID NO: 312)

EVQLVESGGVVQPGRSRSLRLSCAASGFTFSSYGMHWVRQAPGKGL
EWVTLSIYEGRNKYYADSVKGRFTISRDNASKNTLYLQMNSLRAED
TAVYYCAKDRTLYGMDVGQGTTVTVSS

(SEQ ID NO: 313)

QVTLRESPALVKTTQTLTCTFSGESLSTNRMCVTWIRQPPKG
ALEWLARIDWDGVKYYNTSLKTRLTISKDTSKNQVVLMTNMDPV
DTATFYCARSTSLLTFYYFDYWGQGTLTVSS

(SEQ ID NO: 314)

EVQLVESGGGLVQPGGSLRLSCAASEFTVGTNHMNWVRQAPGKGL
EWVSVIYSGGNTFYADSVKGRFTISRHTSKNTLYLQMNSLTAEDT
AVYYCARGLGGMGVWGQGTTVTVSS

(SEQ ID NO: 315)

EVQLVESGGLVQRGESLRLYCAASGFTFSKYWMNWVRQAPGKGL
EWVANIKGDSEKYYVDSVKGRTISRDNAKNSLYLQMNSLRAED
TAVYYCARDYWGSYYFDFWGQGTLTVSS

(SEQ ID NO: 316)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYMSWVRQAPGKGL
EWVANIKQDGSEKYYVDSVKGRTISRDNAKNSLYLQMNSLRAADD

TAVYYCARDDIVVVPPAPMGYYYYYFGMDVGQGTTVTVSS

(SEQ ID NO: 317)

EVQLVESGGGLVQPGGSLRLSCAASGFTFDDFAMHWVRQAPGKGL
EWVSGISWTGGNMDYANSVKGRTISRDAKNSLYLQMNSLRAAD
TALYYCVKDIRGIVATGGAPDIWGRGTMVTVSS

(SEQ ID NO: 318)

EVQLVESGGLVQPGGSLRLSCAASGFTVGTNYMNWVRQAPGKGL
EWISVIYSGGNTFYADSVKGRFTISRQTSQNTLYLQMNSLRPEDT
AVYYCARGIRGFDIWGQGTMVTVSS

(SEQ ID NO: 319)

EVQLVESGGLVQPGGSLRLSCAASGFTISTNYMNWVRQAPGKGL
EWVAVIYSSGTYIDSVDVKGRTISRRLTSKNTVYLQMSSLNSEDT
AVYYCARGIRGFDIWGQGTMVTVSS

(SEQ ID NO: 320)

EVQLVESGGGLVQPGGSLRLSCAASGFTIDDSAMHWVRQTPGKGL
EWVSGISWKSGSIGYADSVRGRFTISRDNAKNSLYLQMNSLRVED
TALYYCVKDIRGNWNYGGNWEDPWGQGTLTVSS

(SEQ ID NO: 321)

EVQLVESGGLVQPGGSLRLSCEASGFTVGVNHNWVRQAPGKGL
EWVSIVFSSGRTFYGYDVKGRLTIPQTSQNTVYLQMNSLRSEDT
AIYYCARGIGGLDIWGRGTMVTVSS

- continued

(SEQ ID NO: 322)

EVQLVESGGGLVQPGRSRSLSCAASGFTFDDYALHWVRQAPGKGL
EWVSGISWTGGTIDYADSVKGRFTISRDNAKNSLYLQMSSLRTED
TAIYYCTRDIRGNWKYGGWDPWGQGTLTVSS

(SEQ ID NO: 323)

QVQLVQSGTEVKPGASVKVSCKASGYTFAYYMHWVRQAPGQGL
DWMGWISPNSGFTNYAQKFQGRVTMTRDTSINTFYMELGLRSDD
TAVYYCAREGSTHNSFDPWGQGTLTVSS

(SEQ ID NO: 324)

EVQLVESGGGLVQPGGSLRLSCAASGFTVGTNFNMNWVRQAPGKGL
EWVSAIYSGGTANYADSVKGRFTISRDTSRNTLYLQMNSLRTEDT
AVYYCARGGGMDVGQGTTVTVSS

(SEQ ID NO: 325)

QVQLVQSGAEVKPGGSVVKVSCKASGGTFNTYVLSWVRQAPGQGL
EWMGEIIPILGAANYAQNQFQGRVTFTDESTNTAYMDLSSLRSED
TAVYYCARDRTSGFDPWGQGTLTVSS

(SEQ ID NO: 326)

QVQLVQSGAEVEKPGASVKVSCKASGYIFTYHGISWVRQAPGQGL
EWVGWISPYNGYTDYAQKLQGRVTLLTDSTTTAYMELRNLRSED
TAMYYCSRGGRGPYWSFDLWGRGTLTVSS
VL Sequences:

(SEQ ID NO: 327)

DIQMTQSPSTLSASVGDRVITTCRASQSIISNWLAWYQQKPGKAPK
LLIYKASSLESGVPSRFSGSGSGTEFTLTISLQPDDFATYYCQQ
YHSYSYTFQGQTKIEIK

(SEQ ID NO: 328)

DIQMTQSPSSLSASVGDRVITTCRASQGIIRNDLGWYQQKPGKAPK
RLIYTASSLQSGVPSRESGSGSGTEFTLTISLQPEDFATYYCLQ
HNSYPLTFGGGTKVAIK

(SEQ ID NO: 329)

DIQMTQSPSSLSASVGDRVITTCRTSQGIIRNDLGWYQQKPGKAPK
RLIYAASSLQSGVPSRFSGSGSGTEFTLTISLQPEDFATYYCLQ
HNNYPYTFQGQTKLEIK

(SEQ ID NO: 330)

DIVMTQTPLSSPVTLGQPASISCRSSQTLVHGDGNTYLSWIQQRP
GQPPRLLIYKVSNQFSGVPDRFSGSGAGTDFTLKISRVEAEDVGL
YFCMQATHEPITFGQGTRLEIK

(SEQ ID NO: 331)

DIVMTQTPLSSPVTLGQPASISCRSSPSLVHSDGNTYLSWLQQRP
GQPPRLLIYKISNRFSGVPDFRSGSGAGTDFTLKISRVEAEDVGV
YYCMQATHFPITFGQGTRLEIR

(SEQ ID NO: 332)

DIQMTQSPSSLSASLGDRVITTCRASQSIISYLNWYQQKPGKAPK
LLIYVASSLQSGVPSRFSGSGSGTEFTLTISNLQPEDFATYYCQQ
SYSTPPITFGQGTRLEIK

-continued

(SEQ ID NO: 333)
DIQMTQSPSSLSASVGDRVITCRASQSISSYLNWYQQKPGKAPK
LLIYVASSLQSGVPSRSGSGSGTDFTLTISSLQPEDFATYYCQQ
SYSTPPITFGQGTRLEIK
(SEQ ID NO: 334)
DIQMTQSPSSLSASVGDRVITCRASQTINIYLWYQQKPGRAPR
LLIYAASSLQSGVPSRESGSMSGTDFTLTISSLQPEDFATYYCHQ
SYSTPPITFGQGTRLEIK
(SEQ ID NO: 335)
DIQMTQSPSSLSASVGDRVITCRASQSMSSYLNWYQQKPGRAPK
LLIFIAASSLQSGVPSRESGSMSGTDFTLTISSLQPEDFATYYCQQ
SYSTPPITFGQGTRLEIK
(SEQ ID NO: 336)
EIVLTQSPGTLSSLSPGERATLSCRASQSFNFNYLAWYQQKPGQAP
RLLIYGAASSRATGIPDRESGSMSGTDFTLTINRLEPEDFGVFYCO
QYESAPWTFGQGKVEIK
(SEQ ID NO: 337)
DIQMTQSPSSLSASVGDRVITCRASQSISSYLNWYQQKPGKLII
YAASSLQSGVPSRESGGSGTDFTLTISSLRPEDFATYYCQQSYC
TPPIITFGQGTRLEIK
(SEQ ID NO: 338)
DIQMTQSPSSLSASVGDRVITCRASQSISSYLNWYQQKPGKAPK
LLIYAASSLQSGVPSRESGSMSGTDFTLTISSLQPEDFATYYCQQ
SYSTPPITFGQGTRLEIK
(SEQ ID NO: 339)
DRVITCRASQVISNYLAWYQQKPGKVPRLLIYAASSTLQSGVPSR
FSGSGSGTDFTLTISSLQPEDFATYYCQKYNASPRTFGQGKVEI
K
(SEQ ID NO: 340)
DIQMTQSPSSLSASVGDRVITCRASQNIINNYLNWYQQKPGKAPK
LLIYAASSFQNAVPSRESGSMSGTDFTLTISSLQPEDFATYYCQQ
SYNTPLTFGGGTKEIK
(SEQ ID NO: 341)
DIQMTQSPSSLSASVGDRVITCRASQGIRNDLGWYQQKPGKAPK
RLIYAASSLQSGVPSRSGSGSGTEFTLTISSLQPEDFATYYCLQ
HNSPYTFGGTKLEIK
(SEQ ID NO: 342)
DIQMTQSPSSLSASVGDRVITCRASQSISSYLNWYQQKPGKAPK
LLIYAASSLQSGVPSRSGSGSGTDFTLTISSLQPEDFATYYCQQ
SYSTPPITFGQGTRLEIK

[0203] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of.

VH Sequences:
(SEQ ID NO: 343)

QSLEESGGRLVKPDETLTITCTVSGIDLSSNGLTWRQAPGEGLE

WIGTINKDASAYYASWAKGRLTISKPSSTKVDLKITSPTTEDTAT

YFCGRIAFKTGTSIWPGPTLTVSS

VL Sequences:
(SEQ ID NO: 344)

AIIVMTQTPSPVSAAVGGTVTINCQASESVYSNNYLSWFQQKPGQP

PKLLIYLASTLASGVPSRFKGSGSGTQFTLTISGVQCDDAATYYC

IGGKSSSTDGNAFGGGTEVVVR

[0204] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:
(SEQ ID NO: 345)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGL

EWMGGIIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSED

TAVYYCARGNIVATITPLDYWGQGTLTVSS

(SEQ ID NO: 346)
QPVLTQPPSVAAPGKVTISCGSSSNIANNYVSWYQQLPGTAP

KLLIFANNKRPSGIPDRESGSKSGTSAALDITGLQTGDEADYYCG

TWDSDLRAGVPGGGTKLTVL

(SEQ ID NO: 347)
EVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGL

EWMGGIIPIFGTANYAQKFQGRVTITADKSTSTAYMELSSLRSED

TAVYYCAREGTIYDSSGYSFDYWQGQGTLTVSS

(SEQ ID NO: 348)
QVQLVESGGVVVQPGRSRLSCAASGFTFSSYAMHWVRQAPGKGL

EWVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQGTLTVSS

(SEQ ID NO: 349)
EVQLVESGGVVVQPGRSRLSCAASGFTFSSYAMHWVRQAPGKGL

EWVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQGTLTVSS

(SEQ ID NO: 350)
QVQLVESGGVVVQPGRSRLSCAASGFTFSSYAMHWVRQAPGKGL

EWVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQGTLTVSS

(SEQ ID NO: 351)
EVQLVESGGVVVQPGRSRLSCAASGFTFSSYAMHWVRQAPGKGL

EWVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQGTLTVSS

- continued

(SEQ ID NO: 352)
EVQLVESGGVVQPGRLSRLSCAASGTFSSYAMHWVRQAPGKGL

EWAVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQTLTVSS

(SEQ ID NO: 353)
QVQLVESGGVVQPGRLSRLSCAASGTFSSYAMHWVRQAPGKGL

EWAVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQTLTVSS

(SEQ ID NO: 354)
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSRYGVHWVRQAPGQGL

EWMGRLIPIVSMTNYAQKFQDRVSITTDKSTGTAYMELRSLTSED

TALYYCASVGQQLPWVFFAWGQGTLTVSS

(SEQ ID NO: 355)
QMQLVQSGGGVVQPGRLSRLSCAASGTFSSYAMHWVRQAPGKGL

EWAVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQTLTVSS

(SEQ ID NO: 356)
QVQLVQSGGGVVQPGRLSRLSCAASGTFSSYAMHWVRQAPGKGL

EWAVAVISEDGSNKYYADSVRGRFTISRDNSKNTLYLQMNSLRTED

TAVYYCARGWLDRDIDYWQGQTLTVSS

(SEQ ID NO: 357)
QMQLVQSGAEVKKPGSSVKVSCKASGGTFSYYAYSWVRQAPGQGL

EWMGGIIPSGFTANYAQKFQGRVTITADESTSTAYMELSSLSED

TAVYYCARGPIVATITPLDYWGQGTLTVSS

(SEQ ID NO: 358)
QMQLVQSGAEVKKPGSSVKVSCKASGGTFSYYAYSWVRQAPGQGL

EWMGGIIPFGTANYAQKEQGRVTITADESTSTAYMELSSLSED

TAVYYCARGPIVATITPLDYWGQGTLTVSS

(SEQ ID NO: 359)
QMQLVQSGAEVKKPGSSVKVSCKASGGTFSYYAYSWVRQAPGQGL

EWMGGIIPSGFTANYAQKFQGRVTITADESTSTAYMELSSLSED

TAVYYCARGPIVATITPLDYWGQGTLTVSS

(SEQ ID NO: 360)
QMQLVQSGAEVKKPGSSVKVSCKASGGTFSYYAYSWVRQAPGQGL

EWMGGIIPFGTANYAQKFQGRVTITADESTSTAYMELSSLSED

TAVYYCARGPIVATITPLDYWGQGTLTVSS

VL Sequences:

(SEQ ID NO: 361)
SYELMQPPSVSVPAGKTATIACGGENIGRKTVHWYQQKPGQAPVL

VIYYDSDRPSGIPERFSGNSGNATLTISRVEAGDEADYYCQW

DSSSDHRIFGGGTKLTVL

(SEQ ID NO: 362)
AIRMTQSPSSLASAVGDRVTITCRASQSISSYLNWYQQKPGKAPK

LLIYTSSLKGVPRESGSGSGTDFTLTISRQLPEDFATYYCQW

SYSSTWTFGRGTKVEIK

- continued

(SEQ ID NO: 363)
QSVLTPPPSVAAPGQKVTCSCGNNSNIANNYVSWYQQLPGTAP

KLLIYDNNYRPSGIPDRESGSKSGTSATLDITGLQTGDEADYYCG

VWDGSLTTGVPGGGTKLTVL

(SEQ ID NO: 364)
LPVLTPASVSGSPGQSITISCTGTTSDIGGYDYYVSWYQQHPGKA

PKLMIYDVSKRPSGVSNRFGSKSGNTASLTISGLQAEDEADYYC

SSYTSSSTHVFGTGTKLTVL

(SEQ ID NO: 365)
QSALTQPPSVSGSPGQSITISCTGTSSDVGYYNYVSWYQQHPGKA

PKLMIYDVSNRPSGVSNRFGSKSGNTASLTISGLQAEDEADYYC

SSYRSSTLGPVFGGGTKLTVL

(SEQ ID NO: 366)
QAGLTQPPSVSEAPRQRVTTCSCGSSSNIGNNAVNWYQQLPGKAP

KLLIYDNNLLPSGVSDRESGSKSGTSASLAISGLQSEDEADYYC

AWDDSLNGYVFVFGTGTKLTVL

(SEQ ID NO: 367)
QSALTQPRSVSGSPGQSVTISCTGTSSDVGYYNYVSWYQQHPGKA

PKLMIYDVSKRPSGVPDRFSGSKSGNTASLTISGLQAEDEADYYC

SSYTSSSTHVFGTGTKLTVL

(SEQ ID NO: 368)
QSVTQPPSVAAPGQKVTCSCGSSSNIGNNYVSWYQQLPGTAP

KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYC

TWDSSLSSVWVEGGTQLTVL

(SEQ ID NO: 369)
QSVLTPPPSVAAPGQKVTCSCGSSSNIGNNYVSWYQQLPGTAP

PRLMIYDVSNRPSGVSNRFGSKSGNTASLTISGLQAEDEGDIY

SSYTSGGTLGPVFGGGTKLTVL

(SEQ ID NO: 370)
QSVTQPPSVAAPGQKVTCSCGSSSNIGNNYVSWYQQLPGTAP

KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYC

TWDSSLSSAVVFGGGTKLTVL

(SEQ ID NO: 371)
QSVTQPPSVAAPGQKVTCSCGSSSNIGNNYVSWYQQVPGTAP

KLLIYDNNKRPSGIPDRESGNSDTSATLGITGLQTGDEADYYC

TWDSSLSSAVVFGGGTKLTVL

(SEQ ID NO: 372)
QSVTQPPSVAAPGQKVTCSCGSSSNIGNNYVSWYQQLPGTAP

KLLIYDNNKRPSGIPDRESGSKSGTSATLGITGLQTGDEADYYC

TWDSSLSSAVVFGGGTKLTVL

(SEQ ID NO: 373)
SYELMQPPSVSVPAGKTATIACGGENIGRKTVHWYQQKPGQAPVL

VIYYDSDRPSGIPERFSGNSGNATLTISRVEAGDEADYYCLW

DSSSDHRIFGGGTKLTVL

-continued

(SEQ ID NO: 374)

SYELMQPPSVVAPGKTATIACGGENIGRKTVHWWQQKPGQAPVL

VIYYDSDRPSGIPERFSGNSGNNTATLTISRVEAGDEADYYCQVV

DSSSDHRIFGGGTKLTVL

(SEQ ID NO: 375)

SYELMQPPSVVAPGKTATIACGGENIGRKTVHWWQQKPGQAPVL

VIYYDSDRPSGIPERFSGNSGNNTATLTISRVEAGDEADYYCQVV

DSSSDHRIFGGGTKLTVL

(SEQ ID NO: 376)

SYELMQPPSVVAPGKTATIACGGENIGRKTVHWWQQKPGQAPVL

VIYYDSDRPSGIPERFSGNSGNNTATLTISRVEAGDEADYYCQVV

DSSSDHRIFGGGTKLTVL

[0205] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:

(SEQ ID NO: 377)

QVQLVQSGSEVKSGSSVKVSCKTSGGTFITNYAINWVRQAPGQ

GLEWMGGILPIFGAAKYAQKFQDRVTITADESTNTAYLELSSLTS

EDTAMYYCARSKRWLQSDLQYWQGQTLTVSS

VL Sequences:

(SEQ ID NO: 378)

QPVLTPASVSGSPGQSITISCTGSSDVGSYDLVSWYQQSPGKV

PKLLIYEGVKRPSGVSNRFSGSKSGNTASLTISGLQAEDADYYC

SSYAGTRNFVFGGTQLTVL

[0206] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a combination of a VH sequence and a VL sequence selected from the group consisting of:

VH Sequences:

(SEQ ID NO: 379)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIYSTGGATAYADSVKGRFTISRDNSKNTLYLQMNSLRAED

TAVYYCAKSSAGQSRPGFDYWGQGTLTVSS

(SEQ ID NO: 380)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIYSTGGATAYADSVKGRFTISRDNSKNTLYLQMNSLRAED

TAVYYCAKSSAGQSRPGFDYWGQGTLTVSS

(SEQ ID NO: 381)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIYSTGGATAYADSVKGRFTISRDNSKNTLYLQMNSLRAED

TAVYYCAKSSAGQSFPGFDYWGQGTLTVSS

-continued

(SEQ ID NO: 382)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIYSTGGATAYADSVKGRFTISRDNSKNTLYLQMNSLRAED

TAVYYCAKWSAAFDFYWGQGTLTVSS

(SEQ ID NO: 383)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIYSTGGATAYADSVKGRFTISRDNSKNTLYLQMNSLRAED

TAVYYCAKWSAGYDYWGQGTLTVSS

(SEQ ID NO: 384)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIYSTGGATAYADSVKGRFTISRDNSKNTLYLQMNSLRAED

TAVYYCAKWSKGFDYWGQGTLTVSS

(SEQ ID NO: 385)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIWKQGMIVTVYDSVKGRTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

(SEQ ID NO: 386)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIWRNGIVTVYDSVKGRTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

(SEQ ID NO: 387)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSDIWKQGMIVTVYDSVKGRTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

(SEQ ID NO: 388)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIWRQGLATAYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

(SEQ ID NO: 389)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSEIVATGILTSYDSVKGRTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

(SEQ ID NO: 390)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIGRQGLITVYDSVKGRTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

(SEQ ID NO: 391)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSSIWYQGLIVTVYDSVKGRTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

(SEQ ID NO: 392)

EVQLESQGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL

EWVSDIWKQGPATADSVKGRTISRDNSKNTLYLQMNSLRAEDT

AVYYCAKSSAGFDYWGQGTLTVSS

-continued

(SEQ ID NO: 393)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIWKQGIVTVYDVSVKGRFTISRDNSKNTLYLQMNSLRAEDT
AVYYCAKSSAGFDYWGQGTIVTVSS

(SEQ ID NO: 394)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIWRQGLATAYDSVKGRFTISRDNSKNTLYLQMNSLRAEDT
AVYYCAKSSAGFDYWGQGTIVTVSS

(SEQ ID NO: 395)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIWRNGIVTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKSSAGFDYWGQGTIVTVSS

(SEQ ID NO: 396)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIWRNGIVTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKSSAGFDYWGQGTIVTVSS

(SEQ ID NO: 397)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIWRNGIVTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKSSAGFDYWGQGTIVTVSS

(SEQ ID NO: 398)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
GLEWVSSIWYQGLTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
RAEDTAVYYCAKSSAGFDYWGQGTIVTVSS

(SEQ ID NO: 399)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIWYQGLTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKSSAGFDYWGQGTIVTVSS

(SEQ ID NO: 400)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIWYQGLTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKSSAGFDYWGQGTIVTVSS

VL Sequences:

(SEQ ID NO: 401)

DIQMTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPK
LLIYYASTLQSGVPSRESGSGSGTDFTLTISSLQPEDFATYYCQQ
DNGYPSTFGQGTIVTVSS

(SEQ ID NO: 402)

DIQMTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPK
LLIYYASTLQSGVPSRESGSGSGTDFTLTISSLQPEDFATYYCQQ
DNGYPSTFGQGTIVTVSS

(SEQ ID NO: 403)

DIQMTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPK
LLIYAASSLQSGVPSRESGSGSGTDFTLTISSLQPEDFATYYCQQ
DNGYPSTFGGGTKVEIKR

[0207] In some embodiments, the PDL1 binding domain comprises or is derived from an antibody sequence or antigen-binding fragment thereof that includes a single chain Fv (scFv) sequence selected from the group consisting of:

(SEQ ID NO: 404)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSDITASQRTTYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCARSKIAFDFYWGQGTIVTVSSGGGGSGGGGGGGGGSTDIQ
MTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPKLLI
YKASRLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQRAL
KPVTFGQGTIVTVSS

(SEQ ID NO: 405)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSINKDHHTSYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKNLDEFDFYWGQGTIVTVSSGGGGSGGGGGGGGGSTDIQ
MTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPKLLI
YAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYS
TPNTFGQGTIVTVSS

(SEQ ID NO: 406)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIMATGAGTLYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKDGAGFDYWGQGTIVTVSSGGGGSGGGGGGGGGSTDIQ
MTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPKLLI
YASASLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQANS
RPSTFGQGTIVTVSS

(SEQ ID NO: 407)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
QWVSTITSSGAATTYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKNYTGFYWGQGTIVTVSSGGGGSGGGGGGGGGSTDIQ
MTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPKLLI
YNASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYTY
GPGTFQGTIVTVSS

(SEQ ID NO: 408)

EVQOLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL
EWVSSIYSTGGATAYADSVKGRFTISRDNSKNTLYLQMNSLRAEDT
TAVYYCAKSSAGFDYWGQGTIVTVSSGGGGSGGGGGGGGGSTDIQ
MTQSPSSLSASVGDRVITCRASQSISYLNWYQQKPGKAPKLLI
YYASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQDNG
YPSTFGQGTIVTVSS

PDL1×41BB Dual Targeting

[0208] In some embodiments, the fusion proteins are bispecific molecules that include a TBD that binds 41BB and a binding domain directed toward PDL1. In these, embodiments, the binding to PDL1 is capable of providing the

additional crosslinking function and TNFRSF activation can be achieved with only one or two anti-41BB TBDs. In these embodiments, the TNFRSF signaling is enhanced and focused by the presence of a PDL1 expressing cell.

Tetravalent 41BB agonist: hzRH3v5-1
 (SEQ ID NO: 448)
EVQLLESGGGEVQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESGRNTVYAESVK
GRFTISRDNAKNTVYLQMSSLRAEDTAVYYCGLLKGNRVVSPSVAYWGQGTLTVKPGGGDKT
HTCPPCPAPGGPSVFLPPPDKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHNAKTK
PREEQYNSTYRVVSLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPS
RDELTQNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCVMHEALHNHYTQKSLSLSPGSGGGGGGSEVQLLESGGEVQPGGSLRLSCAAS
GFSFSINAMGWYRQAPGKRREFVAAIESGRNTVYAESVKGRFTISRDNAKNTVYLQMSSLRAED
TAVYYCGLLKGNRVVSPSVAYWGQGTLTVKPGGGDKT
HTCPPCPAPGGPSVFLPPPDKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHNAKTK
PREEQYNSTYRVVSLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPS
RDELTQNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCVMHEALHNHYTQKSLSLSPGSGGGGGGSEVQLLESGGEVQPGGSLRLSCAAS
GFSFSINAMGWYRQAPGKRREFVAAIESGRNTVYAESVKGRFTISRDNAKNTVYLQMSSLRAED
TAVYYCGLLKGNRVVSPSVAYWGQGTLTVKPGGGDKT

Bispecific PDL1 x 41BB: hz28A2v5 x hzRH3v5-1
 (SEQ ID NO: 449)
EVQLLESGGGEVQPGGSLRLSCAASGGIFAIPKISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFEYWGQGTLTVKPGGGGGSEVQLLESGGGE
VQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIESGRNTVYAESVKGRFTISRDNAK
NTVYLQMSSLRAEDTAVYYCGLLKGNRVVSPSVAYWGQGTLTVKPGGGDKTHTCPCPAPGG
PSVFLFPPPKDKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTQNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQGNVFSCVMH
EALHNHYTQKSLSLSPGK

Bispecific PDL1 x 41BB: hz28A2v5 x hzRH3v5-2
 (SEQ ID NO: 450)
EVQLLESGGGEVQPGGSLRLSCAASGGIFAIPKISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFEYWGQGTLTVKPGGGGGSEVQLLESGGGE
VQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIYSGRNTVYAESVKGRFTISRDNAK
NTVYLQMSSLRAEDTAVYYCGLLKGNRVVSPSVAYWGQGTLTVKPGGGDKTHTCPCPAPGG
PSVFLFPPPKDKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTQNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQGNVFSCVMH
EALHNHYTQKSLSLSPGK

Bispecific PDL1 x 41BB: hz28A2v5 x hzRH3v5-16
 (SEQ ID NO: 451)
EVQLLESGGGEVQPGGSLRLSCAASGGIFAIPKISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFEYWGQGTLTVKPGGGGGSEVQLLESGGGE
VQPGGSLRLSCAASGFSFSINAMGWYRQAPGKRREFVAAIYSGSSTVYAESVKGRFTISRDNAK
NTVYLQMSSLRAEDTAVYYCGLLKGNRVVSPSVAYWGQGTLTVKPGGGDKTHTCPCPAPGG
PSVFLFPPPKDKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTQNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQGNVFSCVMH
EALHNHYTQKSLSLSPGK

- continued

Bispecific PDL1 x 41BB: hz28A2v5 x hz4E01v16 (SEQ ID NO: 452)
EVQLLESGGGEVQPGGSRLSCAASGGIFAIKPISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFYWGQGTLTVKPGGSGGSEVQLLESGG
VQLLESGGGEVQPGGSRLSCAASGWAFGNIGMAWFRQAPGKEREFSRSLAWQGGSTDYVESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRYSRSYDIRTPQTVDYWGQGTLTVKPGG
GDKTHTCPPCPAPGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHN
AKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIKAKGQPREGQVYT
LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Bispecific PDL1 x 41BB: hz28A2v5 x hz4E01v18 (SEQ ID NO: 453)
EVQLLESGGGEVQPGGSRLSCAASGGIFAIKPISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFYWGQGTLTVKPGGSGGSEVQLLESGG
VQLLESGGGEVQPGGSRLSCAASGWAFGNIGMAWFRQAPGKEREFSRSLAWGGGSTDYVESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRYSRSYDIRTPQTVDYWGQGTLTVKPGG
GDKTHTCPPCPAPGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHN
AKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIKAKGQPREGQVYT
LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Bispecific PDL1 x 41BB: hz28A2v5 x hz4E01v21 (SEQ ID NO: 454)
EVQLLESGGGEVQPGGSRLSCAASGGIFAIKPISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFYWGQGTLTVKPGGSGGSEVQLLESGG
VQLLESGGGEVQPGGSRLSCAASGWAFNSNYGMAWFRQAPGKEREFSRSLAWGGGSTDYVESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRYSRSYDIRTPQTVDYWGQGTLTVKPGG
GDKTHTCPPCPAPGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHN
AKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIKAKGQPREGQVYT
LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Bispecific PDL1 x 41BB: hz28A2v5 x hz4E01v22 (SEQ ID NO: 455)
EVQLLESGGGEVQPGGSRLSCAASGGIFAIKPISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFYWGQGTLTVKPGGSGGSEVQLLESGG
VQLLESGGGEVQPGGSRLSCAASGWAFGNIGMAWFRQAPGKEREFSRSLAWGGGSTDYVESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRYSRSYDIRTPQTVDYWGQGTLTVKPGG
GDKTHTCPPCPAPGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHN
AKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIKAKGQPREGQVYT
LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Bispecific PDL1 x 41BB: hz28A2v5 x hz4E01v23 (SEQ ID NO: 456)
EVQLLESGGGEVQPGGSRLSCAASGGIFAIKPISWYRQAPGKQREWVSTTSSGATNYAESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCNVFYWGQGTLTVKPGGSGGSEVQLLESGG

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vQLLESGGGEVQPAGGSRLSCAASGWAFSNYGMWFRQAPGKEREFSRILAWGGSTDYVESVK
GRFTISRDNAKNTLYLQMSSLRAEDTAVYYCARQRSYSRYDIRTPQTYDYGQGTLVTVKPGGG
GDKHTCPCPAPGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHN
AKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREGQVYT
LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESENQGPENNYKTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
```

[0209] In some embodiments, the fusion proteins are multispecific containing a TBD and a binding domain directed toward Folate Receptor Alpha (FR α). In these, embodiments, the binding to FR α is capable of providing the additional crosslinking function and TNFRSF activation

can be achieved with only one or two TBDs. In these embodiments, the TNFRSF signaling is enhanced and focused by the presence of a FR α expressing cell.

[0210] Exemplary FR α -targeting single domain sequences are shown below:

Fra-5:

(SEQ ID NO: 409)

```
QLQLQESGGGLVQAGGSRLSCAASGIMFYISDMGWYRQAPGKQREFVATTITSGGTNYADSVK
```

```
GRFSISRDNAKNTVYLOMNSLEPEDTAVYYCTAHGPTYGSTWDDLWGQGTQVTVKPGG
```

(SEQ ID NO: 410)

CDR1: GIMFYISD

(SEQ ID NO: 411)

CDR2: TITSGGTNY

(SEQ ID NO: 412)

CDR3: TAHGPTYGSTWDDL

Fra-6:

(SEQ ID NO: 413)

```
QVQLQESGGGLVQAGGSRLSCAASETFGVVFTLGWYRQTPGKQREFVARVIGTDTVDYADSVK
```

```
GRFTISSDFARNTVYLQMNNLKPEDTAVYYCNTGAYWGQGTQVTVKPGG
```

(SEQ ID NO: 414)

CDR1: TFGVVFT

(SEQ ID NO: 415)

CDR2: VIGTDTV

(SEQ ID NO: 416)

CDR3: NTGAY

Fra-57:

(SEQ ID NO: 417)

```
QLQLQESGGGLVQAGGSRLSCAASGSIFRFCGARGWYRQAPGKORELVATITSGGTNYADSVQ
```

```
EGRFTISRDIAKNTLYLQMNSLEPEDTAVYYCTAREPTGYDYWGQGTQVTVKPGG
```

(SEQ ID NO: 418)

CDR1: GRTASTYS

(SEQ ID NO: 419)

CDR2: IWSTGST

(SEQ ID NO: 420)

CDR3: TAREPTGYDY

1A3:

(SEQ ID NO: 410)

```
QLQLQESGGGLVQAGGSRLSCAASGSIFRFCGARGWYRQAPGKORELVATITSGGTNYADSVQ
```

```
GRFTISRDNAKNMVLQMNGLKGDTAVYYCAADRSDAVGVGWDYWGQGTQVTVKPGG
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-continued

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CDR1: GSIFREGA (SEQ ID NO: 422)
CDR2: ITSGGST (SEQ ID NO: 423)
CDR3: AADRSDAVGVGWDY (SEQ ID NO: 424)

1F3: (SEQ ID NO: 425)
QVQLQQSGGGLVQTGGSLRLSCAASGRTASTYSMGWFRQAPGKEROFVARIIWSTGSTYYTNSV

EGRFTISRDIAKNTLYLOMNSLEPEDTAVYYCTARDPTGYDYWGQGTQVTVKPGG

CDR1: GRTASTYS (SEQ ID NO: 418)
CDR2: IIWSTGST (SEQ ID NO: 426)
CDR3: TARDPTGYDY (SEQ ID NO: 427)

1G10: (SEQ ID NO: 428)
QLQLQESGGGLVQAGGSLRLSCAASGSIFSIDATAWYRQAPGKORELVAIITSSGSTNYPDSVK

GRFTISRDNAKNTVYLQMNSLNPEPDALYSNAITRMGGSTYDFWGQGTQVTVKPGG

CDR1: GSIFSIDA (SEQ ID NO: 429)
CDR2: ITSSGST (SEQ ID NO: 430)
CDR3: NAITRMGGSTYDF (SEQ ID NO: 431)

```

[0211] The disclosure will be further described in the following examples, which do not limit the scope of the disclosure described in the claims.

EXAMPLES

Example 1. 41BB-Targeting Single Domain Antibodies Bind 41BB

[0212] The 41BB-targeting single domain antibodies (sdAbs) referred to herein as 1G3 (SEQ ID NO: 432), 1H4 (SEQ ID NO: 436), 1H1 (SEQ ID NO: 440), 4H4 (SEQ ID NO: 16), 1H8 (SEQ ID NO: 444), 4F5 (SEQ ID NO: 23), and 4E1 (SEQ ID NO: 20) bind recombinant human 41BB (FIG. 2A), cynomolgus 41BB (FIG. 2B). The 41BB-targeting single domain antibodies (sdAbs) referred to herein as 4F5 (SEQ ID NO: 23), 4H04 (SEQ ID NO: 16), 4E01 (SEQ ID NO: 20), RH03 (SEQ ID NO: 25), and D1 (SEQ ID NO: 29) bind human 41BB expressed on the cell surface of CHO cells (FIG. 3). The 41BB-targeting sdAbs referred to herein as 4H04, RH03, and bind cynomolgus 41BB. For FIG. 2A, FIG. 2B, and FIG. 4, binding was assessed by ELISA wherein recombinant 41BB-mFc fusion protein (a fusion protein containing 41BB operably linked to a mouse Fc region) was immobilized on a Medisorp 96 well plate. For FIG. 3, binding was assessed by flow cytometry using 41BB expressing CHO cells, and the data is presented as median fluorescence intensity.

Example 2. 41BB-Targeting Single Domain Antibodies Block 41BB

[0213] The 41BB-targeting single domain antibodies (sdAbs) referred to herein as 4F05 (SEQ ID NO: 23), 4H04 (SEQ ID NO: 16), 4E01 (SEQ ID NO: 20), RH03 (SEQ ID NO: 25), and D1 (SEQ ID NO: 29) block the interaction between 41BB and its ligand 41BBL. All single domain antibodies tested, with the exception of RH3 blocks the interaction between 41BB and 41BBL. Blocking was assessed by flow cytometry using a recombinant 41BB fusion protein and 41BB expressing CHO cells, data is presented as median fluorescence intensity.

[0214] In contrast to the 41BB sdAbs of the disclosure, conventional bivalent anti-41BB antibodies do not induce 41BB signaling unless further clustered with an exogenous crosslinking anti-human IgG antibody. FIG. 6 demonstrates the inability of a conventional bivalent anti-41BB antibody PF-05082566, which is disclosed in U.S. Pat. No. 8,337,850, to induce 41BB signaling unless further clustered with an exogenous crosslinking anti-human IgG antibody. In FIG. 6, 41BB signaling was monitored using a NF- κ B reporter 293 cell line expressing 41BB.

Example 3. PDL1-Targeting Single Domain Antibodies Bind PDL1 and Block the Interaction Between PLD1 and PD1

[0215] The studies presented herein use an exemplary PDL1 single domain antibody (sdAb), referred to herein as

28A10 (SEQ ID NO: 100) to demonstrate that the PDL1-targeting sdAbs of the disclosure bind cell surface PDL1 (FIG. 7A) and block the interaction of PDL1 with PD1 (FIG. 7B). Binding was assessed by flow cytometry on PDL1-expressing CHO cells, and blocking was assessed by flow cytometry using a recombinant PD1 fusion protein and PDL1-expressing CHO cells. The data presented in FIGS. 7A and 7B are presented as median fluorescence intensity.

Example 4. PDL1-41BB Targeting Fusion Proteins

[0216] The disclosure provides fusion proteins that target at least PDL1 and 41BB. These bispecific PDL1-41BB targeting fusion proteins are agonists of PDL1-dependent 41BB mediated signaling. FIGS. 8A and 8B are conceptual schematics wherein the bispecific fusion proteins have minimal 41BB agonistic properties (FIG. 8A) unless bound by a PD-L1 expressing cell (FIG. 8B). FIG. 8C demonstrates the ability of a PDL1-positive cell, in this case, a population of PDL1 transfected CHO cells, to mediate 41BB signaling and the inability of PDL1-negative cell, in this case, a population of untransfected CHO cells, to mediate 41BB signaling. Two distinct bispecific fusion proteins are shown in this figure, each containing a distinct 41BB binding VHH (e.g., 4E01 or RH3) and the same PD-L1 VHH, 28A10. 41BB signaling was monitored using a NF- κ B reporter 293 cell line expressing 41BB. This reporter cell line implements an NF- κ B driven secreted alkaline phosphatase, to monitor NF- κ B signaling.

[0217] The PDL1-41BB targeting fusion proteins of the disclosure include a humanized anti-41BB sequence. In the studies presented herein, the PDL1-41BB targeting fusion proteins of the disclosure include a humanized anti-41BB sequence such as hzRH3v5-1 (SEQ ID NO: 30) and/or hzRH3v9 (SEQ ID NO: 82) bind both human and cynomolgus 41BB (FIGS. 9A, 9B), including human 41BB and cynomolgus 41BB expressed on the surface of CHO cells (FIGS. 9C, 9D). Binding was assessed by flow cytometry on 41BB expressing 293freestyle cells.

[0218] The humanized variants hzRH3v5-1 and hzRH3v9 do not block binding of 41BBL to cell surface 41BB as shown in FIG. 9E. In these studies, a recombinant fusion protein 41BBL-mFc, containing a mouse Fc region, was used, and bound 41BBL was detected using an anti-mouse IgG-Fc specific secondary antibody.

[0219] The humanized variant hzRH3v5-1 specifically binds 41BB as compared to the other TNFRSF members OX40 and GITR (FIG. 10). Binding was assessed by flow cytometry using CHO cells expressing the given TNFRSF member.

[0220] Additional humanized 41BB variants were analyzed. FIGS. 11A, 11B, 11C, and 11D demonstrate the binding to human (FIG. 11A and FIG. 11C) or cynomolgus monkey (FIG. 11B) 41BB of the humanized 4E01 variants. Binding was assessed by flow cytometry on 41BB expressing 293freestyle cells. FIG. 11D demonstrates that the humanized variants hz4E01v16, hz4E01v18, hz4E01v21, hz4E01v22 and hz4E01v23 block binding of 41BBL to cell surface 41BB. In these studies, a recombinant fusion protein 41BBL-mFc, containing a mouse Fc region was used and bound 41BBL was detected using an anti-mouse IgG-Fc specific secondary antibody.

[0221] The PDL1-41BB targeting fusion proteins of the disclosure also include a humanized anti-PDL1 sequence. In the studies presented herein, the PDL1-41BB targeting

fusion proteins of the disclosure include a humanized anti-PDL1 sequence such as hz28A2v1 (SEQ ID NO: 120), hz28A2v2 (SEQ ID NO: 121), hz28A2v3 (SEQ ID NO: 122), and hz28A2v4-1 (SEQ ID NO: 123). FIG. 12 demonstrates binding of humanized single domain antibodies targeting PDL1. Binding was assessed by flow cytometry on PDL1-expressing CHO cells.

[0222] FIG. 13 is a schematic of two exemplary formats of a PDL1 \times 41BB bispecific fusion protein of the disclosure, referred to herein as INBRX-105-1. INBRX-105-1-A (left) has the PDL1 and 41BB binding domains located at opposing terminal positions with a central Fc region, whereas INBRX-105-1-B (right) has the PDL1 and 41BB binding domains positioned in tandem, N-terminal to an Fc region.

[0223] These two formats were further evaluated for their ability to bind human or cynomolgus monkey 41BB, to block the interaction between 41BB and 41BBL, to bind PDL1, and to block the interaction between PDL1 and PD1.

[0224] In particular, FIGS. 14A, 14B, and 14C demonstrate the equivalent binding to human (FIG. 14A) or cynomolgus monkey (FIG. 14B) 41BB by the two distinct formats of a bispecific fusion protein targeting PDL1 and 41BB referred to herein as INBRX-105-1-A and INBRX-105-1-B and illustrated in FIG. 13. Binding was assessed by flow cytometry on 41BB expressing 293freestyle cells. In the studies presented herein, hzRH3v5-1 (SEQ ID NO: 124) is the 41BB binding domain used in both formats. As shown in FIG. 14C, the bispecific fusion protein containing hzRh3v5-1 does not block 41BBL binding to cell surface 41BB. In these studies, a recombinant fusion protein of 41BBL and a mouse Fc region was used, and bound 41BBL was detected using an anti-mouse IgG-Fc specific secondary antibody.

[0225] Furthermore, FIGS. 15A, 15B, 15C, and 15D demonstrate the equivalent binding (FIG. 15A and FIG. 15C) and PD1 blocking (FIG. 15B and FIG. 15D) by the two distinct formats of a bispecific fusion protein targeting PDL1 and 41BB referred to herein as INBRX-105-1-A and INBRX-105-1-B. Binding was assessed by flow cytometry on human (FIG. 15A) or cynomolgus monkey (FIG. 15C) PDL1 expressing 293freestyle cells. Blocking was assessed by flow cytometry using on human (FIG. 15B) or cynomolgus monkey (FIG. 15D) PDL1 expressing 293freestyle cells with either recombinant human (FIG. 15B) or cynomolgus monkey (FIG. 15D) PD1-mFc fusion protein. Bound PD1 was detected using an anti-mouse IgG-Fc specific secondary antibody. In the studies presented herein, hz28A2v5 is the PDL1-binding domain used in both formats.

[0226] The PDL1 \times 41BB bispecific fusion proteins were evaluated for their ability to induce PDL1-dependent 41BB agonism. FIG. 16 demonstrates the ability of humanized versions of a PDL1 \times 41BB bispecific fusion protein (INBRX-105-1) to induce PDL1-dependent 41BB agonism. Compared herein are two distinct formats, INBRX-105-1-A vs INBRX-105-1-B, having the PDL1 and 41BB binding domains positioned at opposite termini or in tandem within the fusion protein, respectively. Notably, INBRX-105-1-A vs INBRX-105-1-B demonstrate equivalent PDL1-dependent agonistic activities. A 41BB-expressing HEK293 NF- κ B reporter cell line was used to assess 41BB signaling and a PDL1-expressing CHO cell line was used as the source of PDL1. This reporter cell line implements an NF- κ B driven secreted alkaline phosphatase, to monitor NF- κ B signaling.

[0227] The ability of the 41BB-specific binding and the PDL1-specific binding by the binding domains in the PDL1 \times 41BB bispecific fusion proteins was evaluated. FIGS. 17A and 17B demonstrate the 41BB-specific binding by the 41BB-binding portion of a PDL1 \times 41BB bispecific fusion protein (INBRX-105-1) of the present disclosure. Binding was assessed on 41BB (FIG. 17A) or the closest homolog, TNFRSF21/DR6 (FIG. 17B), expressing 293freestyle cells by flow cytometry. An anti-DR6 antibody (Invitrogen) was used to as positive control for DR6 expression. In addition, FIGS. 18A, 18B, and 18C demonstrate the PDL1-specific binding by the PDL1-binding portion of a PDL1 \times 41BB bispecific fusion protein (INBRX-105-1) of the present disclosure. Binding was assessed on PDL1 (FIG. 18A), the closest homologs PDL2 (FIG. 18B) or VISTA/PDL3 (FIG. 18C), expressing 293freestyle cells by flow cytometry. An anti-PDL2 antibody and an anti-VISTA antibody known as VSTB174, which is disclosed in PCT Publication No. WO 2015/097536, were used to as positive controls for PDL2 and PDL3 expression respectively.

[0228] The ability of the PDL1 \times 41BB bispecific fusion proteins to simultaneously bind both 41BB and PDL1 was evaluated. FIGS. 19A and 19B demonstrate the ability of a PDL1 \times 41BB bispecific fusion protein to simultaneously bind PDL1 and 41BB. INBRX-105-1 was titrated onto PDL1 expressing K562 cells and 25 nM recombinant 41BB-mFc proteins was added. Bound 41BB was detected using an anti-mouse IgG-Fc specific secondary antibody. FIG. 19A is a graph showing the binding of INBRX-105-1 to the PDL1 expressing K562 cells. FIG. 19B is a graph showing the binding of recombinant 41BB to INBRX-105-1 on the PDL1 expressing cells.

[0229] FIG. 20 demonstrates the ability of a PDL1 \times 41BB bispecific fusion protein to simultaneously bind recombinant PDL1 and recombinant 41BB in an ELISA. INBRX-105-1 was titrated on to immobilized (Medisorp plate) recombinant PDL1, subsequently either 2 or 10 g/ml biotinylated recombinant 41BB (His-tagged) was added. Bound recombinant 41BB was detected via streptavidin-HRP.

[0230] The effect of the PDL1 \times 41BB bispecific fusion proteins to on T-cell activation and proliferation was evaluated. FIGS. 21A, 21B, and 21C demonstrate the effect of a PDL1 \times 41BB bispecific fusion protein (INBRX-105-1) of the present disclosure on T-cell activation and proliferation. Herein an autologous *in vitro* co-culture system implementing immature DC (iDC) and donor matched T-cells was conducted for 7 days. PDL1 $^+$ iDC were derived by enriching the monocyte population (EasySep™ Human Monocyte Enrichment Kit, STEMCELL Technologies Inc.) from human donor PBMCs and culturing them in 500 U/ml GM-CSF and 250 U/ml IL-4 for 7 days. Autologous T-cells were enriched at the same time (EasySep™ Human T-cell Enrichment Kit, STEMCELL Technologies Inc.) and cryo-preserved until iDC derivation was complete. Enriched T-cells were added to iDC at approximately 20:1 (T-cell: iDC) and co-cultured for at least 7 days in the presence of IL-7. The PDL1 \times 4TBB bispecific, INBRX-105-1, is superior to the monospecific PDL1 sdAb-Fc fusion protein (hz28A2v5-Fc), the 41BB sdAb-Fc fusion protein (hzRH3v5-1-Fc), the combination of the hz28A2v5-Fc and hzRH3v5-1-Fc, the anti-PDL1 antibody Atezolizumab, the anti-41BB antibody, Utomilumab (PF-05082566, disclosed in U.S. Pat. No. 8,337,850), or the anti-PD1 antibody Pembrolizumab, and combinations thereof, at inducing

INF γ (FIG. 21A) or mediating CD8 $^+$ T-cell proliferation (FIG. 21B) and activation (FIG. 21C). INF γ production in the cell supernatant was monitored using an ELISA and normalized to the standard curve. T-cell proliferation was monitored by flow cytometry using CTV labeling of T-cells. T-cell activation was assessed by the presence of the activation marker CD25 monitored by flow cytometry. Antibodies were used at 10 nM. INBRX-105-1 seemingly augments low level and/or tonic T-cell activation/signaling events that is damped by the PDL1:PD1 interaction.

[0231] FIGS. 22A and 22B demonstrate PDL1-dependent 41BB agonism mediated by a PDL1 \times 41BB bispecific fusion protein (INBRX-105-1) of the present disclosure. In these studies, T-cells were cultured alone or with autologous immature DCs (iDC, PDL1-expressing), a PDL1-expressing K562 cell line or the parental K562 cell line (PDL1-negative) in the presence or absence of 10 nM INBRX-105-1 for 7 days. CD8 $^+$ T-cell proliferation (FIG. 22A) was monitored using CTV labeling and INF γ production (FIG. 22B) in the cell supernatant was monitored using an ELISA and normalized to the standard curve.

[0232] FIG. 23 demonstrates the capacity of a PDL1 \times 41BB bispecific fusion protein (INBRX-105-1) of the present disclosure to enhance the Th1 lineage defining transcription factor, T-bet, expression in T-cell populations. Herein T-cells were co-cultured with autologous immature DCs for 7 days in the presence or absence of INBRX-105-1. T-bet expression was assessed on CD4 $^+$ and CD8 $^+$ T-cell population by flow cytometry via intracellular staining following fixation and permeabilization. INBRX-105-1 has a more dramatic effect on T-bet expression in CD8 $^+$ T-cells.

[0233] The PDL1 \times 41BB bispecific fusion proteins of the disclosure were compared to various known monospecific antibodies. FIGS. 24A and 24B contrast the capacity of a PDL1 \times 41BB bispecific fusion protein (INBRX-105-1) of the present disclosure and the combination of monospecific antibodies Atezolizumab (anti-PDL1) and Utomilumab (anti-41BB) to induce INF γ (FIG. 24A) or TNF α (FIG. 24B) production from CD4 $^+$ or CD8 $^+$ T-cells. Herein T-cells were co-cultured with autologous immature DCs for 7 days in the presence or absence of INBRX-105-1 or the combination of the monospecific antibodies. INBRX-105-1 is far superior at T-cell co-stimulation compared to monospecific antibodies targeting the same antigens. Cytokine expression was assessed on CD4 $^+$ and CD8 $^+$ T-cell population by flow cytometry via intracellular staining following fixation and permeabilization.

[0234] FIGS. 25A and 25B demonstrate the agonistic capacity of a tetravalent 41BB-binding fusion protein and PDL1 \times 41BB bispecific fusion proteins of the present disclosure in the presence of an additional PDL1 positive (FIG. 25A) or negative (FIG. 25B) cell line. Notably only the tetravalent 41BB binding fusion protein is capable of inducing 41BB signaling in the absence of a PDL1 expressing cell line. The bispecific PDL1 \times 41BB fusion proteins (INBRX-105-1, INBRX-105-2 and INBRX-105-16) only induced 41BB signaling when bound to cell surface PDL1 as shown in FIG. 25A. This demonstrates that bivalent engagement of 41BB, as is the case of INBRX-105, is insufficient to effectively cluster and mediate productive 41BB signaling. Engagement of a second cell surface antigen, PDL1 as in the present example, enables further clustering of 41BB and productive signaling. Herein a 41BB-expressing HEK293

NF- κ B reporter cell was used and co-incubated with either the PDL1-negative K562 cell line (FIG. 25B) or a stably transfected, PDL1-expressing K562 cell line (FIG. 25A). INBRX-105-1 incorporates the 41BB-targeting sdAb: hzRH3v5-1, INBRX-105-2 incorporates the 41BB-targeting

sdAb: hzRH3v5-2 and INBRX-105-16 incorporates the 41BB-targeting sdAb: hzRH3v5-16 and all incorporate the hz28A2v5 PDL1-targeting sdAb. The tetravalent 41BB-targeting fusion protein used herein has the following format comprising hzRH3v5-1-Fc-hzRH3v5-1.

SEQUENCE LISTING

```

Sequence total quantity: 456
SEQ ID NO: 1      moltype = AA  length = 218
FEATURE          Location/Qualifiers
REGION           1..218
note = chemically synthesized
source            1..218
mol_type = protein
organism = synthetic construct

SEQUENCE: 1
PAPELLGGPS VFLFPPKPKD TLMISRTPEV TCVVVVDVSHE DPEVKFNWYV DGVEVHNNAKT 60
KPREEQYNST YRVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKKA KGQPREPQVY 120
TLPPSRDELT KNQVSLTCLV KGFPYPSDIAV EWESNGQOPEN NYKTPPVLD SDGSFFLYSK 180
LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK                           218

SEQ ID NO: 2      moltype = AA  length = 215
FEATURE          Location/Qualifiers
REGION           1..215
note = chemically synthesized
source            1..215
mol_type = protein
organism = synthetic construct

SEQUENCE: 2
PAPGGPSVFL FPPPKPKDTLM ISRTPEVTCV VVDVSHE DPEVKFNWYV DGVEVHNNAKT 60
EEQYNSTYRV VSVLTVLHQD WLNGKEYKCK VSNKALPAPI EKTISKAKGQ PREPVQVYTL 120
PSRDELTKNQ VSLTCLVKGF YPSDIAVEWE SNGQOPENNYK TTTPVLDSDG SFFLYSKLTV 180
DKSRWQQGNV FSCSVMHEALHNHYTQKSLS LSPGK                               215

SEQ ID NO: 3      moltype = AA  length = 217
FEATURE          Location/Qualifiers
REGION           1..217
note = chemically synthesized
source            1..217
mol_type = protein
organism = synthetic construct

SEQUENCE: 3
PAPPVAGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSHED PEVQFNWYVD GVEVHNNAKT 60
PREEQFNSTF RVVSVLTVQD HQDWLNGKEYKCK VSNKGLPAPI EKTISKAKGQ QGPREPQVY 120
LPPSRREEMTK NQVSLTCLV KGFPYPSDIIVE WESNGQOPEN YKTTPPMLDS DGSFFLYSK 180
TVDKSRWQQG NVFSCSVMHE ALHNHYTQKSLS LSLSPGK                           217

SEQ ID NO: 4      moltype = AA  length = 218
FEATURE          Location/Qualifiers
REGION           1..218
note = chemically synthesized
source            1..218
mol_type = protein
organism = synthetic construct

SEQUENCE: 4
PAPELLGGPS VFLFPPKPKD TLMISRTPEV TCVVVVDVSHE DPEVKFNWYV DGVEVHNNAKT 60
KPREEQYNST YRVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKKA KGQPREPQVY 120
TLPPSRREEMT KNQVSLTCLV KGFPYPSDIAV EWESSNGQOPEN NYNTTPPMULD SDGSFFLYSK 180
LTVDKSRWQQ GNIIFSCSVMH EALHNRTQK SLSLSPGK                           218

SEQ ID NO: 5      moltype = AA  length = 218
FEATURE          Location/Qualifiers
REGION           1..218
note = chemically synthesized
source            1..218
mol_type = protein
organism = synthetic construct

SEQUENCE: 5
PAPEFLGGPS VFLFPPKPKD TLMISRTPEV TCVVVVDVSQE DPEVKFNWYV DGVEVHNNAKT 60
KPREEQFNST YRVSVLTVL HQDWLNGKEY KCKVSNKGLPSSIEKTISKKA KGQPREPQVY 120
TLPPSQEEMT KNQVSLTCLV KGFPYPSDIAV EWESNGQOPEN NYKTPPVLD SDGSFFLYSK 180
LTVDKSRWQEG NVFSCSVMH EALHNHYTQK SLSLSPGK                           218

SEQ ID NO: 6      moltype = AA  length = 218
FEATURE          Location/Qualifiers

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REGION          1..218
source          note = chemically synthesized
                1..218
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 6
PAPELLGGPS VFLFPPPKD TLMISRTPEV TCVVVVDVSQE DPEVQFNWYV DGVEVHNAKT 60
KPREEQFNST YRVVSVLTVL HQDWLNGKEY KCKVSNKGKP SSIEKTISKA KGQPREGQVY 120
TLPPSQEEMT KNQVSLTCLV KGFYPDSIAV EWESNGQOPEN NYKTTPPVLD SDGSFFLYSR 180
LTVDKSRWQE GNVFSCSVMH EALHNHYTQK SLSLSLGK 218

SEQ ID NO: 7      moltype = AA length = 14
FEATURE          Location/Qualifiers
REGION           1..14
source            note = chemically synthesized
                1..14
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 7
EPKSSDKTHT CPPC                                         14

SEQ ID NO: 8      moltype = AA length = 9
FEATURE          Location/Qualifiers
REGION           1..9
source            note = chemically synthesized
                1..9
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 8
DKTHTCPPC                                                 9

SEQ ID NO: 9      moltype = AA length = 11
FEATURE          Location/Qualifiers
REGION           1..11
source            note = chemically synthesized
                1..11
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 9
ESKYGPPCPP C                                              11

SEQ ID NO: 10     moltype = AA length = 6
FEATURE          Location/Qualifiers
REGION           1..6
source            note = chemically synthesized
                1..6
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 10
GGSGGS                                         6

SEQ ID NO: 11     moltype = AA length = 9
FEATURE          Location/Qualifiers
REGION           1..9
source            note = chemically synthesized
                1..9
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 11
GGSGGGSGGS                                              9

SEQ ID NO: 12     moltype = AA length = 12
FEATURE          Location/Qualifiers
REGION           1..12
source            note = chemically synthesized
                1..12
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 12
GGSGGGSGGS GS                                         12

SEQ ID NO: 13     moltype = AA length = 15
FEATURE          Location/Qualifiers
REGION           1..15
source            note = chemically synthesized
                1..15

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mol_type = protein
organism = synthetic construct
SEQUENCE: 13
GGSAGGGSGGG GSGGS                                15

SEQ ID NO: 14          moltype = AA length = 12
FEATURE
REGION
1..12
note = chemically synthesized
source
1..12
mol_type = protein
organism = synthetic construct
SEQUENCE: 14
GQGTLVTVKP GG                                12

SEQ ID NO: 15          moltype = AA length = 12
FEATURE
REGION
1..12
note = chemically synthesized
source
1..12
mol_type = protein
organism = synthetic construct
SEQUENCE: 15
GQGTLVTVEP GG                                12

SEQ ID NO: 16          moltype = AA length = 123
FEATURE
REGION
1..123
note = chemically synthesized
source
1..123
mol_type = protein
organism = synthetic construct
SEQUENCE: 16
QVQLQESGGG LVQAGDSLRL SCAASGWAFD NYGMAWFROA PGKEREFIGR LAWNGGSTDY 60
ADSVVKGRFTI SRDNPKNTLY LQMNNLKPED TAVYYCARQR SYSGYGIRTP QTYDYWGQGT 120
QVT                                         123

SEQ ID NO: 17          moltype = AA length = 8
FEATURE
REGION
1..8
note = chemically synthesized
source
1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 17
GWAFDNYG                                8

SEQ ID NO: 18          moltype = AA length = 8
FEATURE
REGION
1..8
note = chemically synthesized
source
1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 18
LAWNGGST                                8

SEQ ID NO: 19          moltype = AA length = 19
FEATURE
REGION
1..19
note = chemically synthesized
source
1..19
mol_type = protein
organism = synthetic construct
SEQUENCE: 19
ARQRYSYSGYG IRTPQTYDY                                19

SEQ ID NO: 20          moltype = AA length = 123
FEATURE
REGION
1..123
note = chemically synthesized
source
1..123
mol_type = protein
organism = synthetic construct
SEQUENCE: 20
QVQLQQSGGG LVQAGDSLRL SCAASGWAFG NYGMAWFRRG PGKEREFIGR LAWNGGSTDY 60

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VDSVKGRFTI SRDNPKNLTY LQMNNLKPDD TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
QVT                                         123

SEQ ID NO: 21      moltype = AA  length = 8
FEATURE          Location/Qualifiers
REGION           1..8
note = chemically synthesized
source            1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 21
GWAFGNYG                                         8

SEQ ID NO: 22      moltype = AA  length = 19
FEATURE          Location/Qualifiers
REGION           1..19
note = chemically synthesized
source            1..19
mol_type = protein
organism = synthetic construct

SEQUENCE: 22
ARQRYSRYSYD IRTPQTYDY                                         19

SEQ ID NO: 23      moltype = AA  length = 123
FEATURE          Location/Qualifiers
REGION           1..123
note = chemically synthesized
source            1..123
mol_type = protein
organism = synthetic construct

SEQUENCE: 23
QVQLVQSGGG LVQPGGSLRL SCAASGWAFD NYGMAWFRQA PGKEREFIGR LAWNGGSTDY 60
ADSVKGRFTI SRDNPKNLTY LQMNSLKPED TAVYYCARQR SYSRYGIRAP QTYDYWGQGT 120
QVT                                         123

SEQ ID NO: 24      moltype = AA  length = 19
FEATURE          Location/Qualifiers
REGION           1..19
note = chemically synthesized
source            1..19
mol_type = protein
organism = synthetic construct

SEQUENCE: 24
ARQRYSRYSYD IRAPQTYDY                                         19

SEQ ID NO: 25      moltype = AA  length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source            1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 25
QVQLQESGGG LVQPGGSLRL SCAAVGFSFS INAMGWYRQA PGKRREFLAA IDSGRNTVYA 60
VSVKGRFTIS RDNAKNTVYL QMNSLKPED AIYYCGLLKG NRVVSPSVAY WGQGTQVT 118

SEQ ID NO: 26      moltype = AA  length = 8
FEATURE          Location/Qualifiers
REGION           1..8
note = chemically synthesized
source            1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 26
GFSFSINA                                         8

SEQ ID NO: 27      moltype = AA  length = 7
FEATURE          Location/Qualifiers
REGION           1..7
note = chemically synthesized
source            1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 27
IDSGRNT                                         7

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SEQ ID NO: 28      moltype = AA length = 15
FEATURE           Location/Qualifiers
REGION            1..15
note = chemically synthesized
source             1..15
mol_type = protein
organism = synthetic construct

SEQUENCE: 28
GLLKGNRVS PSVAY                                         15

SEQ ID NO: 29      moltype = AA length = 120
FEATURE           Location/Qualifiers
REGION            1..120
note = chemically synthesized
source             1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 29
EVQPVQSGGG LVQAGESLRL SCAASATIFS NNAMGWYRQA PGKQRELVAT ITTGGFTNYR 60
DSVKGRFDIS RDNAKNTVYL QMNNLKPEDT AVYYCNVVLR YSRDYSYTTV KEYWGQGTQV 120

SEQ ID NO: 30      moltype = AA length = 8
FEATURE           Location/Qualifiers
REGION            1..8
note = chemically synthesized
source             1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 30
ATIFSNNA                                                 8

SEQ ID NO: 31      moltype = AA length = 7
FEATURE           Location/Qualifiers
REGION            1..7
note = chemically synthesized
source             1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 31
ITTGGFT                                              7

SEQ ID NO: 32      moltype = AA length = 18
FEATURE           Location/Qualifiers
REGION            1..18
note = chemically synthesized
source             1..18
mol_type = protein
organism = synthetic construct

SEQUENCE: 32
NVVLRYSRDY SYTTVKEY                                         18

SEQ ID NO: 33      moltype = AA length = 126
FEATURE           Location/Qualifiers
REGION            1..126
note = chemically synthesized
source             1..126
mol_type = protein
organism = synthetic construct

SEQUENCE: 33
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKGLEWVAR LAWNGGSTDY 60
AESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP                                         126

SEQ ID NO: 34      moltype = AA length = 126
FEATURE           Location/Qualifiers
REGION            1..126
note = chemically synthesized
source             1..126
mol_type = protein
organism = synthetic construct

SEQUENCE: 34
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKGREFVAR LAWNGGSTDY 60
AESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP                                         126

SEQ ID NO: 35      moltype = AA length = 126

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FEATURE          Location/Qualifiers
REGION          1..126
source           note = chemically synthesized
                1..126
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 35
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREVFSR LAWNGGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP          126

SEQ ID NO: 36      moltype = AA length = 126
FEATURE          Location/Qualifiers
REGION          1..126
source           note = chemically synthesized
                1..126
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 36
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFIGR LAWNGGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP          126

SEQ ID NO: 37      moltype = AA length = 126
FEATURE          Location/Qualifiers
REGION          1..126
source           note = chemically synthesized
                1..126
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 37
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREVFSR LAWNGGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP          126

SEQ ID NO: 38      moltype = AA length = 126
FEATURE          Location/Qualifiers
REGION          1..126
source           note = chemically synthesized
                1..126
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 38
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREVFSR LAWNGGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP          126

SEQ ID NO: 39      moltype = AA length = 126
FEATURE          Location/Qualifiers
REGION          1..126
source           note = chemically synthesized
                1..126
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 39
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFIGR LAWNGGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP          126

SEQ ID NO: 40      moltype = AA length = 126
FEATURE          Location/Qualifiers
REGION          1..126
source           note = chemically synthesized
                1..126
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 40
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFIGR LAWNGGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP          126

SEQ ID NO: 41      moltype = AA length = 126
FEATURE          Location/Qualifiers
REGION          1..126
source           note = chemically synthesized
                1..126

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mol_type = protein
organism = synthetic construct

SEQUENCE: 41
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFIGR LAWQGGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP 126

SEQ ID NO: 42      moltype = AA length = 8
FEATURE           Location/Qualifiers
REGION            1..8
source             note = chemically synthesized
                  1..8
                  mol_type = protein
                  organism = synthetic construct

SEQUENCE: 42
LAWQGGST 8

SEQ ID NO: 43      moltype = AA length = 126
FEATURE           Location/Qualifiers
REGION            1..126
source             note = chemically synthesized
                  1..126
                  mol_type = protein
                  organism = synthetic construct

SEQUENCE: 43
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFIGR LAWNAGSTDY 60
VESVKGRFTI SRDNPKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP 126

SEQ ID NO: 44      moltype = AA length = 8
FEATURE           Location/Qualifiers
REGION            1..8
source             note = chemically synthesized
                  1..8
                  mol_type = protein
                  organism = synthetic construct

SEQUENCE: 44
LAWNAGST 8

SEQ ID NO: 45      moltype = AA length = 126
FEATURE           Location/Qualifiers
REGION            1..126
source             note = chemically synthesized
                  1..126
                  mol_type = protein
                  organism = synthetic construct

SEQUENCE: 45
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFVSR LAWQGGSTDY 60
VESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP 126

SEQ ID NO: 46      moltype = AA length = 126
FEATURE           Location/Qualifiers
REGION            1..126
source             note = chemically synthesized
                  1..126
                  mol_type = protein
                  organism = synthetic construct

SEQUENCE: 46
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFVSR LAWNAGSTDY 60
VESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP 126

SEQ ID NO: 47      moltype = AA length = 126
FEATURE           Location/Qualifiers
REGION            1..126
source             note = chemically synthesized
                  1..126
                  mol_type = protein
                  organism = synthetic construct

SEQUENCE: 47
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREFVSR LAWGGGSTDY 60
VESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYWGQGT 120
LVTVKP 126

SEQ ID NO: 48      moltype = AA length = 8

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FEATURE	Location/Qualifiers
REGION	1..8
source	note = chemically synthesized
	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 48	
LAWGGGST	8
SEQ ID NO: 49	moltype = AA length = 126
FEATURE	Location/Qualifiers
REGION	1..126
source	note = chemically synthesized
	1..126
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 49	
EVQLLESGGG EVQPGGSLRL SCAASGWAFS NYGMAWFROA PGKEREVFSR LAWGGGSTDY	60
VESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYGQGT	120
LVTVKP	126
SEQ ID NO: 50	moltype = AA length = 8
FEATURE	Location/Qualifiers
REGION	1..8
source	note = chemically synthesized
	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 50	
GWAFSNYG	8
SEQ ID NO: 51	moltype = AA length = 126
FEATURE	Location/Qualifiers
REGION	1..126
source	note = chemically synthesized
	1..126
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 51	
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREVFSR LAWSGGSTDY	60
VESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYGQGT	120
LVTVKP	126
SEQ ID NO: 52	moltype = AA length = 8
FEATURE	Location/Qualifiers
REGION	1..8
source	note = chemically synthesized
	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 52	
LAWGGGST	8
SEQ ID NO: 53	moltype = AA length = 126
FEATURE	Location/Qualifiers
REGION	1..126
source	note = chemically synthesized
	1..126
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 53	
EVQLLESGGG EVQPGGSLRL SCAASGWAFS NYGMAWFROA PGKEREVFSR LAWSGGSTDY	60
VESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSRYDIRTP QTYDYGQGT	120
LVTVKP	126
SEQ ID NO: 54	moltype = AA length = 126
FEATURE	Location/Qualifiers
REGION	1..126
source	note = chemically synthesized
	1..126
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 54	
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFROA PGKEREVFSR LAWGGGSTDY	60
VESVKGRFTI SRDNAKNTLY LQMSSLRAED TAVYYCARQR SYSGYDIRTP QTYDYGQGT	120
LVTVKP	126

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SEQ ID NO: 55      moltype = AA  length = 19
FEATURE          Location/Qualifiers
REGION           1..19
source            note = chemically synthesized
                  1..19
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 55
ARQRYSYSGYD IRTPQTYDY                                         19

SEQ ID NO: 56      moltype = AA  length = 126
FEATURE          Location/Qualifiers
REGION           1..126
source            note = chemically synthesized
                  1..126
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 56
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFRQA PGKEREVFSR LAWGGGSTDY  60
VESVKGRFTI SRDNNAKNTLY LQMSSLRAED TAVYYCARQR SYSRGYIRTP QTYDYWGQGT 120
LVTVKP                                         126

SEQ ID NO: 57      moltype = AA  length = 19
FEATURE          Location/Qualifiers
REGION           1..19
source            note = chemically synthesized
                  1..19
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 57
ARQRYSYSGYD IRTPQTYDY                                         19

SEQ ID NO: 58      moltype = AA  length = 126
FEATURE          Location/Qualifiers
REGION           1..126
source            note = chemically synthesized
                  1..126
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 58
EVQLLESGGG EVQPGGSLRL SCAASGWAFG NYGMAWFRQA PGKEREVFSR LAWGGGSTDY  60
VESVKGRFTI SRDNNAKNTLY LQMSSLRAED TAVYYCARQR SYSGYGIRTP QTYDYWGQGT 120
LVTVKP                                         126

SEQ ID NO: 59      moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source            note = chemically synthesized
                  1..121
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 59
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKGLEWVA 1DSGRNTVYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCGLLK  NRVVSPSVAY WGQGTLVTVK 120
P                                         121

SEQ ID NO: 60      moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source            note = chemically synthesized
                  1..121
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 60
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IESGRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLK  NRVVSPSVAY WGQGTLVTVK 120
P                                         121

SEQ ID NO: 61      moltype = AA  length = 7
FEATURE          Location/Qualifiers
REGION           1..7
source            note = chemically synthesized
                  1..7
                  mol_type = protein
                  organism = synthetic construct

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SEQUENCE: 61
IESGRNT                                         7

SEQ ID NO: 62          moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source            1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 62
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IESGRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKQ NRVVSPSVAY WGQGTLVTVK 120
P                                         121

SEQ ID NO: 63          moltype = AA  length = 7
FEATURE          Location/Qualifiers
REGION           1..7
note = chemically synthesized
source            1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 63
IYSGRNT                                         7

SEQ ID NO: 64          moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source            1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 64
EVQLLESGGG EVQPGGSLRL SCAASGFTFS INAMGWYRQA PGKRREFVAA IESGRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKQ NRVVSPSVAY WGQGTLVTVK 120
P                                         121

SEQ ID NO: 65          moltype = AA  length = 8
FEATURE          Location/Qualifiers
REGION           1..8
note = chemically synthesized
source            1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 65
GFTFSINA                                         8

SEQ ID NO: 66          moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source            1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 66
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMSWYRQA PGKRREFVAA IESGRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKQ NRVVSPSVAY WGQGTLVTVK 120
P                                         121

SEQ ID NO: 67          moltype = AA  length = 8
FEATURE          Location/Qualifiers
REGION           1..8
note = chemically synthesized
source            1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 67
GFSFSINA                                         8

SEQ ID NO: 68          moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source            1..121
mol_type = protein
organism = synthetic construct

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SEQUENCE: 68
EVOLLESGGG EVQPGGSLRL SCAASGFTFS SNAMGWYRQA PGKRREFVAA IESGRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKG NRVVSPSVAY WGQGTLVTVK 120
P 121

SEQ ID NO: 69      moltype = AA length = 8
FEATURE          Location/Qualifiers
REGION           1..8
source            note = chemically synthesized
                 1..8
                 mol_type = protein
                 organism = synthetic construct
SEQUENCE: 69
GFTFSSNA

SEQ ID NO: 70      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source            note = chemically synthesized
                 1..121
                 mol_type = protein
                 organism = synthetic construct
SEQUENCE: 70
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IECSRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKG NRVVSPSVAY WGQGTLVTVK 120
P 121

SEQ ID NO: 71      moltype = AA length = 7
FEATURE          Location/Qualifiers
REGION           1..7
source            note = chemically synthesized
                 1..7
                 mol_type = protein
                 organism = synthetic construct
SEQUENCE: 71
IESSRNT          7

SEQ ID NO: 72      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source            note = chemically synthesized
                 1..121
                 mol_type = protein
                 organism = synthetic construct
SEQUENCE: 72
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IESGSNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKG NRVVSPSVAY WGQGTLVTVK 120
P 121

SEQ ID NO: 73      moltype = AA length = 7
FEATURE          Location/Qualifiers
REGION           1..7
source            note = chemically synthesized
                 1..7
                 mol_type = protein
                 organism = synthetic construct
SEQUENCE: 73
IESGSNT          7

SEQ ID NO: 74      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source            note = chemically synthesized
                 1..121
                 mol_type = protein
                 organism = synthetic construct
SEQUENCE: 74
EVOLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IESGRSTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKG NRVVSPSVAY WGQGTLVTVK 120
P 121

SEQ ID NO: 75      moltype = AA length = 7
FEATURE          Location/Qualifiers
REGION           1..7
source            note = chemically synthesized
                 1..7

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mol_type = protein
organism = synthetic construct
SEQUENCE: 75
IESGRST                                         7

SEQ ID NO: 76          moltype = AA length = 121
FEATURE
REGION
1..121
note = chemically synthesized
source
1..121
mol_type = protein
organism = synthetic construct
SEQUENCE: 76
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IESGRNTYYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKKG NRVVSPSVAY WGQGTLVTVK 120
P                                                 121

SEQ ID NO: 77          moltype = AA length = 7
FEATURE
REGION
1..7
note = chemically synthesized
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 77
IESGRNT                                         7

SEQ ID NO: 78          moltype = AA length = 121
FEATURE
REGION
1..121
note = chemically synthesized
source
1..121
mol_type = protein
organism = synthetic construct
SEQUENCE: 78
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IYGSSTTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKKG NRVVSPSVAY WGQGTLVTVK 120
P                                                 121

SEQ ID NO: 79          moltype = AA length = 7
FEATURE
REGION
1..7
note = chemically synthesized
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 79
IYGSST                                         7

SEQ ID NO: 80          moltype = AA length = 121
FEATURE
REGION
1..121
note = chemically synthesized
source
1..121
mol_type = protein
organism = synthetic construct
SEQUENCE: 80
EVQLLESGGG EVQPGGSLRL SCAAVGFSFS INAMGWYRQA PGKRREFVAA IESGRNTYYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKKG NRVVSPSVAY WGQGTLVTVK 120
P                                                 121

SEQ ID NO: 81          moltype = AA length = 121
FEATURE
REGION
1..121
note = chemically synthesized
source
1..121
mol_type = protein
organism = synthetic construct
SEQUENCE: 81
EVQLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFVAA IESGRNTYYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKKG NRVVSPSVAY WGQGTLVTVK 120
P                                                 121

SEQ ID NO: 82          moltype = AA length = 121
FEATURE
REGION
1..121

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source          note = chemically synthesized
               1..121
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 82
EVOLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKGREFVAA IESGRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKG NRVVSPSVAY WGQGTLVTVK 120
P                                         121

SEQ ID NO: 83      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source          note = chemically synthesized
               1..121
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 83
EVOLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQA PGKRREFLAA IESGRNTVYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKG NRVVSPSVAY WGQGTLVTVK 120
P                                         121

SEQ ID NO: 84      moltype = AA length = 119
FEATURE          Location/Qualifiers
REGION           1..119
source          note = chemically synthesized
               1..119
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 84
QVQLVQSGAE VKKPGSSVKV SCKASGGTFN SYAISWVRQA PGQGLEWMGG IIPGPGTANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARKN EEDGGFDHWG QGTLTVSS 119

SEQ ID NO: 85      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
source          note = chemically synthesized
               1..118
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 85
QVOLVESGGG LVQPGGSLRL SCAASGFTFS DYYMHWVRQA PGKGLEWVSV ISGSGSNTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARLY AQFEGDFWGQ GTLTVSS 118

SEQ ID NO: 86      moltype = AA length = 116
FEATURE          Location/Qualifiers
REGION           1..116
source          note = chemically synthesized
               1..116
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 86
QVQLVQSGAE VKKPGESLKI SCKGSGYSFS TYWISWVRQM PGKGLEWMGK IYPGDSYTNY 60
SPSFQGQVTI SADKSISTAY LQWSSLKASD TAMYYCARGY GIFDYWGQGT LTVSS 116

SEQ ID NO: 87      moltype = AA length = 116
FEATURE          Location/Qualifiers
REGION           1..116
source          note = chemically synthesized
               1..116
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 87
EVOLVQSGAE VKKPGESLRI SCKGSGYSFS TYWISWVRQM PGKGLEWMGK IYPGDSYTNY 60
SPSFQGQVTI SADKSISTAY LQWSSLKASD TAMYYCARGY GIFDYWGQGT LTVSS 116

SEQ ID NO: 88      moltype = AA length = 107
FEATURE          Location/Qualifiers
REGION           1..107
source          note = chemically synthesized
               1..107
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 88
DIELTQPPSV SVAPGQTARI SCSDNLGDY YASWYQQKPG QAPVLVIYDD SNRPSGIPER 60
FSGSNNSGNTA TLTISGTQAE DEADYYCQTW DGTLHFVFGG GTKLTVL 107

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SEQ ID NO: 89      moltype = AA length = 107
FEATURE          Location/Qualifiers
REGION           1..107
note = chemically synthesized
source            1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 89
DIELTQPPSV SVAPGQTARI SCSGDNIGSK YVSWYQQKPG QAPVLVIYSD SERPSGIPER 60
FSGSNNSGNTA TLTISGTQAE DEADYYCQSW DGSISRVPFG GTKLTVL 107

SEQ ID NO: 90      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 90
DIELTQPPSV SVAPGQTARI SCSGDNIGDQ YAHWYQQKPG QAPVVVIYQD KNRPSGIPER 60
FSGSNNSGNTA TLTISGTQAE DEADYYCATY TGFGSLAVFG GGTKLTVL 108

SEQ ID NO: 91      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 91
SYELTQPPSV SVSPGQTASI TCSGDNIGDQ YAHWYQQKPG QSPVLVIYQD KNRPSGIPER 60
FSGSNNSGNTA TLTISGTQAM DEADYYCATY TGFGSLAVFG GGTKLTVL 108

SEQ ID NO: 92      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 92
SYELTQPPSV SVSPGQTASI TCSGDNIGDQ YAHWYQQKPG QSPVVVIYQD KNRPSGIPER 60
FSGSNNSGNTA TLTISGTQAM DEADYYCATY TGFGSLAVFG GGTKLTVL 108

SEQ ID NO: 93      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 93
DIELTQPPSV SVAPGQTARI SCSGDNIGDQ YAHWYQQKPG QAPVVVIYQD KNRPSGIPER 60
FSGSNNSGNTA TLTISGTQAE DEADYYCSTY TFVGFTTVFG GGTKLTVL 108

SEQ ID NO: 94      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 94
SYELTQPPSV SVSPGQTASI TCSGDNIGDQ YAHWYQQKPG QSPVLVIYQD KNRPSGIPER 60
FSGSNNSGNTA TLTISGTQAM DEADYYCSTY TFVGFTTVFG GGTKLTVL 108

SEQ ID NO: 95      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 95
SYELTQPPSV SVSPGQTASI TCSGDNIGDQ YAHWYQQKPG QSPVVVIYQD KNRPSGIPER 60
FSGSNNSGNTA TLTISGTQAM DEADYYCSTY TFVGFTTVFG GGTKLTVL 108

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SEQ ID NO: 96      moltype = AA length = 448
FEATURE          Location/Qualifiers
REGION           1..448
note = chemically synthesized
source            1..448
mol_type = protein
organism = synthetic construct

SEQUENCE: 96
QVQLQQWGAG LLKPSETLSL TCAVYGGGSFS GYYWSWIROS PEKGLEWIGE INHGGYVTYN 60
PSLESRVTIS VDTSKNQFSL KLSSVTAADT AVYVCARDYG PGNYDWYFDL WGRGTLVTVS 120
SASTKGPSPV PLAPCSRSTS ESTAAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGKT TYTCNVDHKP SNTKVDKRVE SKYGPCCPC PAPEFLGGPS 240
VFLFPPKPKD TLMISRTPEV TCVVVDSVQE DPEVQFNWVY DGVEVHNNAKT KPREQFNST 300
YRVSVLTVL KQDWLNGKEY KCKVSNKGLP SIEKTISKKA QGQPREGQVY TLPPSQEEMT 360
KNQVSLTCLV KGFPYPSDIAY EWESNGQOPEN NYKTTTPVLD SDGSFFLYSR LTVDKSRWQE 420
GNVFSCSVMH EALHNHYTQK SLSLSLGK 448

SEQ ID NO: 97      moltype = AA length = 451
FEATURE          Location/Qualifiers
REGION           1..451
note = chemically synthesized
source            1..451
mol_type = protein
organism = synthetic construct

SEQUENCE: 97
QVQLQQWGAG LLKPSETLSL TCAVYGGGSFS GYYWSWIROS PEKGLEWIGE INHGGYVTYN 60
PSLESRVTIS VDTSKNQFSL KLSSVTAADT AVYVCARDYG PGNYDWYFDL WGRGTLVTVS 120
SASTKGPSPV PLAPSSKSTS GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGKT TYICNVNHNKP SNTKVDKRVE PKSCDKTHTC PPCPAPELLG 240
GPSVFLPPPK PDKDTLMISRT PEVTCVVVD SHEDPEVKFN WYVVDGEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG ALPKCIEKTI SKAKGQPREP QVYTLPPSRD 360
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTPV LDSDGSFFL YSKLTVDKSR 420
WQQGNVFCSCS VMHEALHNHY TQKSLSLSPG K 451

SEQ ID NO: 98      moltype = AA length = 216
FEATURE          Location/Qualifiers
REGION           1..216
note = chemically synthesized
source            1..216
mol_type = protein
organism = synthetic construct

SEQUENCE: 98
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWSQQPK QGAPRLLIYD ASN RATGIPA 60
RFGSGSGSTD FTLTISLEP EDFAVYYCQQ RSNWPPALTF GGGTKVEIKR TVAAPSIF 120
PPSDEQLKSG TASVVCALLNN FYPREAKVQW KVDNALQSGN SQESVTEQDS KDSTYLSST 180
LTLSKADYEK HKVYACEVTH QGLSSPVTKS FNRGEC 216

SEQ ID NO: 99      moltype = AA length = 178
FEATURE          Location/Qualifiers
REGION           1..178
note = chemically synthesized
source            1..178
mol_type = protein
organism = synthetic construct

SEQUENCE: 99
QDSTSDFLIPA PPLSKVPLQQ NFQDNQFHGK WYVVGQAGNI RLREDKDPIK MMATIYELKE 60
DKSYDVTMVK FDDKKCMYDI WTFVPGSQPG EFTLGKIKSF PGHTSSLVRV VSTNYNQHAM 120
VFFKFVFQNR EEFYITLYGR TKELTSELKE NFIRFSKSLG LPENHIVFPV PIDQCIDG 178

SEQ ID NO: 100     moltype = AA length = 109
FEATURE          Location/Qualifiers
REGION           1..109
note = chemically synthesized
source            1..109
mol_type = protein
organism = synthetic construct

SEQUENCE: 100
QVQLQESGGG LVQAGGSLRL ACTTSGGIFN IRPISWYRQP PGMQREWVAT IAFGGATNYA 60
NSIKGRFTAS RDNAKNTVYL QMNGLKPEDT AVYYCNAFEI WGQGTQVTV 109

SEQ ID NO: 101     moltype = AA length = 8
FEATURE          Location/Qualifiers
REGION           1..8
note = chemically synthesized
source            1..8

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mol_type = protein
organism = synthetic construct
SEQUENCE: 101
GGIFNIRP                                         8

SEQ ID NO: 102          moltype = AA length = 7
FEATURE           Location/Qualifiers
REGION            1..7
source             note = chemically synthesized
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 102
IAFGGAT                                         7

SEQ ID NO: 103          moltype = AA length = 5
FEATURE           Location/Qualifiers
REGION            1..5
source             note = chemically synthesized
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 103
NAPEI                                         5

SEQ ID NO: 104          moltype = AA length = 109
FEATURE           Location/Qualifiers
REGION            1..109
source             note = chemically synthesized
1..109
mol_type = protein
organism = synthetic construct
SEQUENCE: 104
QLQLQESGGG LVRAGGSSLRL ACTTSGGIFA IKPISWYRQP PGQEREWVTT TTSSGATNYA 60
NSIKGRFTVA RDNAKNTVYL QMNDLKLEDT AVYYCNFPEY WGQGTQVTW                         109

SEQ ID NO: 105          moltype = AA length = 8
FEATURE           Location/Qualifiers
REGION            1..8
source             note = chemically synthesized
1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 105
GGIFAIKP                                         8

SEQ ID NO: 106          moltype = AA length = 7
FEATURE           Location/Qualifiers
REGION            1..7
source             note = chemically synthesized
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 106
TTSSGAT                                         7

SEQ ID NO: 107          moltype = AA length = 5
FEATURE           Location/Qualifiers
REGION            1..5
source             note = chemically synthesized
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 107
NVFPEY                                         5

SEQ ID NO: 108          moltype = AA length = 109
FEATURE           Location/Qualifiers
REGION            1..109
source             note = chemically synthesized
1..109
mol_type = protein
organism = synthetic construct
SEQUENCE: 108
QVQLQESGGD LVQAGSSLRL ACATSGGVFN IRPISWYRQP PGKQREWVAT IASGGATNYA 60
NSIKGRFTAS RDNAKNTVYL QMNGLKPEDT AVYYCNAFPEY WGQGTQVTW                         109

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SEQ ID NO: 109      moltype = AA  length = 8
FEATURE
REGION
1..8
note = chemically synthesized
source
1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 109
GGVFNIRP

SEQ ID NO: 110      moltype = AA  length = 7
FEATURE
REGION
1..7
note = chemically synthesized
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 110
IASGGAT

SEQ ID NO: 111      moltype = AA  length = 5
FEATURE
REGION
1..5
note = chemically synthesized
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 111
NAFEV

SEQ ID NO: 112      moltype = AA  length = 109
FEATURE
REGION
1..109
note = chemically synthesized
source
1..109
mol_type = protein
organism = synthetic construct
SEQUENCE: 112
QVQLQQSGGG LVQAGGSLRL ACTTSGGIFN IRPISWYRQP PGMQREWVAT IASGGATNYA 60
NSIKGRFTAS RDNAKNTVYL QMNGLKPEDT AVYYCNTLNF WGRGTQVTV 109

SEQ ID NO: 113      moltype = AA  length = 5
FEATURE
REGION
1..5
note = chemically synthesized
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 113
NTLNF

SEQ ID NO: 114      moltype = AA  length = 109
FEATURE
REGION
1..109
note = chemically synthesized
source
1..109
mol_type = protein
organism = synthetic construct
SEQUENCE: 114
QVOLQESGGG LVQAGGSLRL ACTTSGGIFN IRPISWYRQP PGMQREWVAT IASGGATNYA 60
NSIKGRFTAS RDNAKNTVYL QMNGLKPEDT AVYYCNVFEI WGQGTQVTV 109

SEQ ID NO: 115      moltype = AA  length = 5
FEATURE
REGION
1..5
note = chemically synthesized
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 115
NVFEI

SEQ ID NO: 116      moltype = AA  length = 109
FEATURE
REGION
1..109

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source          note = chemically synthesized
               1..109
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 116
QVQLQQSGGG LVQAGGSSLRL ACITSGGIFN IRPISWYRQP PGKQREWVAT IASGGAANYA 60
NSIKGRFTAS RDNAKNTVYL QMNGLKPEDT AVYYCNAFEN WGQGTQVTW                      109

SEQ ID NO: 117      moltype = AA length = 7
FEATURE          Location/Qualifiers
REGION           1..7
note = chemically synthesized
source          1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 117
IASGGAA                                                 7

SEQ ID NO: 118      moltype = AA length = 5
FEATURE          Location/Qualifiers
REGION           1..5
note = chemically synthesized
source          1..5
mol_type = protein
organism = synthetic construct

SEQUENCE: 118
NAFEN                                                 5

SEQ ID NO: 119      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
note = chemically synthesized
source          1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 119
QVQLQESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLTVK P                      111

SEQ ID NO: 120      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
note = chemically synthesized
source          1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 120
EVQLQESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLTVK P                      111

SEQ ID NO: 121      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
note = chemically synthesized
source          1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 121
EVQLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLTVK P                      111

SEQ ID NO: 122      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
note = chemically synthesized
source          1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 122
EVQLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLTVK P                      111

SEQ ID NO: 123      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
note = chemically synthesized

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source          1..111
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 123
EVQVLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVTT TTSSGATNYA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCNVFEY WGQGTLTVK P           111

SEQ ID NO: 124      moltype = AA  length = 111
FEATURE          Location/Qualifiers
REGION           1..111
note = chemically synthesized
source            1..111
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 124
EVOLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLTVK P           111

SEQ ID NO: 125      moltype = AA  length = 111
FEATURE          Location/Qualifiers
REGION           1..111
note = chemically synthesized
source            1..111
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 125
PTFSPALLVV TEGDNATFTC SFSNTSESFV LNWYRMSPSN QTDKLAAFP E DRSQPGQDCR 60
FRVTQLPNR DFHMSVVRAR RNDSGTYLCG AISLAPKAQI KESLRAELRV T           111

SEQ ID NO: 126      moltype = AA  length = 117
FEATURE          Location/Qualifiers
REGION           1..117
note = chemically synthesized
source            1..117
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 126
QVQLVQSGAE VKKPGASVKV SCKASGYTFT DYGFISWVRQA PGQGLEWMGW ITAYNGNTNY 60
AQKLQGRVTM TTDTSSTVY MELSSLRSDD TAVYYCARDY FYGMDVWGQG TTVTVSS    117

SEQ ID NO: 127      moltype = AA  length = 123
FEATURE          Location/Qualifiers
REGION           1..123
note = chemically synthesized
source            1..123
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 127
QVQLVQSGAE VKKPGSSVKV SCKTSGDTFS TYAISWVRQA PGQGLEWMGG IIPIFGKAHY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYFCARKF HFVSGSPFGM DVWGQGTTVT 120
VSS              123

SEQ ID NO: 128      moltype = AA  length = 112
FEATURE          Location/Qualifiers
REGION           1..112
note = chemically synthesized
source            1..112
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 128
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYDVHWWVRQA PGQRLEWMGW LHADTGITKF 60
SQKFQGRVTI TRDTSASTAY MELSSLRSED TAVYYCARER IQLWFDYWGQ GT           112

SEQ ID NO: 129      moltype = AA  length = 120
FEATURE          Location/Qualifiers
REGION           1..120
note = chemically synthesized
source            1..120
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 129
QVQLVQSGAE VKKPGSSVKV SCKVSGGIFS TYAINWVRQA PGQGLEWMGG IIPIFGTANH 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARDQ GIAAALFDYW GQGTLTVSS    120

SEQ ID NO: 130      moltype = AA  length = 110
FEATURE          Location/Qualifiers

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REGION          1..110
source          note = chemically synthesized
                1..110
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 130
EVQLVESGGG LVQPGRSLRL SCAVSGFTFD DYVVHWVRQA PGKGLEWVSG NSGNIGYADS 60
VKGRFTISRD NAKNSLYLQM NSLRAEDTAL YYCAVPFDYW QQGTLVTVSS           110

SEQ ID NO: 131      moltype = AA length = 123
FEATURE          Location/Qualifiers
REGION           1..123
source            note = chemically synthesized
                1..123
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 131
QVQLVQSGAE VKKPGSSVKV SCKTSGDTFS SYAISWVRQA PGQGLEWMGG IIPIFGRAHY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYFCARKF HFVSGSPFGM DVWGQQTTVT 120
VSS                           123

SEQ ID NO: 132      moltype = AA length = 123
FEATURE          Location/Qualifiers
REGION           1..123
source            note = chemically synthesized
                1..123
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 132
QVQLVQSGAE VKKPGSSVKV SCKTSGGTFS SYAISWVRQA PGQGLEWMGG IIPIPGKAHY 60
AQKFQGRVTI TADESTTTAY MELSSLRSED TAVYYCARKY DYVSGSPFGM DVWGQQTTVT 120
VSS                           123

SEQ ID NO: 133      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source            note = chemically synthesized
                1..121
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 133
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAINWVRQA PGQGLEWMGG IIPIPGSANY 60
AQKFQDRVTI TADESTSAAY MELSSLRSED TAVYYCARDS SGWSRYYMDV WGQGTTVVS 120
S                           121

SEQ ID NO: 134      moltype = AA length = 123
FEATURE          Location/Qualifiers
REGION           1..123
source            note = chemically synthesized
                1..123
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 134
QVQLVQSGAE VKEPGSSVKV SCKASGGTFN SYAISWVRQA PGQGLEWMGG IIPLFGIAHY 60
AQKFQGRVTI TADESTNTAY MDLSSLRSED TAVYYCARKY SYVSGSPFGM DVWGQQTTVT 120
VSS                           123

SEQ ID NO: 135      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source            note = chemically synthesized
                1..121
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 135
EVQLVESGGG LVQPGRSLRL SCAASGITFD DYGMHWVRQA PGKGLEWVSG ISWNRGRIEY 60
ADSVVKGRFTI SRDNAKNSLY LQMNSLRAED TALYYCAKGR FRYFDWFLDY WGQGTLVTVS 120
S                           121

SEQ ID NO: 136      moltype = AA length = 120
FEATURE          Location/Qualifiers
REGION           1..120
source            note = chemically synthesized
                1..120
                mol_type = protein
                organism = synthetic construct

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SEQUENCE: 136
QMLVLQSGGG LVQPGGSLRL SCAASGFTFS SYWMSWVRQA PGKGLEWVAN IKQDGSEKYY 60
VDSVKGRFTI SRDNNAKNSLY LQMNSLRAED TAVYYCARDY FWSGFSAFDI WGKGTLVTVS 120

SEQ ID NO: 137      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
source             note = chemically synthesized
                   1..107
                   mol_type = protein
                   organism = synthetic construct
SEQUENCE: 137
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLVWYQQKP GQAPRLLIYD ASN RATGIPA 60
RFSGSGSGTD FTLLTISLEP EDFAVYYCQQ RSNWPTFGQ GTKVEIK 107

SEQ ID NO: 138      moltype = AA length = 106
FEATURE           Location/Qualifiers
REGION            1..106
source             note = chemically synthesized
                   1..106
                   mol_type = protein
                   organism = synthetic construct
SEQUENCE: 138
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA 60
RFSGSGSGTD FTLLTISLEP EDFAVYYCQQ RSNWPTFGQ TKVEIK 106

SEQ ID NO: 139      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
source             note = chemically synthesized
                   1..107
                   mol_type = protein
                   organism = synthetic construct
SEQUENCE: 139
DIQMTQSPSS LSASVGDRVT ITCRASQGIS SWLAWYQQKP EKAPKSLIYA ASSLQSGVPS 60
RFSGSGSGTD FTLLTISLQP EDFATYYCQQ YNSYPYTFQGQ GTKLEIK 107

SEQ ID NO: 140      moltype = AA length = 108
FEATURE           Location/Qualifiers
REGION            1..108
source             note = chemically synthesized
                   1..108
                   mol_type = protein
                   organism = synthetic construct
SEQUENCE: 140
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAQYQQK PGQAPRLLIY GASSRATGIP 60
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSSPWTFG QGTKVEIK 108

SEQ ID NO: 141      moltype = AA length = 106
FEATURE           Location/Qualifiers
REGION            1..106
source             note = chemically synthesized
                   1..106
                   mol_type = protein
                   organism = synthetic construct
SEQUENCE: 141
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAQYQQK PGQAPRLLIY GASSRATGIP 60
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSSPWTFGG TKVEIK 106

SEQ ID NO: 142      moltype = AA length = 106
FEATURE           Location/Qualifiers
REGION            1..106
source             note = chemically synthesized
                   1..106
                   mol_type = protein
                   organism = synthetic construct
SEQUENCE: 142
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAQYQQK GQAPRLLIYD ASN RATGIPA 60
RFSGSGSGTD FTLLTISLEP EDFAVYYCQQ RSNWPTFGQ TRLEIK 106

SEQ ID NO: 143      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
source             note = chemically synthesized
                   1..107
                   mol_type = protein

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SEQUENCE: 143          organism = synthetic construct
AIQLTQSPSS LSASVGDRVT ITCRASQGIS SALAWYQQKP GKAPKLLIYD ASSLESGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ FNSYPFTFGP GTKVDIK           107

SEQ ID NO: 144          moltype = AA length = 107
FEATURE
REGION
1..107
note = chemically synthesized
source
1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 144          moltype = AA length = 107
DIVMTQSPST LSASVGDRVT ITCRASQGIS SWLAWYQQKP GRAPKVLIYK ASTLESGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYSTPWTFGQ GTKLEIK           107

SEQ ID NO: 145          moltype = AA length = 121
FEATURE
REGION
1..121
note = chemically synthesized
source
1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 145          moltype = AA length = 121
EVQLVESGGG LVQPGGSLRL SCAASGFTFS RYWMSWVRQA PGKGLEWVAN IKQDGSEKYY 60
VDSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCAREG GWFGELAFDY WGQGTLVTVS 120
S                                         121

SEQ ID NO: 146          moltype = AA length = 108
FEATURE
REGION
1..108
note = chemically synthesized
source
1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 146          moltype = AA length = 108
EIVLTQSPGT LSLSPGERAT LSCRASQRVS SSYLAWSQQK PGQAPRLLIY DASSRATGIP 60
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSLPWTFG QGTKVKEIK           108

SEQ ID NO: 147          moltype = AA length = 118
FEATURE
REGION
1..118
note = chemically synthesized
source
1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 147          moltype = AA length = 118
EVQLVESGGG LVQPGGSLRL SCAASGFTFS DSWIHWWVRQA PGKGLEWVAW ISPYGGSTYY 60
ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCARRH WPGGFWDYWGQ GTLTVSA           118

SEQ ID NO: 148          moltype = AA length = 118
FEATURE
REGION
1..118
note = chemically synthesized
source
1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 148          moltype = AA length = 118
EVOLVESGGG LVQPGGSLRL SCAASGFTFS GSWIHWWVRQA PGKGLEWVAW ILPYGGSSYY 60
ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCARRH WPGGFWDYWGQ GTLTVSA           118

SEQ ID NO: 149          moltype = AA length = 108
FEATURE
REGION
1..108
note = chemically synthesized
source
1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 149          moltype = AA length = 108
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YLYHPATFGQ GTKVEIKR           108

SEQ ID NO: 150          moltype = AA length = 108
FEATURE
REGION
1..108
note = chemically synthesized

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source          1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 150
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YYNVPWTFGQ GTKVEIKR           108

SEQ ID NO: 151      moltype = AA  length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 151
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YYAPPWTFGQ GTKVEIKR           108

SEQ ID NO: 152      moltype = AA  length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 152
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YYTVPRTFGQ GTKVEIKR           108

SEQ ID NO: 153      moltype = AA  length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 153
DIQMTQSPSS LSASVGDRVT ITCRASQVIN TFLAWYQQKP GKAPKLLIYS ASTLASGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YYTVPRTFGQ GTKVEIKR           108

SEQ ID NO: 154      moltype = AA  length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 154
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ GYGVPRTFGQ GTKVEIKR           108

SEQ ID NO: 155      moltype = AA  length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 155
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YLFTPPTFGQ GTKVEIKR           108

SEQ ID NO: 156      moltype = AA  length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 156
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YFITPTTFGQ GTKVEIKR           108

SEQ ID NO: 157      moltype = AA  length = 108
FEATURE          Location/Qualifiers
REGION           1..108

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source          note = chemically synthesized
               1..108
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 157
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YYTTPPTFGQ GTKVEIKR           108

SEQ ID NO: 158      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 158
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ FFYTPPTFGQ GTKVEIKR           108

SEQ ID NO: 159      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 159
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ SLFTPPTFGQ GTKVEIKR           108

SEQ ID NO: 160      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 160
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ SLYTPPTFGQ GTKVEIKR           108

SEQ ID NO: 161      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 161
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ SWYHPPTFGQ GTKVEIKR           108

SEQ ID NO: 162      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 162
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YFYIPPTFGQ GTKVEIKR           108

SEQ ID NO: 163      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
note = chemically synthesized
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 163
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD FTLTSSLQP EDFATYYCQQ YWYTPPTFGQ GTKVEIKR           108

SEQ ID NO: 164      moltype = AA length = 108
FEATURE          Location/Qualifiers

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REGION          1..108
source          note = chemically synthesized
                1..108
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 164
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKQ GKAPKLLIYS ASFLYSGVPS 60
RFSGSGSGTD PTLTISSLQP EDFATYYCQQ SYFIPPTFGQ GTKVEIKR           108

SEQ ID NO: 165      moltype = AA length = 141
FEATURE          Location/Qualifiers
REGION           1..141
source            note = chemically synthesized
                1..141
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 165
METGLRLWLLL VAVLKGVQCL SVEESGGRLV TPGTPLTLTC TASGFTITNY HMFWVRQAPG 60
KGLEWIGVIT SSGIGSSSTT YYATWAKGRF TISKTTSTVN LRITSPTTED TATYFCARDY 120
FTNTYYALDI WGPGLTVTS S                           141

SEQ ID NO: 166      moltype = AA length = 123
FEATURE          Location/Qualifiers
REGION           1..123
source            note = chemically synthesized
                1..123
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 166
QVQLVQSGAE VKKPGSSVKV SCKTSGDTFS TYAISWVRQA PGQGLEWMGG IIPIPGKAHY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYFCARKF HFVSGSPFGM DVWGQGTTVT 120
VSS                           123

SEQ ID NO: 167      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
source            note = chemically synthesized
                1..118
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 167
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYDVHWRQQA PGQRLEWMGW LHADTGITKF 60
SQKFQGRVTI TRDTSASTAY MELSSLRSED TAVYYCARER IQLWFDYWQ GTLTVSS       118

SEQ ID NO: 168      moltype = AA length = 120
FEATURE          Location/Qualifiers
REGION           1..120
source            note = chemically synthesized
                1..120
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 168
QVQLVQSGAE VKKPGSSVKV SCKVSGGIFS TYAINWVRQA PGQGLEWMGG IIPIPGTANH 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARQD GIAAAFLDYW GQGTLTVSS 120

SEQ ID NO: 169      moltype = AA length = 113
FEATURE          Location/Qualifiers
REGION           1..113
source            note = chemically synthesized
                1..113
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 169
EVQLVESGGG LVQPGRSRL SCAVSGFTFD DYVWHWRQQA PGKGLEWVSG ISGNNSGNIGY 60
ADSVKGRFTI SRDNNAKNSLY LQMNSLRAED TALYYCAVPF DYWGQGTLVTVSS        113

SEQ ID NO: 170      moltype = AA length = 123
FEATURE          Location/Qualifiers
REGION           1..123
source            note = chemically synthesized
                1..123
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 170
QVQLVQSGAE VKKPGSSVKV SCKTSGDTFS SYAISWVRQA PGQGLEWMGG IIPIFGRAHY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYFCARKF HFVSGSPFGM DVWGQGTTVT 120

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VSS		123
SEQ ID NO: 171	moltype = AA length = 123	
FEATURE	Location/Qualifiers	
REGION	1..123	
	note = chemically synthesized	
source	1..123	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 171		
QVQLVQSGAE VKKPGSSVKV SCKTSGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGKAHY	60	
AQKFQGRVTI TADESTTAY MELSSLRSED TAVYYCARKY DYVSGSPFGM DVWGQQTTVT	120	
VSS	123	
SEQ ID NO: 172	moltype = AA length = 121	
FEATURE	Location/Qualifiers	
REGION	1..121	
	note = chemically synthesized	
source	1..121	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 172		
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAINWVRQA PGQGLEWMGG IIPIFGSANY	60	
AQKFQDRVTI TADESTSAAY MELSSLRSED TAVYYCARSKY SYVSGSPFGM DVWGQTTTVS	120	
S	121	
SEQ ID NO: 173	moltype = AA length = 123	
FEATURE	Location/Qualifiers	
REGION	1..123	
	note = chemically synthesized	
source	1..123	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 173		
QVQLVQSGAE VKEPGSSVKV SCKASGGTFN SYAISWVRQA PGQGLEWMGG IIPLFGIAHY	60	
AQKFQGRVTI TADESTNTAY MDLSSLRSED TAVYYCARSKY SYVSGSPFGM DVWGQTTTVS	120	
VSS	123	
SEQ ID NO: 174	moltype = AA length = 121	
FEATURE	Location/Qualifiers	
REGION	1..121	
	note = chemically synthesized	
source	1..121	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 174		
EVOLVESGGG LVQPGRSLRL SCAASGITFD DYGMHWVRQA PGKGLEWVSG ISWNRGRIEY	60	
ADSVVKGRPTI SRDNAKNSLY LQMNSLRAED TALYYCAKGR FRYFDWFLDY WGQGTLVTVS	120	
S	121	
SEQ ID NO: 175	moltype = AA length = 116	
FEATURE	Location/Qualifiers	
REGION	1..116	
	note = chemically synthesized	
source	1..116	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 175		
MDTRAPTQLL GLLLLWLPGA RCALVMTQTP SSTSTAVGGT VTIKCQASQS ISVYLAWYQQ	60	
KPGQPPKLLI YSASTLASGV PSRFKGSRSRTEYTLTISGV QREDAATYYC LGSAGS	116	
SEQ ID NO: 176	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
REGION	1..107	
	note = chemically synthesized	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 176		
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLVWYQQKP QQAPRLLIYD ASN RATGIPA	60	
RFSGSGSGTD FTLTISLEP EDFAVYYCQQ RSNWPRTFGQ GTKVEIK	107	
SEQ ID NO: 177	moltype = AA length = 106	
FEATURE	Location/Qualifiers	
REGION	1..106	
	note = chemically synthesized	

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source          1..106
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 177
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA 60
RFSGSGSGTD FTLTISSLQP EDFAVYYCQQ RSNWPTFGQG TKVEIK                106

SEQ ID NO: 178      moltype = AA  length = 107
FEATURE           Location/Qualifiers
REGION            1..107
note = chemically synthesized
source             1..107
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 178
DIQMTQSPSS LSASVGDRVT ITCRASQGIS SWLAWYQQKP EKAPKSLIYA ASSLQSGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YNSYPYTFQG GTKLEIK                107

SEQ ID NO: 179      moltype = AA  length = 108
FEATURE           Location/Qualifiers
REGION            1..108
note = chemically synthesized
source             1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 179
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWYQQK PGQAPRLLIY GASSRATGIP 60
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSSPWTFG QGTKVEIK                108

SEQ ID NO: 180      moltype = AA  length = 106
FEATURE           Location/Qualifiers
REGION            1..106
note = chemically synthesized
source             1..106
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 180
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWYQQK PGQAPRLLIY GASSRATGIP 60
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSSPFGGG TKVEIK                106

SEQ ID NO: 181      moltype = AA  length = 106
FEATURE           Location/Qualifiers
REGION            1..106
note = chemically synthesized
source             1..106
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 181
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA 60
RFSGSGSGTD FTLTISSLQP EDFAVYYCQQ RSNWPTFGQG TRLEIK                106

SEQ ID NO: 182      moltype = AA  length = 107
FEATURE           Location/Qualifiers
REGION            1..107
note = chemically synthesized
source             1..107
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 182
AIQLTQSPSS LSASVGDRVT ITCRASQGIS SALAWYQQKP GKAPKLLIYD ASSLESGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ FNSYPFTFGP GTKVDIK                107

SEQ ID NO: 183      moltype = AA  length = 120
FEATURE           Location/Qualifiers
REGION            1..120
note = chemically synthesized
source             1..120
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 183
EVOLLESGGG LVQPGGSLRL SCAASGFTFS SYIMMWVRQKA PGKGLEWVSS IYPSGGITFY 60
ADTVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARIK LGTVTTVDYW GQGTLVTVSS 120

SEQ ID NO: 184      moltype = AA  length = 110
FEATURE           Location/Qualifiers
REGION            1..110

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source          note = chemically synthesized
               1..110
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 184
QSALTQPASV SGSPGQSQTI SCTGTSSDV GYNYVSWYQQ HPGKAPKLMI YDVSNRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSSTRV FGTGTVTQL 110

SEQ ID NO: 185      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source            1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 185
EVKLQESGPS LVKPSQTL SL TCSVTGYSIT SDYWNWIRKF PGNKLEYVGY ISYTGSTYYN 60
PSLKSRSI SIT RDT SKN QYYL QLNSVTSEDT ATYYCARYGG WLSPFDYWGQ GTTLTVSS 118

SEQ ID NO: 186      moltype = AA length = 120
FEATURE          Location/Qualifiers
REGION           1..120
note = chemically synthesized
source            1..120
mol_type = protein
organism = synthetic construct
SEQUENCE: 186
EVQLQESGPV LVAPSQSL SI TCTVSGFSL TYSINWIRO PPGKGLEWLGV MWAGGGTNSN 60
SVLKSRLII S KDN SKS QVFL KMNSLQTD DT ARYYCARYGG NSPYAIDYW GQGTSVTVSS 120

SEQ ID NO: 187      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source            1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 187
EVKLQESGPS LVKPSQTL SL TCSVTGYSII SDYWNWIRKF PGNKLEYLG Y ISYTGSTYYN 60
PSLKSRSI SIT RDT SKN QYYL QLNSVTTEDT ATYYCARRGG WLSPFDYWGQ GTTLTVSS 118

SEQ ID NO: 188      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source            1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 188
EVKLQESGPS LVKPGASVKL SCKASGYTFT SYDINWVKQR PGQGLEWIGW IFPRDNNTKY 60
NENFKKGATL TVD TSSTTAY MELHSLTSED SAVYFCTKEN WVGDFDYWGQ GTTLTLSS 118

SEQ ID NO: 189      moltype = AA length = 114
FEATURE          Location/Qualifiers
REGION           1..114
note = chemically synthesized
source            1..114
mol_type = protein
organism = synthetic construct
SEQUENCE: 189
EVOLQOQSGPD LVTPGASVRI SCQASGYTFF DYMMNWKQS HGKSLEWIGD IDPNYGGTTY 60
NQKFKKGAIL TVDRSSSTAY MELRSLTSED SAVYYCARGA LTDWGQGTSL TVSS 114

SEQ ID NO: 190      moltype = AA length = 106
FEATURE          Location/Qualifiers
REGION           1..106
note = chemically synthesized
source            1..106
mol_type = protein
organism = synthetic construct
SEQUENCE: 190
EIVLTQSPAT LSLSPGERAT LSCRASSSVS YIYWFQQKPG QSPRPLIYAA FN RATGIPAR 60
FSGSGSGTDY TLTISSLEPE DFAVYYCQW SN NPLTFGQG TKVEIK 106

SEQ ID NO: 191      moltype = AA length = 114
FEATURE          Location/Qualifiers

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REGION          1..114
source          note = chemically synthesized
                1..114
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 191
QVQLVQSGAE VKKPGASVKV SCKASGYTFF DYMMNWRQQA PGQGLEWMGD IDPNYGGTNY 60
AQKFQGRVTM TRDTSISTAY MELSRLRSDD TAVYYCARGA LTDWGQGTMV TVSS      114

SEQ ID NO: 192      moltype = AA length = 114
FEATURE          Location/Qualifiers
REGION           1..114
source            note = chemically synthesized
                1..114
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 192
QVQLVQSGAE VKKPGASVKV SCKASGYTFF DYMMNWRQQA PGQSLEWMGD IDPNYGGTNY 60
NQKFQGRVTM TRDTSISTAY MELSRLRSDD TAVYYCARGA LTDWGQGTMV TVSS      114

SEQ ID NO: 193      moltype = AA length = 114
FEATURE          Location/Qualifiers
REGION           1..114
source            note = chemically synthesized
                1..114
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 193
EVQLVQSGAE VKKPGASVKV SCKASGYTFF DYMMNWRQQA PGQSLEWMGD IDPNYGGTNY 60
NQKFQGRVTM TVDRSSSTAY MELSRLRSDD TAVYYCARGA LTDWGQGTMV TVSS      114

SEQ ID NO: 194      moltype = AA length = 114
FEATURE          Location/Qualifiers
REGION           1..114
source            note = chemically synthesized
                1..114
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 194
EVQLVESGGG LVQPGRSLRL SCTASGYTFF DYMMNWRQQA PGKGLEWVGD IDPNYGGTTY 60
AASVKGRFTI SVDRSKSIAY LQMSSLKTED TAVYYCTRGA LTDWGQGTMV TVSS      114

SEQ ID NO: 195      moltype = AA length = 114
FEATURE          Location/Qualifiers
REGION           1..114
source            note = chemically synthesized
                1..114
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 195
EVQLVESGGG LVQPGRSLRL SCTASGYTFF DYMMNWRQQA PGKGLEWVGD IDPNYGGTTY 60
NASVKGRFTI SVDRSKSIAY LQMSSLKTED TAVYYCARGA LTDWGQGTMV TVSS      114

SEQ ID NO: 196      moltype = AA length = 107
FEATURE          Location/Qualifiers
REGION           1..107
source            note = chemically synthesized
                1..107
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 196
DIVMTQSHKL MSTSVGDRVS ITCKASQDVG TAVAWYQQKP GQSPKLLIYW ASTRHTGVPD 60
RFTGSGSGTD FTLTISNVQS EDLADYFCQQ DSSYPLTFGA GTKVELK      107

SEQ ID NO: 197      moltype = AA length = 107
FEATURE          Location/Qualifiers
REGION           1..107
source            note = chemically synthesized
                1..107
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 197
DIVTTQSHKL MSTSVGDRVS ITCKASQDVG TAVAWYQQKP GQSPKLLIYW ASTRHTGVPD 60
RFTGSGSGTD FTLTISNVQS EDLADYFCQQ DSSYPLTFGA GTKVELK      107

SEQ ID NO: 198      moltype = AA length = 113

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FEATURE	Location/Qualifiers
REGION	1..113
source	note = chemically synthesized 1..113 mol_type = protein organism = synthetic construct
SEQUENCE: 198	
DIVMTQSPSS LAVSVGEKVS MGCKSSQSLL YSSNQKNSLA WYQQKPGQSP KLLIDWASTR	60
ESGPVPDRFTG SGSGTDFTLT ISSVKAEDLA VYYCQQYYGY PLTFGAGTKL ELK	113
SEQ ID NO: 199	moltype = AA length = 106
FEATURE	Location/Qualifiers
REGION	1..106
source	note = chemically synthesized 1..106 mol_type = protein organism = synthetic construct
SEQUENCE: 199	
DIVMTQSPAI MSASPGEKVT MTCASSSIR YMHWYQQKPG TSPKRWISDT SKLTSGVPAR	60
FSGSGSGTSY ALTISSMEAE DAATYYCHQR SSYPWTFGGG TKLEIK	106
SEQ ID NO: 200	moltype = AA length = 106
FEATURE	Location/Qualifiers
REGION	1..106
source	note = chemically synthesized 1..106 mol_type = protein organism = synthetic construct
SEQUENCE: 200	
QIVLSQSPAI LSASPGEKVT MTCRASSSVS YIYWFQQKPG SSPKPWIYAT FNLASGVPAR	60
FSGSGSGTSY SLTISRVETE DAATYYCQOW SNNPLTFGAG TKLELK	106
SEQ ID NO: 201	moltype = AA length = 106
FEATURE	Location/Qualifiers
REGION	1..106
source	note = chemically synthesized 1..106 mol_type = protein organism = synthetic construct
SEQUENCE: 201	
EIVLTQSPAT LSLSPGERAT LSCRASSSVS YIYWFQQKPG QAPRLLIYAA FNRATGIPAR	60
FSGSGSGTDY TLTISSLEPE DFAVYYCQOW SNNPLTFGQG TKVEIK	106
SEQ ID NO: 202	moltype = AA length = 106
FEATURE	Location/Qualifiers
REGION	1..106
source	note = chemically synthesized 1..106 mol_type = protein organism = synthetic construct
SEQUENCE: 202	
QIVLTQSPAT LSLSPGERAT LSCRASSSVS YIYWFQQKPG QSPPRLIYAT FNLASGIPAR	60
FSGSGSGTSY TLTISSLEPE DFAVYYCQOW SNNPLTFGQG TKVEIK	106
SEQ ID NO: 203	moltype = AA length = 106
FEATURE	Location/Qualifiers
REGION	1..106
source	note = chemically synthesized 1..106 mol_type = protein organism = synthetic construct
SEQUENCE: 203	
DIQLTQSPSS LSASVGDRVT ITCRASSGVY YIYWFQQKPG KAPKLLIYAA FNLASGVPSR	60
FSGSGSGTEY TLTISSLQPE DFATYYCQOW SNNPLTFGQG TKVEIK	106
SEQ ID NO: 204	moltype = AA length = 106
FEATURE	Location/Qualifiers
REGION	1..106
source	note = chemically synthesized 1..106 mol_type = protein organism = synthetic construct
SEQUENCE: 204	
DIQLTQSPSS LSASVGDRVT ITCRASSGVY YIYWFQQKPG KAPKPLIYAA FNLASGVPSR	60
FSGSGSGTEY TLTISSLQPE DFATYYCQOW SNNPLTFGQG TKVEIK	106

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SEQ ID NO: 205      moltype = AA length = 106
FEATURE          Location/Qualifiers
REGION           1..106
note = chemically synthesized
source            1..106
mol_type = protein
organism = synthetic construct
SEQUENCE: 205
DIQLTQSPSI LSASVGRVT ITCRASSVS YIYWFQQKPG KAPKPLIYAT FNLASGVPSR 60
FSGSGSGTSY TLTISSLQPE DFATYYCQW SNNPLTFGQG TKVEIK 106

SEQ ID NO: 206      moltype = AA length = 124
FEATURE          Location/Qualifiers
REGION           1..124
note = chemically synthesized
source            1..124
mol_type = protein
organism = synthetic construct
SEQUENCE: 206
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYGISWVRQA PGQGLEWMGW ISAYNGNTNY 60
AQKLQGRVTM TTDSTSTAY MELRSLRSDD TAVYYCARAL PSGTILVGGW FDPWGQGTLV 120
TVSS                           124

SEQ ID NO: 207      moltype = AA length = 124
FEATURE          Location/Qualifiers
REGION           1..124
note = chemically synthesized
source            1..124
mol_type = protein
organism = synthetic construct
SEQUENCE: 207
EVQLVQSGGG VVQPGRLRL SCAASGFTPS SYALSWVRQA PGKGLEWVSA ISGGGGSTYY 60
ADSVKGRTI SRDNNSKNTLY LQMNSLRAED TAVYYCAKDV FPETFSMNYG MDVWGQGTLV 120
TVSS                           124

SEQ ID NO: 208      moltype = AA length = 128
FEATURE          Location/Qualifiers
REGION           1..128
note = chemically synthesized
source            1..128
mol_type = protein
organism = synthetic construct
SEQUENCE: 208
QVQLVQSGGG VVQPGGSLRL SCAASGFTFD DYAMHWVRQA PGKGLEWVSL ISGDGGSTYY 60
ADSVKGRTI SRDNNSKNLTY LQMNSLRTEA TALYYCAKVL LPCSSTSCYG SVGAPDIWGQ 120
GTTTVVSS                         128

SEQ ID NO: 209      moltype = AA length = 117
FEATURE          Location/Qualifiers
REGION           1..117
note = chemically synthesized
source            1..117
mol_type = protein
organism = synthetic construct
SEQUENCE: 209
QVQLVQSGGS VVRPGESLRL SCVASGFIFD NYDMMSWVRQV PGKGLEWVSR VNWNNGGTTY 60
ADAVKGRTI SRDNNTKNSLY LQMNNLRAED TAVYYCVREF VGAYDLWGQG TTWTVSS 117

SEQ ID NO: 210      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source            1..121
mol_type = protein
organism = synthetic construct
SEQUENCE: 210
QVQLVQSGAE VKKPGATVKV SCKVFGDTFR GLYIHWRQQA PGQGLEWMGG IIPIFGTANY 60
AQKFQGRVTI TTDESTSTAY MELSSLRSED TAVYYCASGL RWGIWGWFDP WGQGTLVTVS 120
S                           121

SEQ ID NO: 211      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source            1..121
mol_type = protein

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SEQUENCE: 211          organism = synthetic construct
EVQLVQSGAE LKKPGSSVKV SCKAFGGTFS DNAISWVRQA PGQGPEWMGG IIPIFGKPNY 60
AQKFQGRVTI TADESTSTAY MVLSSLRSED TAVYYCARTM VRGFLGVMDV WGQGTTVTVS 120
S                                         121

SEQ ID NO: 212          moltype = AA length = 125
FEATURE
REGION
1..125
note = chemically synthesized
source
1..125
mol_type = protein
organism = synthetic construct

SEQUENCE: 212          organism = synthetic construct
QVQLVQSGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA ISGSGGSTYY 60
ADSVVKGRFTI SRDNSKNLY LQMNLSRAED TAVYYCAKDO FVTIFGVPRY GMDVWGQGTT 120
VTVSS                                         125

SEQ ID NO: 213          moltype = AA length = 120
FEATURE
REGION
1..120
note = chemically synthesized
source
1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 213          organism = synthetic construct
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGTANY 60
AQKFQGRVTI TADKSTSTAY MELSSLRSED TAVYYCARGR QMFGAGIDFW GPGTLTVSS 120

SEQ ID NO: 214          moltype = AA length = 118
FEATURE
REGION
1..118
note = chemically synthesized
source
1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 214          organism = synthetic construct
EVQLVESGAE VKKPGSSVKV SCKVSGGTFG TYALNWVRQA PGQGLEWMGR IVPLIGLVNY 60
AHNFEGRISI TADKSTGTAY MELSNLRSDD TAVYYCAREV YGGNSDYWGQ GTLTVSS 118

SEQ ID NO: 215          moltype = AA length = 120
FEATURE
REGION
1..120
note = chemically synthesized
source
1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 215          organism = synthetic construct
QVQLVQSGGE VKKPGASVKV SCKASGYTLS SHGITWVRQA PGQGLEWMGW ISAHNGHASN 60
AQKVVEDRVTM TTDTSTNTAY MELRSLTADD TAVYYCARVH AALYYGMDVW GQGTLTVSS 120

SEQ ID NO: 216          moltype = AA length = 121
FEATURE
REGION
1..121
note = chemically synthesized
source
1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 216          organism = synthetic construct
QVQLQESGGG VVQPGRSLRL SCSASGFTFS RHGMHWVRQA PGKGLEWVAV ISHDGSVKYY 60
ADSMKGRFSI SRDNNNNTLY LQMDSLRADD TAVYYCARGL SYQVSGWFDP WGQGTLTVS 120
S                                         121

SEQ ID NO: 217          moltype = AA length = 110
FEATURE
REGION
1..110
note = chemically synthesized
source
1..110
mol_type = protein
organism = synthetic construct

SEQUENCE: 217          organism = synthetic construct
NFMLTQPHSV SESPGKTVTI SCTRSGGSIA SNYVQWYQQR PGSSPTTVIY EDNQRPSGVP 60
DRFSGSIDTS SNSASLTISG LTKDEADYY CQSYDGITVI FGGGTLTVL 110

SEQ ID NO: 218          moltype = AA length = 111
FEATURE
Location/Qualifiers

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REGION          1..111
source          note = chemically synthesized
                1..111
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 218
NFMLTQPHSV SGSPGKTVTL PCTRSGSIA SHYVQWYQQR PGSAPTTVIY EDNKRPSGVP 60
DRFSGSIDSS SNSASLSISG LKTEDEADYY CQSYDSSNRW VFGGGTKLTV L           111

SEQ ID NO: 219      moltype = AA length = 115
FEATURE          Location/Qualifiers
REGION           1..115
source            note = chemically synthesized
                1..115
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 219
LPVLTQPAKL SASPGASASL TCTLRSGLNV GSYRIYWYQQ KPGSRPQYLL NYKSDSNKQQ 60
ASGVPSRFSG SKDASANAGI LLISGLQSED EADYYCMIWY SSAVVFGGGT KLTVL     115

SEQ ID NO: 220      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
source            note = chemically synthesized
                1..111
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 220
NFMLTQPHSV SESPGKTVTI SCTRSGSIA SNYVQWYQQR PGSAPTTVIY EDNQRPSGVP 60
DRFSGSIDSS SNSASLTISG LKTEDEADYY CQSYDSSNLW VFGGGTKLTV L           111

SEQ ID NO: 221      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
source            note = chemically synthesized
                1..108
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 221
SSELTLQDPAV SVALGQTVRI TCQGDLSLRSY YASWYQQKPG QAPVLVIYGK NNRPSGIPDR 60
FSGSSSGNTA SLTITGAQAE DEADYYCNSR DSSGNHYVFG TGTKVTVL             108

SEQ ID NO: 222      moltype = AA length = 108
FEATURE          Location/Qualifiers
REGION           1..108
source            note = chemically synthesized
                1..108
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 222
LPVLTQAPSV SVAPGKTARI TCGGSDIGRK SVHWHYQQKPG QAPALVIYSD RDRPSGISER 60
FSGSNNSGNTA TLTISRVEAG DEADYYCQWV DNNNSDHVYVFG AGTELIVL             108

SEQ ID NO: 223      moltype = AA length = 109
FEATURE          Location/Qualifiers
REGION           1..109
source            note = chemically synthesized
                1..109
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 223
QSALTQPASV SGSPGQSITI SCTGTSSDVG GYNYVSWYQQ HPGKAPKLMY YDVSNRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSTLPF GGGTKLTVL             109

SEQ ID NO: 224      moltype = AA length = 107
FEATURE          Location/Qualifiers
REGION           1..107
source            note = chemically synthesized
                1..107
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 224
EIVLTQSPAT LSLSPGERAT LSCRASQSISG NSLAWYQQKPG QOAPRLLMYG ASSRATGIPD 60
RFSGSGAGTD FTLTISLEP EDFATYYCQQ HTIPTFSFGP GTKVEVK             107

SEQ ID NO: 225      moltype = AA length = 107

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FEATURE	Location/Qualifiers
REGION	1..107
source	note = chemically synthesized 1..107 mol_type = protein organism = synthetic construct
SEQUENCE: 225	
DIVMTQTPSF LSASIGDRVT ITCRASQGIG SYLAWYQQRP GEAPKLLIYA ASTLQSGVPS	60
RFSGSGSGTD FTLTISNLQP EDFATYYCQQ LNNYPITFGQ GTRLEIK	107
SEQ ID NO: 226	moltype = AA length = 105
FEATURE	Location/Qualifiers
REGION	1..105
source	note = chemically synthesized 1..105 mol_type = protein organism = synthetic construct
SEQUENCE: 226	
QSALTQPPSV SVSPGQTANI PCSGDKLGNK YAYWYQQKPG QSPVLLIYQD IKRPSRIPER	60
FSGSNSADTA TLTISGTQAM DEADYYCQTW DNSVVFGGGT KLTVL	105
SEQ ID NO: 227	moltype = AA length = 112
FEATURE	Location/Qualifiers
REGION	1..112
source	note = chemically synthesized 1..112 mol_type = protein organism = synthetic construct
SEQUENCE: 227	
NFMLTQPHSV SESPGKTVTI SCTRSGSID SNYVQWYQQR PGSAPTTVIY EDNQRPSGVP	60
DRFSGSIDSS SNSASLTISG LKTEDEADYY CQSYDSNNRH VIFGGGTLKLT VL	112
SEQ ID NO: 228	moltype = AA length = 110
FEATURE	Location/Qualifiers
REGION	1..110
source	note = chemically synthesized 1..110 mol_type = protein organism = synthetic construct
SEQUENCE: 228	
NFMLTQPHSV SESPGKTVTI SCTRSGGNIG TNYVQWYQQR PGSAPVALIY EDYRRPSGVP	60
DRFSGSIDSS SNSASLIISG LKPEDEADYY CQSYHSSGW FGGGTLKLT VL	110
SEQ ID NO: 229	moltype = AA length = 108
FEATURE	Location/Qualifiers
REGION	1..108
source	note = chemically synthesized 1..108 mol_type = protein organism = synthetic construct
SEQUENCE: 229	
QSVLTQPPSV SVAPGQTARI TCGGNIGNSK GVHWYQQKPG QAPVLVYDD SDRPSGIPER	60
FSGSNSNGNTA TLTISRVEAG DEADYYCQW DSSSDHWVFG GGTKLTVL	108
SEQ ID NO: 230	moltype = AA length = 111
FEATURE	Location/Qualifiers
REGION	1..111
source	note = chemically synthesized 1..111 mol_type = protein organism = synthetic construct
SEQUENCE: 230	
NFMLTQPHSV SESPGKTVTI SCTRSGSIA SNYVQWYQQR PGSAPTTVIY EDNQRPSGVP	60
DRFSGSIDSS SNSASLTISG LKTEDEADYY CQSYDSTTPS VFGGGTLTV L	111
SEQ ID NO: 231	moltype = AA length = 120
FEATURE	Location/Qualifiers
REGION	1..120
source	note = chemically synthesized 1..120 mol_type = protein organism = synthetic construct
SEQUENCE: 231	
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYGISWVRQA PGQGLEWMGW TSPHNGLTAF	60
AQILEGRVTM TTDTSNTAY MELRNLTFFD TAVYFCAKVH PVFSYALDVW GQGTLTVSS	120

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SEQ ID NO: 232      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source            1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 232
EVQLVESGAE VMNPNGSSVRV SCRGSGGDFS TYAFSWVRQA PGQGLEWMGR IIPILGIANY 60
AQKFQGRVTI TADKSTSTAY MELSSLRSDD TAVYYCARDG YGSDPVLWGQ GTLTVSS 118

SEQ ID NO: 233      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source            1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 233
EVOLVQSGAE VKKPGASVKV SCKASGYTFT NYGISWVRQA PGQGLEWMGW ISAYNGNTNY 60
AQKVQGRVTM TTDTSTSTGY MELSLRSDD TAVYYCARGD FRKPFWDYWGQ GTLTVSS 118

SEQ ID NO: 234      moltype = AA length = 115
FEATURE          Location/Qualifiers
REGION           1..115
note = chemically synthesized
source            1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 234
EVQLVQSGPE LKKPGASVKM SCKASGYTFT SYVMHWVKQA PGQRLEWIGY VNPFNDGKY 60
NEMFKGRATL TSDKSTSTAY MELSSLRSED SAVYYCARQA WGYPWGQGTL VTVSS 115

SEQ ID NO: 235      moltype = AA length = 115
FEATURE          Location/Qualifiers
REGION           1..115
note = chemically synthesized
source            1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 235
EVQLVQSGAE VKKPGASVKM SCKASGYTFT SYVMHWVKQA PGQRLEWIGY VNPFNDGKY 60
NEMFKGRATL TSDKSTSTAY MELSSLRSED TAVYYCARQA WGYPWGQGTL VTVSS 115

SEQ ID NO: 236      moltype = AA length = 115
FEATURE          Location/Qualifiers
REGION           1..115
note = chemically synthesized
source            1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 236
EVOLVQSGAE VKKPGASVKM SCKASGYTFT SYVMHWVRQA PGQRLEWIGY VNPFNDGKY 60
NEMFKGRATL TSDKSTSTAY MELSSLRSED TAVYYCARQA WGYPWGQGTL VTVSS 115

SEQ ID NO: 237      moltype = AA length = 115
FEATURE          Location/Qualifiers
REGION           1..115
note = chemically synthesized
source            1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 237
EVQLVQSGAE VKKPGASVKV SCKASGYTFT SYVMHWVRQA PGQRLEWIGY VNPFNDGKY 60
NEMFKGRATL TSDKSTSTAY MELSSLRSED TAVYYCARQA WGYPWGQGTL VTVSS 115

SEQ ID NO: 238      moltype = AA length = 115
FEATURE          Location/Qualifiers
REGION           1..115
note = chemically synthesized
source            1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 238
EVQLVQSGAE VKKPGASVKV SCKASGYTFT SYVMHWVRQA PGQRLEWIGY VNPFNDGKY 60
NEMFKGRATI TSDKSTSTAY MELSSLRSED TAVYYCARQA WGYPWGQGTL VTVSS 115

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SEQ ID NO: 239      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
source            note = chemically synthesized
                  1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 239
DIVLTQSPAS LALSPGERAT LSCRATESVE YYGTSLVQWY QQKPGQPPKL LIYAASSVDS 60
GVPSRFSGSG SGTDFTLTIN SLEEDAAMY FCQQSRRVPY TFGQGTKLEI K       111

SEQ ID NO: 240      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
source            note = chemically synthesized
                  1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 240
DIVLTQSPAT LSLSPGERAT LSCRATESVE YYGTSLVQWY QQKPGQPPKL LIYAASSVDS 60
GVPSRFSGSG SGTDFTLTIN SLEAEDAAMY FCQQSRRVPY TFGQGTKLEI K       111

SEQ ID NO: 241      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
source            note = chemically synthesized
                  1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 241
EIVLTQSPAT LSLSPGERAT LSCRATESVE YYGTSLVQWY QQKPGQPPKL LIYAASSVDS 60
GVPSRFSGSG SGTDFTLTIN SLEAEDAAMY FCQQSRRVPY TFGQGTKLEI K       111

SEQ ID NO: 242      moltype = AA length = 111
FEATURE          Location/Qualifiers
REGION           1..111
source            note = chemically synthesized
                  1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 242
DIVLTQSPAT LSLSPGERAT LSCRATESVE YYGTSLVQWY QQKPGQPPKL LIYAASSVDS 60
GVPSRFSGSG SGTDFTLTIN SLEAEDAATY FCQQSRRVPY TFGQGTKLEI K       111

SEQ ID NO: 243      moltype = AA length = 123
FEATURE          Location/Qualifiers
REGION           1..123
source            note = chemically synthesized
                  1..123
mol_type = protein
organism = synthetic construct

SEQUENCE: 243
EVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGTANY 60
AQKFQGRVTI TADKSTSTAY MELSSLRSED TAVYYCAREG TIYDSSGYSF DYWGQGTLVT 120
VSS              123

SEQ ID NO: 244      moltype = AA length = 124
FEATURE          Location/Qualifiers
REGION           1..124
source            note = chemically synthesized
                  1..124
mol_type = protein
organism = synthetic construct

SEQUENCE: 244
EVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGI INPSGGTSY 60
AQKFQGRVSM TRDTSTSTVY MELSSLTSED TAVYYCARLD FPHIYGNYYG MDIWGQGTTV 120
TVSS             124

SEQ ID NO: 245      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
source            note = chemically synthesized
                  1..118
mol_type = protein
organism = synthetic construct

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SEQUENCE: 245
 QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGTANY 60
 AQKFQGRVTI TADKSTSTAY MELSSLRSED TAVYYCARLA VPGAFDIWGQ GTMVTVSS 118

SEQ ID NO: 246 moltype = AA length = 116
 FEATURE Location/Qualifiers
 REGION 1..116
 note = chemically synthesized
 source 1..116
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 246
 EVQLVESGGG VVQPGRSLRL SCAASGFTFS SYAMHWWVRQA PGKGLAVISY DGSNKYYADS 60
 VKGRFTISR NSKNLTYLQM NSLRAEDTAV YYCARGQWLW TELDYWGQGT LVTVSS 116

SEQ ID NO: 247 moltype = AA length = 122
 FEATURE Location/Qualifiers
 REGION 1..122
 note = chemically synthesized
 source 1..122
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 247
 EVQLVESGSE VEKPGSSVKV SCKASGGTFS DSGISWVRQA PGQGLEWMGG IIPMFATPY 60
 AQKFQDRVTI TADESTSTVY MELSGLRSD TAVFYCARDR GRGHLPWYFD LWGRGTLTV 120
 SS 122

SEQ ID NO: 248 moltype = AA length = 119
 FEATURE Location/Qualifiers
 REGION 1..119
 note = chemically synthesized
 source 1..119
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 248
 EVQLVESGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGTANY 60
 AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARAP YYYYYMDVWG QGTTVTVSS 119

SEQ ID NO: 249 moltype = AA length = 124
 FEATURE Location/Qualifiers
 REGION 1..124
 note = chemically synthesized
 source 1..124
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 249
 EVQLVESGEE VKKPGSSVKV SCKASGGTLS RYALSWVRQA PGQGPFWVGA IIPIFGTPHY 60
 SKFQDRVII TVDTSTNTAF MELSSLRFED TALYFCARGH DEYDISGYHR LDYWQGTLV 120
 TVSS 124

SEQ ID NO: 250 moltype = AA length = 121
 FEATURE Location/Qualifiers
 REGION 1..121
 note = chemically synthesized
 source 1..121
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 250
 QVQLVQSGSE LKKPGSSVKV SCKASGYSFS GYYIHWWVRQA PGQGLEWMGW IDPNSGVTNY 60
 VRRFQGRVTM TRDTSLSTAY MELSGLTADD TAVYYCARDE NLWQFGYLDY WGQTLTVVS 120
 S 121

SEQ ID NO: 251 moltype = AA length = 120
 FEATURE Location/Qualifiers
 REGION 1..120
 note = chemically synthesized
 source 1..120
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 251
 QVQLVQSGAE VKKPGSSVKV SCKASGGTFS RYGVHWWVRQA PGQGLEWMGR LIPIVSMTNY 60
 AQKFQDRVSI TTDKSTGTAY MELRSLTSED TALYYCASVG QQLPWFFAW GQGTLTVSS 120

SEQ ID NO: 252 moltype = AA length = 118
 FEATURE Location/Qualifiers
 REGION 1..118

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source          note = chemically synthesized
               1..118
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 252
EVQLVESGGG VVQPGRSRLR SCAASGFTFS SYAMHWVRQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNLY LQMNSLRTED TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 253      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source          1..118
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 253
EVQLVESGGG VVQPGRSRLR SCAASGFTFS SYAMHWVRQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNLY LQMNSLRTED TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 254      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source          1..121
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 254
EVQLVQSGGG LVQPGGSLRL SCAASGFTFS DYGMHWVRQP PGKGLEWLAV ISYDGSYKIH 60
ADSVQGRFTI SRDNAKNSVF LQMNSLKTED TAVYYCTTDR KWLAWHGMDV WGQGTTVTVS 120
S                 121

SEQ ID NO: 255      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source          1..118
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 255
EVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIPGTANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARDG IVADFQHWGQ GTLTVSS 118

SEQ ID NO: 256      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source          1..121
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 256
EVOLVESGAE VKKPGASVKV SCKASGDTFS RYGITWVRQA PGRGLEWMGN IVPFFGATNY 60
AQKFQGRVTI TADHSTSTAY MDLSSLRSDD TAVYYCARDH FYGSGGYFDY WGQGTLVTVS 120
S                 121

SEQ ID NO: 257      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source          1..121
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 257
EVOLLESGAE VKKPGASVKV SCKASGYTFN SYDINWVRQA PGQGLEWMGG IIIPVPGTANY 60
AESFQGRVTM TADHSTSTAY MELNNLRSED TAVYYCARDR WHYESRPMDV WGQGTTVTVS 120
S                 121

SEQ ID NO: 258      moltype = AA length = 119
FEATURE          Location/Qualifiers
REGION           1..119
note = chemically synthesized
source          1..119
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 258
EVQLVESGGG LVRPGGSLRL ACAASGFSFS DYYMTWIROA PGRGLEWIAY ISDSGQTVHY 60
ADSVKGRFTI SRDNTKNSLF LQVNTRLAED TAVYYCARED LLGYYLQSWG QGTLTVSS 119

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SEQ ID NO: 259      moltype = AA length = 131
FEATURE
REGION
1..131
note = chemically synthesized
source
1..131
mol_type = protein
organism = synthetic construct
SEQUENCE: 259
QVQLQQSGPG LVKPSQTLSL TCAISGDSVS SNSAAWNWIR QSPSRGLEWL GRTYYRSKWF 60
NDYAVSVKSR ITINPDTSKN QFSQLNNSVT PDETAVYYCA RDEPRAVAGS QAYYYYGMDV 120
WGQGTTVTVS S 131

SEQ ID NO: 260      moltype = AA length = 124
FEATURE
REGION
1..124
note = chemically synthesized
source
1..124
mol_type = protein
organism = synthetic construct
SEQUENCE: 260
EVQLVQSGAE VKKPGASVKV SCKASGYFT SYAMHWRQAF PGKGLEWMGI INPSDGSTS 60
AQKFQGRVTM TRDTSTSTVH MELSSLRSED TAVYYCARDL FPHIYGNYYG MDIWQGTTV 120
TVSS 124

SEQ ID NO: 261      moltype = AA length = 118
FEATURE
REGION
1..118
note = chemically synthesized
source
1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 261
QMQLVQSGGG VVQPGRSLRL SCAASGFTFS SYAMHWRQAF PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTE D TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 262      moltype = AA length = 118
FEATURE
REGION
1..118
note = chemically synthesized
source
1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 262
QVQLVQSGGG VVQPGRSLRL SCAASGFTFS SYAMHWRQAF PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTE D TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 263      moltype = AA length = 110
FEATURE
REGION
1..110
note = chemically synthesized
source
1..110
mol_type = protein
organism = synthetic construct
SEQUENCE: 263
QSVLTQPPSV SAAPGQKVTI SCSCGNNSNIA NNYVSWYQQQL PGTAPKLLIY DNNYRPMSGIP 60
DRFGSGSKSGT SATLDITGLQ TGDEADYYCG VWDGSLTTGV FGGGTKLTVL 110

SEQ ID NO: 264      moltype = AA length = 107
FEATURE
REGION
1..107
note = chemically synthesized
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 264
AIQMTQSPSS LSASVGDRVT ITCRASQGIS NYLAWYQQKP GKVPKLLIYA ASTLESGVPS 60
RFSGSGSGTD FTLTISSSLQP EDLATYYCQQ LHTFPPLTFGG GTKVEIK 107

SEQ ID NO: 265      moltype = AA length = 111
FEATURE
REGION
1..111
note = chemically synthesized
source
1..111
mol_type = protein
organism = synthetic construct

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SEQUENCE: 265
QVLTQPPSA SGSPGQSVTI SCTGTSSDVG AYNFVSWYRQ HPGKAPKLMI YEVNKRPSGV 60
PDRFSGSKSG NTASLTIVSGL QAEDEADYYC SSYAGTNSLG IFGTGKLTIV L 111

SEQ ID NO: 266      moltype = AA length = 111
FEATURE           Location/Qualifiers
REGION            1..111
note = chemically synthesized
source             1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 266
QSVTQPPSV SAAPGQKVTI SCSGSSSDIG NHYVSWYQQ PGTAPKLLIY DNNQRPSGIP 60
DRFSGSKSGT SATLAITGLQ TGDEADYYCG TWDNSLSPHL LFGGTAKLTIV L 111

SEQ ID NO: 267      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein
organism = synthetic construct

SEQUENCE: 267
QSVLTQPPSV SAAPGQKVTI SCGSSSNMG NNYVSWYKQV PGTAPKLLIY ENDKRPSGIP 60
DRFSGSKSGT SATLGITGLQ TGDEADYYCG TWDNSLSGFV FASGKVTIVL 110

SEQ ID NO: 268      moltype = AA length = 109
FEATURE           Location/Qualifiers
REGION            1..109
note = chemically synthesized
source             1..109
mol_type = protein
organism = synthetic construct

SEQUENCE: 268
QSALTQPA SV SGSQGSVTI SCTGTSSDVG SYNLVSWYQQ HPGKAPNLMI YDVSKRSGVS 60
NRFSGSKSGN TASLTISGLQ AEDEADYYCS SYTGISTVVF GGGTAKLTIVL 109

SEQ ID NO: 269      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein
organism = synthetic construct

SEQUENCE: 269
QSVLTQPA SV SGSPGQSITI SCTGTSSDVG SYNLVSWYQQ HPGKAPKLMI YEVSKRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYGGFNNLL FGGGAKLTIVL 110

SEQ ID NO: 270      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
note = chemically synthesized
source             1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 270
DIVMTQSPSS LSASIGDRVT ITCRASQRIS AYVNWYQQKP GKAPKVLIIYA ASSLRSGVPS 60
RFSFGSGSGTD FTLTISSSLQP EDFATYYCQQ TYSSPWTFGQ GTKVEIK 107

SEQ ID NO: 271      moltype = AA length = 112
FEATURE           Location/Qualifiers
REGION            1..112
note = chemically synthesized
source             1..112
mol_type = protein
organism = synthetic construct

SEQUENCE: 271
QSVLTQPPSA SGSPGQSVTI SCTGTSSDVG GYDSVSWYQQ HPGKAPKLMI YDVSKRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSSIFF YVFGTAKTVT VL 112

SEQ ID NO: 272      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein

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SEQUENCE: 272          organism = synthetic construct
LPVLTQPVASV SGSPGQSITI SCTGTTSIDIG GYDYVSWYQQ HPGKAPKLMI YDVSKRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSSTHV FGTGKLTQL 110

SEQ ID NO: 273          moltype = AA length = 111
FEATURE               Location/Qualifiers
REGION                1..111
source                 note = chemically synthesized
                      1..111
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 273          moltype = AA length = 111
QSALTQPVASV SGSPGQSITI SCTGTSSDV GYNVYVSWYQQ HPGKAPKLMI YDVSNRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYRSSTLGP VFGGGTKLTV L 111

SEQ ID NO: 274          moltype = AA length = 110
FEATURE               Location/Qualifiers
REGION                1..110
source                 note = chemically synthesized
                      1..110
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 274          moltype = AA length = 110
QAGLTQPPSV SEAPRQRVTI SCSGSSSNIG NNAVNWYQQL PGKAPKLLIY YDDLLPSGV 60
DRFSGSKSGT SASLAISGLQ SEDEADYYCA AWDDSLNNGV FGTGKLTQL 110

SEQ ID NO: 275          moltype = AA length = 110
FEATURE               Location/Qualifiers
REGION                1..110
source                 note = chemically synthesized
                      1..110
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 275          moltype = AA length = 110
QSALTQPRSV SGSPGQSITI SCTGTSSDV GYNVYVSWYQQ HPGKAPKLMI YDVSKRPSGV 60
PDRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSSTHV FGTGKVTQL 110

SEQ ID NO: 276          moltype = AA length = 110
FEATURE               Location/Qualifiers
REGION                1..110
source                 note = chemically synthesized
                      1..110
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 276          moltype = AA length = 110
QSVTQPPSV SAAPGQKVTI SCSGSSSNIG NNYVSWYQQL PGTAPKLLIY DNNKRPSGIP 60
DRFSGSKSGT SATLGITGLQ TGDEADYYCG TWDSLSVWV FGGGTQLTQL 110

SEQ ID NO: 277          moltype = AA length = 112
FEATURE               Location/Qualifiers
REGION                1..112
source                 note = chemically synthesized
                      1..112
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 277          moltype = AA length = 112
QSVLTQPVASV SGSPGQSITI SCTGTSSDV GYNVYVSWYQQ HPGRAPRLMI YDVSNRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEGDYYC SSYTSGGTLG PVFGGGTKLT VL 112

SEQ ID NO: 278          moltype = AA length = 110
FEATURE               Location/Qualifiers
REGION                1..110
source                 note = chemically synthesized
                      1..110
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 278          moltype = AA length = 110
QAGLTQPPSA SGTPGQRVTI SCSGSSSNIG SNTVNWYQQL PGTAPKLLIY SNNQRPSGVP 60
DRFSGSKSGT SASLAISGLQ SEDEADYYCA AWDDSLNNGVW FGGGTQLTQL 110

SEQ ID NO: 279          moltype = AA length = 107
FEATURE               Location/Qualifiers
REGION                1..107
source                 note = chemically synthesized
                      1..107

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mol_type = protein
organism = synthetic construct

SEQUENCE: 279
AIRMTQSPSS LSASVGDRVT ITCRASQSIIS NYLNWYQQRQ GKAPNLLIYA ASSLQSGVPS 60
RFSFGSGSGTD FTLTISLQP EDFATYYCQQ TYSTPYTFQG GTKLEIK 107

SEQ ID NO: 280      moltype = AA length = 111
FEATURE           Location/Qualifiers
REGION            1..111
note = chemically synthesized
source             1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 280
QSVLTQPASV SGSPGQSITI SCTGTSSDVG GYNVWSWYRQ HPGKAPKLMY YDVSYRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTDSSTRY VFGTGTKLTV L 111

SEQ ID NO: 281      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein
organism = synthetic construct

SEQUENCE: 281
QPVLTQPPSA SGTPGQRVAI SCGSRSNIE INSVNWYQQL PGTAPKLLIY DNNKRPSGIP 60
DRFSGSKSGT SATLGITGLQ TGDEADYYCG SWDSSLSSADV FGGTGTKLTVL 110

SEQ ID NO: 282      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein
organism = synthetic construct

SEQUENCE: 282
QSVLTQPPSV SAAPGKKVTI SCGSSSNIG NNYVWSWYQQL PGTAPKLLIY RNNQRPSGVP 60
DRFSGSKSGT SASLAISGLQ SEDEADYYCA TWDDSLNGWV FGGTGTKLTVL 110

SEQ ID NO: 283      moltype = AA length = 111
FEATURE           Location/Qualifiers
REGION            1..111
note = chemically synthesized
source             1..111
mol_type = protein
organism = synthetic construct

SEQUENCE: 283
QSVVVTQPPSV SGAPGQRVTI SCTGSSSNIG AGYDVHWYQQ LPGTAPKLLI YGNNNRHSGV 60
PDRFSGSKSG TSASLAITGL QAEDEAEFFC GTWDSRLTTY VFGSGTKLTV L 111

SEQ ID NO: 284      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein
organism = synthetic construct

SEQUENCE: 284
QSVVVTQPPSV SAAPGQKVTI SCGSSSNIG NNYVWSWYQQL PGTAPKLLIY DNNKRPSGIP 60
DRFSGSKSGT SATLGITGLQ TGDEADYYCG TWDSSLSSAVV FGGTGTKLTVL 110

SEQ ID NO: 285      moltype = AA length = 103
FEATURE           Location/Qualifiers
REGION            1..103
note = chemically synthesized
source             1..103
mol_type = protein
organism = synthetic construct

SEQUENCE: 285
VIWMTQSPSS LSASVGDRVT ITCAASSLQS WYQQKPGKAP KLLIYEASTL ESGVPSRFSG 60
SGSGSTEFTLT ISSLQPEDFA TYYCQQSYST PYTFGQQGTLK EIK 103

SEQ ID NO: 286      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized

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SEQ ID NO: 293	moltype = AA length = 440
FEATURE	Location/Qualifiers
REGION	1..440
	note = chemically synthesized
source	1..440
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 293	
QVQLVESGGG VVQPGRLRL DCKASGITFS NSGMHWVRQA PGKGLEWVAV IWYDGSKRYY	60
ADSVKGRFTI SRDNNSKNTLF LQMNSLRAED TAVYYCATND DYWGQGLVT VSSASTKGPS	120
VFVFLAPCRS TSESTAALGC LVKDYFPEPV TVSWNSGALT SGVHTFPFAVL QSSGLYSLSS	180
VVTVPSSSLG KTKTYTCNVDH KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPKPK	240
KDTLMISRTP EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN STYRVVSVLT	300
VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREGQ VYTLPPSQEE MTKNQVSLTC	360
LVKGFYPDSI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SRLTVDKSRW QEGNVFSCSV	420
MHEALHNHYT QKSLSLSLGK	440
SEQ ID NO: 294	moltype = AA length = 218
FEATURE	Location/Qualifiers
REGION	1..218
	note = chemically synthesized
source	1..218
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 294	
EIVLTQSPAT LSLSPGERAT LSCRASKGV S TSGYSYLHWY QQKPGQAPRL LIYLASYLES	60
GVPARFSGSG S GTDFTLTIS SLEPEDFAVY YCQHHSRDLPL TFGGGTKVIEI KRTVAAPS VF	120
IFPPSDEQLK SGTASVVC LL NNFYPREAKV QWKVDNALQS GNSQESVTEQ DSKDSTYSL S	180
STLTLSKADY EKHKVYACEV THQGLSSPVT KSFNRGEC	218
SEQ ID NO: 295	moltype = AA length = 214
FEATURE	Location/Qualifiers
REGION	1..214
	note = chemically synthesized
source	1..214
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 295	
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA	60
RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ SSNWPRTFGQ GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQW KV DNALQSGNSQ ESVTEQDSKD STYSL SSTLT	180
LSKADYEKHK VVACEVTHQG LSSPVTKSFN RGEC	214
SEQ ID NO: 296	moltype = AA length = 122
FEATURE	Location/Qualifiers
REGION	1..122
	note = chemically synthesized
source	1..122
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 296	
EVQLVESGGG LVQPGGSLRL SCAASGFTFS DSWIHWRQA PGKGLEWVAW ISPYGGSTYY	60
ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCARRH WPGGF DYWGQ GTLTVSS AS	120
TK	122
SEQ ID NO: 297	moltype = AA length = 118
FEATURE	Location/Qualifiers
REGION	1..118
	note = chemically synthesized
source	1..118
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 297	
EVQLVESGGG LVQPGGSLRL SCAASGFTFS DSWIHWRQA PGKGLEWVAW ISPYGGSTYY	60
ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCARRH WPGGF DYWGQ GTLTVSS	118
SEQ ID NO: 298	moltype = AA length = 447
FEATURE	Location/Qualifiers
REGION	1..447
	note = chemically synthesized
source	1..447
	mol_type = protein
	organism = synthetic construct

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SEQUENCE: 298
 EVQLVESGGG LVQPGGSLRL SCAASGFTFS DSWIHWVRQA PGKGLEWVAW ISPYGGSTYY 60
 ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCARRH WPGGFWDYWGQ GTLVTSSAS 120
 TKGPSVFPFLA PSSKSTSGGT AALGCLVKDY FPEPVTVWSN SGALTSGVHT FPAVLQSSGL 180
 YSLSSVVTVP SSSLGTQTYI CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC PAPELLGGPS 240
 VFLFPPKPKD TLMIISRTPEV TCVVVDSHE DPEVKFNWVY DGVEVHNAAKT KPREEQYAST 300
 YRVVSVLTVL HQDWLNGKEY CCKVSNKALP APIEKTTSKA KGQPREPQVY TLPPSREEMT 360
 KNQVSLTCLV KGFYPSDIAV EWEWSNGQPN NYKTTTPVLD SDGSFFLYSK LTVDKSRWQQ 420
 GNVFSCSVMH EALHNHYTQK SLSLSPG 447

SEQ ID NO: 299 moltype = AA length = 108
 FEATURE Location/Qualifiers
 REGION 1..108
 note = chemically synthesized
 source 1..108
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 299
 DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
 RFSGSGSGTD FTLTISLQP EDFATYYCQQ YLYHPATFGQ GTKVEIKR 108

SEQ ID NO: 300 moltype = AA length = 214
 FEATURE Location/Qualifiers
 REGION 1..214
 note = chemically synthesized
 source 1..214
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 300
 DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS 60
 RFSGSGSGTD FTLTISLQP EDFATYYCQQ YLYHPATFGQ GTKVEIKRTV AAPSVFIFPP 120
 SDEQQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT 180
 LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC 214

SEQ ID NO: 301 moltype = AA length = 121
 FEATURE Location/Qualifiers
 REGION 1..121
 note = chemically synthesized
 source 1..121
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 301
 EVQLVESGGG LVQPGGSLRL SCAASGFTFS RFWMSWVRQA PGKGLEWVAN INQDGTEKYY 60
 ADSVKGRFTI SRDNNAKNSLY LQMNSLRAGD TAVYYCANTY YDFWSGHFDY WGQGTLVTVS 120
 S 121

SEQ ID NO: 302 moltype = AA length = 121
 FEATURE Location/Qualifiers
 REGION 1..121
 note = chemically synthesized
 source 1..121
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 302
 QEHLVESGGG VVQPGRSRL SCAASGFTFS NFGMHWVRQA PGKGLEWVAA LWSDGSNKYY 60
 ADSVKGRVTI SRDNNSKNTLY LQMNSLRAED TAVYYCARGR GAPGIPIFGY WGQGTLVTVS 120
 S 121

SEQ ID NO: 303 moltype = AA length = 130
 FEATURE Location/Qualifiers
 REGION 1..130
 note = chemically synthesized
 source 1..130
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 303
 EVQLVESGGG LVKPGGSLRL SCAASGFTFS NAWMSWVRQA PGKGLEWVGR IKRKTDGGTT 60
 DYAAPVKGRF TISRDDSKNT LHLQMNSLKT EDTAVYYCTT DDIVVVPAVM REYYPGMDVW 120
 GQQTTTVTVSS 130

SEQ ID NO: 304 moltype = AA length = 121
 FEATURE Location/Qualifiers
 REGION 1..121
 note = chemically synthesized
 source 1..121
 mol_type = protein

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SEQUENCE: 304          organism = synthetic construct
QVQLVQSGAE VKKPGASVQV SCKASGYSFT GYYIHWVRQA PGQGLEWMGW INPNSGTTKY 60
AHKFQGRVTM TRDTSIDTAY MILSSLISDD TAVYYCARDE DWNFGSWFDS WGQGTLVTVS 120
S                                         121

SEQ ID NO: 305          moltype = AA length = 121
FEATURE
REGION
1..121
note = chemically synthesized
source
1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 305          organism = synthetic construct
QVHLVQSGAE VKKPGASVKV SCKASGYTFT GYYIHWVRQA PGHGLEWMGW LNPNTGTTKY 60
IQNFQGRVTM TRDTSSSTAY MELTRLRSDD TAVYYCARDE DWNYGSWFDT WGQGTLVTVS 120
S                                         121

SEQ ID NO: 306          moltype = AA length = 120
FEATURE
REGION
1..120
note = chemically synthesized
source
1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 306          organism = synthetic construct
EVQLVESGGG VVRPGGSLRL SCAASGFTFD DYGMTWVRQA PGRGLEWVSG IHWHGKRTGY 60
ADSVKGRFTI SRDNNAKSLY LQMNSLKGED TALYHCVRGG MSTGDWFDPW GQGTLVIVSS 120

SEQ ID NO: 307          moltype = AA length = 120
FEATURE
REGION
1..120
note = chemically synthesized
source
1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 307          organism = synthetic construct
EVQLVESGGG VVRPGGSLRL SCAASGFTFD DYGMTWVRQV PGKGLEWVSG IHWSGRSTGY 60
ADSVKGRFTI SRDNNAKNSLY LQMNSLRAED TALYYCARGG MSTGDWFDPW GQGTLTVSS 120

SEQ ID NO: 308          moltype = AA length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 308          organism = synthetic construct
EVQLVESGGG LVQPGGSLRL SCAASGFTVG SNYMNWVRQA PGKGLEWVSV IYSGGSTYYA 60
DSVKGRFTIS RLTSKNTLYL QMSSLRPEDT AVYYCARGIR GLDVWGQQGT TTVSS      115

SEQ ID NO: 309          moltype = AA length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 309          organism = synthetic construct
EERLVESGGD LVQPGGSLRL SCAASGITVG TNYMNWVRQA PGKGLEWVSV ISSGGNTHYA 60
DSVKGRFIMS RQTSKNTLYL QMNSLETEDT AVYYCARGIR GLDVWGQQGT VTVSS      115

SEQ ID NO: 310          moltype = AA length = 118
FEATURE
REGION
1..118
note = chemically synthesized
source
1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 310          organism = synthetic construct
QVQLVQSGAE VKMPGSSVRV SCKASGGIFS SSTISWVRQA PGQGLEWMGE IIPVPGTVNY 60
AQKFQDRVF TADESTTTAY MELSSLKSGD TAVYFCARNW GLGSFYIWGQ GTMVTVSS      118

SEQ ID NO: 311          moltype = AA length = 115
FEATURE
REGION
1..115

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source          note = chemically synthesized
               1..115
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 311
EVQLVESGGD LVHPGRSLRL SCAASGFPFD EYAMHWRQV PGKGLEWVSG ISWSNNNIGY 60
ADSVKGRFTI SRDNAKNSLY LQMNSLRPED TAFYYCAKSG IFDSWGQGTL VTVSS      115

SEQ ID NO: 312      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION           1..118
note = chemically synthesized
source            1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 312
EVQLVESGGG VVQPGRSLRL SCAASGFTFS SYGMHWVRQA PGKGLEWVTL ISYEGRNKY 60
ADSVKGRFTI SRDNNSKNTLY LQMNSLRAED TAVYYCAKDR TLYGMDVWQG GTTVTVSS    118

SEQ ID NO: 313      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION           1..121
note = chemically synthesized
source            1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 313
QVTLRESPGA LVKTTQTLTL TCTFSGFSL S TNRMCVTWIR QPPGKALEWL ARIDWDGVKY 60
YNTSLKTRLT ISKDTSKNQV VLTMTNMDPV DTATFYCARS TSLTFYYFDY WGQGTLVTVS 120
S

SEQ ID NO: 314      moltype = AA length = 115
FEATURE          Location/Qualifiers
REGION           1..115
note = chemically synthesized
source            1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 314
EVQLVESGGG LVQPGGSLRL SCAASEFTVG TNHMNWVRQA PGKGLEWVSV IYSGGNTFYA 60
DSVKGRFTIS RHTSKNTLYL QMNSLTAEDT AVYYCARGLG GMDVWGQGTT VTVSS      115

SEQ ID NO: 315      moltype = AA length = 120
FEATURE          Location/Qualifiers
REGION           1..120
note = chemically synthesized
source            1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 315
EVQLVESGGG LVQRGESLRL YCAASGFTFS KYWMNWVRQA PGKGLEWVAN IKGDGSEKYY 60
VDSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARDY WGSGYYFDW GQGTLVTVSS 120

SEQ ID NO: 316      moltype = AA length = 130
FEATURE          Location/Qualifiers
REGION           1..130
note = chemically synthesized
source            1..130
mol_type = protein
organism = synthetic construct

SEQUENCE: 316
EVQLVESGGG LVQSGGSLRL SCAASGFTFS SYWMSWVRQA PGKGLEWVAN IKQDGSEKYY 60
VDSVKGRFTI SRDNAKNSLY LQMNSLRADD TAVYYCARDY IVVVPAPMGY YYYYFGMDW 120
GQQTTVTVSS      130

SEQ ID NO: 317      moltype = AA length = 123
FEATURE          Location/Qualifiers
REGION           1..123
note = chemically synthesized
source            1..123
mol_type = protein
organism = synthetic construct

SEQUENCE: 317
EVQLVESGGG LVQPGRSLRL SCAASGFTFD DFAMHWRQV PGKGLEWVSG ISWTGGNMDY 60
ANSVKGRFTI SREDAKNSLY LQMNSLRAAD TALYYCVKDI RGIVATGGAF DIWGRGTMVT 120
VSS             123

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SEQ ID NO: 318      moltype = AA length = 115
FEATURE
REGION          Location/Qualifiers
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 318
EVQLVESGGG LVQPGGSLRL SCAASGFTVG TNYMNWRQQA PGKGLEWISV IYSGGSTFYA 60
DSVKGRFTIS RQTSQNTLYL QMNSLRPDT AVYYCARGIR GFDIWGQQGTM VTVSS     115

SEQ ID NO: 319      moltype = AA length = 115
FEATURE
REGION          Location/Qualifiers
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 319
EVQLVESGGG LVQPGGSLRL SCAASGFTIS TNYMNWRQQA PGKGLEWAVV IYSSGSTYYI 60
DSVKGRFTIS RLTSKNTVYL QMSSLNSEDT AVYYCARGIR GFDIWGQQGTM VTVSS     115

SEQ ID NO: 320      moltype = AA length = 124
FEATURE
REGION          Location/Qualifiers
1..124
note = chemically synthesized
source
1..124
mol_type = protein
organism = synthetic construct

SEQUENCE: 320
EVQLVESGGG LVQPGRSRLR SCAASGFTID DSAMHWVRQTA PGKGLEWVSG ISWKSGSIGY 60
ADSVGRFTI SRDNAKNSLY LQMNSLRVED TALYYCVKDI RGNWNYGGNW FDPWGQGTLV 120
TVSS                           124

SEQ ID NO: 321      moltype = AA length = 115
FEATURE
REGION          Location/Qualifiers
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct

SEQUENCE: 321
EVQLVESGGG LVQPGGSLRL SCEASGFTVG VNHMNWRQQA PGKGLEWVSV IFSSGRTFYG 60
DVVKGRLTIF RQTSQNTVYL QMNSLRSEDT AIYYCARGIG GLDIWGRGTM VTVSS     115

SEQ ID NO: 322      moltype = AA length = 123
FEATURE
REGION          Location/Qualifiers
1..123
note = chemically synthesized
source
1..123
mol_type = protein
organism = synthetic construct

SEQUENCE: 322
EVQLVESGGG LVQPGRSRLR SCAASGFTFD DYALHWVRQQA PGKGLEWVSG ISWTGGTIDY 60
ADSVKGRFTI SRDNAKNSLY LQMSSLRTED TAIYYCTRDI RGNWKYGGWF DPWGQGTLVT 120
VSS                           123

SEQ ID NO: 323      moltype = AA length = 120
FEATURE
REGION          Location/Qualifiers
1..120
note = chemically synthesized
source
1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 323
QVQLVQSGTE VKKPGASVKV SCKASGYTFT AYYMHWRQQA PGQGLDWMGW ISPNSGFTNY 60
AQKFQGRVTM TRDTSINTFY MELSGLRSDA TAVYYCAREG STHHNSFDPW GQGTLTVSS 120

SEQ ID NO: 324      moltype = AA length = 114
FEATURE
REGION          Location/Qualifiers
1..114
note = chemically synthesized
source
1..114
mol_type = protein
organism = synthetic construct

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SEQUENCE: 324
EVOLVESGGGVQPGGSLRL SCAASGFTVG TNFMNWVRQA PGKGLEWVA IYSGGTANYA 60
DSVKGGRFTIS RDTSRNTLYL QMNSLRTEDT AVYYCARGGG MDVWGQGTTV TVSS 114

SEQ ID NO: 325      moltype = AA length = 118
FEATURE           Location/Qualifiers
REGION            1..118
note = chemically synthesized
source             1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 325
QVQLVQSGAE VVKPGSSVKV SCKASGGTFN TYVLSWVRQA PGQGLEWMGE IIPILGAANY 60
AQNFQGRVTF TTDESTNTAY MDLSSLRSDD TAVYYCARDR TSGGFDPWGQ GTLTVSS 118

SEQ ID NO: 326      moltype = AA length = 119
FEATURE           Location/Qualifiers
REGION            1..119
note = chemically synthesized
source             1..119
mol_type = protein
organism = synthetic construct

SEQUENCE: 326
QVQLVQSGAE VEKPGASVKV SCKASGYIFT HYGISWVRQA PGQGLEWVGW ISPYNGYTDY 60
AQKLQGRVTL TTDTSTTAY MELRNLRSD TAMYYCSRGR GPYWSFDLWG RGTLTVSS 119

SEQ ID NO: 327      moltype = AA length = 106
FEATURE           Location/Qualifiers
REGION            1..106
note = chemically synthesized
source             1..106
mol_type = protein
organism = synthetic construct

SEQUENCE: 327
DIQMTQSPST LSASVGDRVT ITCRASQSIS NWLAWYQQKP GKAPKLLIYK ASSLEGVPS 60
RFSGSGSGTE FTLTISSLQP DDFATYYCQQ YHSYSYTFGQ GTKEIK 106

SEQ ID NO: 328      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
note = chemically synthesized
source             1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 328
DIQMTQSPSS LSASVGDRVT ITCRASQGIR NDLGWYQQKP GKAPKRLIYT ASSLQSGVPS 60
RFSGSGSGTE FTLTISSLQP EDFATYYCLQ HNSYPLTFGG GTKVAIK 107

SEQ ID NO: 329      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
note = chemically synthesized
source             1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 329
DIQMTQSPSS LSASVGDRVT ITCRTSQGIR NDLGWYQQKP GKAPKRLIYA ASSLQSGVPS 60
RFSGSGSGTE FTLTISSLQP EDFATYYCLQ HNNYPYTFGG GTKLEIK 107

SEQ ID NO: 330      moltype = AA length = 112
FEATURE           Location/Qualifiers
REGION            1..112
note = chemically synthesized
source             1..112
mol_type = protein
organism = synthetic construct

SEQUENCE: 330
DIVMTQTPLS SPVTLGQPAS ISCRSSQTLV HGDGNTYLSW IQQRPGQPPR LLIYKVSNQF 60
SGVPDRFSGS GAGTDFTLKI SRVEAEDVGL YFCMQATHFP ITFGQGTRLE IK 112

SEQ ID NO: 331      moltype = AA length = 112
FEATURE           Location/Qualifiers
REGION            1..112
note = chemically synthesized
source             1..112
mol_type = protein

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SEQUENCE: 331          organism = synthetic construct
DIQMTQTPLS SPVTLGQPAS ISCRSSPSLV HSDGNTYLSW LQQRPGQQPR LLIYKISNRF 60
SGVPDRFSGS GAGTDFTLKI SRVEAEDVGV YYCMQATHFP ITFGQQTRLE IR           112

SEQ ID NO: 332          moltype = AA length = 108
FEATURE               Location/Qualifiers
REGION                1..108
                      note = chemically synthesized
source                 1..108
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 332          moltype = AA length = 108
DIQMTQSPSS LSASLGDRVVT ITCRASQSIN SYLNWYQQKP GKAPKLLIYV ASSLQSGVPS 60
RFSGSGSGTE FTLTISNLQP EDFATYYCQQ SYSTPPITFG QGTRLEIK             108

SEQ ID NO: 333          moltype = AA length = 108
FEATURE               Location/Qualifiers
REGION                1..108
                      note = chemically synthesized
source                 1..108
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 333          moltype = AA length = 108
DIQMTQSPSS LSASVGDRVVT ITCRASQSIS SYLNWYQQKP GKAPKLLIYV ASSLQSGVPS 60
RFSGSGSGTD FTLTISSSLQP EDFATYYCQQ SYSTPPITFG QGTRLEIK             108

SEQ ID NO: 334          moltype = AA length = 108
FEATURE               Location/Qualifiers
REGION                1..108
                      note = chemically synthesized
source                 1..108
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 334          moltype = AA length = 108
DIQMTQSPSS LSASVGDRVVT ITCRASQTIN IYLNWYQQKP GRAPRLLIYA ASSLQSGVPS 60
RFSGSGSGTD FTLTISSSLQP EDFATYYCQQ SYSTPPITFG QGTRLEIK             108

SEQ ID NO: 335          moltype = AA length = 108
FEATURE               Location/Qualifiers
REGION                1..108
                      note = chemically synthesized
source                 1..108
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 335          moltype = AA length = 108
DIQMTQSPSS LSASVGDRVVT ITCRASQSMS SYLNWYQQKP GRAPKLLIFA ASSLQSGVPS 60
RFSGSGSGTD FTLTISSSLQP EDFATYYCQQ SYSTPPITFG QGTRLEIK             108

SEQ ID NO: 336          moltype = AA length = 108
FEATURE               Location/Qualifiers
REGION                1..108
                      note = chemically synthesized
source                 1..108
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 336          moltype = AA length = 108
EIVLTQSPGT LSLSPGERAT LSCRASQSFN FNYLAWYQQK PGQAPRLLIY GASSRATGIP 60
DRFSGSGSGT DFTLTINRLE PEDFGVFYCQ QYESAPWTFG QGTKVEIK             108

SEQ ID NO: 337          moltype = AA length = 105
FEATURE               Location/Qualifiers
REGION                1..105
                      note = chemically synthesized
source                 1..105
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 337          moltype = AA length = 105
DIQMTQSPSS LSASVGDRVVT ITCRASQSIS SYLNWYQQKP GKLLIYAASS LQSGVPSRFS 60
GGGSQGTDFTL TISSLRPEDF ATYYCQQSYC TPPITFGQQGT RLEIK             105

SEQ ID NO: 338          moltype = AA length = 108
FEATURE               Location/Qualifiers
REGION                1..108
                      note = chemically synthesized
source                 1..108

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mol_type = protein
organism = synthetic construct
SEQUENCE: 338
DIQMTQSPSS LSASVGDRVT ITCRASQSI SYLNWYQQKP GKAPKLLIYA ASSLQSGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYSTPPITFG QGTRLEIK 108

SEQ ID NO: 339      moltype = AA length = 91
FEATURE           Location/Qualifiers
REGION            1..91
note = chemically synthesized
source             1..91
mol_type = protein
organism = synthetic construct
SEQUENCE: 339
DRVTTITCRAS QVISNYLAWY QQKPGKVPRL LIYAASTLQS GVPSRFSGSG SGTDFTLTIS 60
SLQPEDDVATY YCQKYNSAPR TFGQGTKVEIK K 91

SEQ ID NO: 340      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
note = chemically synthesized
source             1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 340
DIQMTQSPSS LSASVGDRVT ITCRASQNIN NYLNWYQQKP GKAPKLLIYA ASSFQNAVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYNTPLTFGG GTKVEIK 107

SEQ ID NO: 341      moltype = AA length = 107
FEATURE           Location/Qualifiers
REGION            1..107
note = chemically synthesized
source             1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 341
DIQMTQSPSS LSASVGDRVT ITCRASQGIR NDLGWYQQKP GKAPKRLIYA ASSLQSGVPS 60
RFSGSGSGTE FTLTISSLQP EDFATYYCLQ HNSYPYTFGQ GTKLEIK 107

SEQ ID NO: 342      moltype = AA length = 108
FEATURE           Location/Qualifiers
REGION            1..108
note = chemically synthesized
source             1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 342
DIQMTQSPSS LSASVGDRVT ITCRASQSI SYLNWYQQKP GKAPKLLIYA ASSLQSGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYSTPPITFG QGTRLEIK 108

SEQ ID NO: 343      moltype = AA length = 115
FEATURE           Location/Qualifiers
REGION            1..115
note = chemically synthesized
source             1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 343
QSELEESGRL VKPDETLTIT CTVSGIDLSS NGLTWVRQAP GEGLEWIGTI NKDASAYYAS 60
WAKGRLTISK PSSTKVDLKI TSPTTEDTAT YFCGRIAFKT GTSIWPGTLE VTVSS 115

SEQ ID NO: 344      moltype = AA length = 112
FEATURE           Location/Qualifiers
REGION            1..112
note = chemically synthesized
source             1..112
mol_type = protein
organism = synthetic construct
SEQUENCE: 344
AIVMTQTPSP VSAAVGGTWT INCQASESVY SNNYLSWFQQ KPGQPPKLLI YLASTLASGV 60
PSRFKGSGSG TQFTLTISGV QCDDAATYYC IGGKSSSTDG NAFFGGTEVV VR 112

SEQ ID NO: 345      moltype = AA length = 121
FEATURE           Location/Qualifiers
REGION            1..121
note = chemically synthesized

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source          1..121
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 345
QMQLVQSGAE VVKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGTANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGN IVATITPLDY WGQGTLTVS 120
S                                         121

SEQ ID NO: 346      moltype = AA  length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein
organism = synthetic construct
SEQUENCE: 346
QPVLTQPPSV SAAPGQKVTI SCSGSSSNIA NNYVSWYQQL PGTAPKLLIF ANNKRPSGIP 60
DRFSGSKSGT SAALDITGLQ TGDEADYYCG TWDSLRLAGV FGGGTKLTVL 110

SEQ ID NO: 347      moltype = AA  length = 123
FEATURE           Location/Qualifiers
REGION            1..123
note = chemically synthesized
source             1..123
mol_type = protein
organism = synthetic construct
SEQUENCE: 347
EVOLVQSGAE VVKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGTANY 60
AQKFQGRVTI TADKSTSTAY MELSSLRSED TAVYYCAREG TIYDSSGYSF DYWGQGTLVT 120
VSS                                         123

SEQ ID NO: 348      moltype = AA  length = 118
FEATURE           Location/Qualifiers
REGION            1..118
note = chemically synthesized
source             1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 348
QVQLVESGGG VVQPGRSRLR SCAASGFTFS SYAMHWVRQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWQG GTLTVSS 118

SEQ ID NO: 349      moltype = AA  length = 118
FEATURE           Location/Qualifiers
REGION            1..118
note = chemically synthesized
source             1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 349
EVOLVESGGG VVQPGRSRLR SCAASGFTFS SYAMHWVRQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWQG GTLTVSS 118

SEQ ID NO: 350      moltype = AA  length = 118
FEATURE           Location/Qualifiers
REGION            1..118
note = chemically synthesized
source             1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 350
QVQLVESGGG VVQPGRSRLR SCAASGFTFS SYAMHWVRQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWQG GTLTVSS 118

SEQ ID NO: 351      moltype = AA  length = 118
FEATURE           Location/Qualifiers
REGION            1..118
note = chemically synthesized
source             1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 351
EVOLVESGGG VVQPGRSRLR SCAASGFTFS SYAMHWVRQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWQG GTLTVSS 118

SEQ ID NO: 352      moltype = AA  length = 118

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FEATURE          Location/Qualifiers
REGION          1..118
source           note = chemically synthesized
                1..118
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 352
EVOLVESGGG VVQPGRSLRL SCAASGFTFS SYAMHWRQQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 353      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION          1..118
source           note = chemically synthesized
                1..118
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 353
QVQLVQSGGG VVQPGRSLRL SCAASGFTFS SYAMHWRQQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 354      moltype = AA length = 120
FEATURE          Location/Qualifiers
REGION          1..120
source           note = chemically synthesized
                1..120
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 354
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS RYGVHWRQQA PGQGLEWMGR LIPIVSMTNY 60
AQKFQDRVTI TTDKSTGTAY MELRSLTSED TALYYCASVG QQLPWFFAW GQGTLTVSS 120

SEQ ID NO: 355      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION          1..118
source           note = chemically synthesized
                1..118
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 355
QVQLVQSGGG VVQPGRSLRL SCAASGFTFS SYAMHWRQQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 356      moltype = AA length = 118
FEATURE          Location/Qualifiers
REGION          1..118
source           note = chemically synthesized
                1..118
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 356
QVQLVQSGGG VVQPGRSLRL SCAASGFTFS SYAMHWRQQA PGKGLEWVAV ISFDGSNKYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCARGW LDRDIDYWGQ GTLTVSS 118

SEQ ID NO: 357      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION          1..121
source           note = chemically synthesized
                1..121
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 357
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAYSWRQQA PGQGLEWMGG IIIPSPGTANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGP IVATITPLDY WGQGTLTVVS 120
S 121

SEQ ID NO: 358      moltype = AA length = 121
FEATURE          Location/Qualifiers
REGION          1..121
source           note = chemically synthesized
                1..121
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 358
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAYSWRQQA PGQGLEWMGG IIPIFGTANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGP IVATITPLDY WGQGTLTVVS 120

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S		121
SEQ ID NO: 359	moltype = AA length = 121	
FEATURE	Location/Qualifiers	
REGION	1..121	
	note = chemically synthesized	
source	1..121	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 359		
QMQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAYSWVRQA PGQGLEWMGG IIPSPGTANY	60	
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGP IVATITPLDY WGQGTLTVS	120	
S	121	
SEQ ID NO: 360	moltype = AA length = 121	
FEATURE	Location/Qualifiers	
REGION	1..121	
	note = chemically synthesized	
source	1..121	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 360		
QMQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPAFGTANY	60	
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGP IVATITPLDY WGQGTLTVS	120	
S	121	
SEQ ID NO: 361	moltype = AA length = 108	
FEATURE	Location/Qualifiers	
REGION	1..108	
	note = chemically synthesized	
source	1..108	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 361		
SYELMQPPSV SVAPGKTATI ACGGENIGRK TVHWYQQKPG QAPVLVIYYD SDRPSGIPER	60	
FSGSNNSGNTA TLTISRVEAG DEADYYCQW DSSSDHRIFG GGTKLTVL	108	
SEQ ID NO: 362	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
REGION	1..107	
	note = chemically synthesized	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 362		
AIRMTQSPSS LSASVGDRV TICRASQSI SYLNWYQQKPK GKAPKLLIYT TSSLKSGVPS	60	
RFSGSGSGTD FTLTISRLQP EDFATYYCQ SYsstwtfgr GTKVEIK	107	
SEQ ID NO: 363	moltype = AA length = 110	
FEATURE	Location/Qualifiers	
REGION	1..110	
	note = chemically synthesized	
source	1..110	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 363		
QSVLTQPPSV SAAPGQKV TI SCGNNSNIA NNYVSWYQQL PGTAPKLLIY DNNYRPMSGIP	60	
DRFSGSKSGT SATLDITGLQ TGDEADYYCG VWDGSLTTGV FGGGTLTVL	110	
SEQ ID NO: 364	moltype = AA length = 110	
FEATURE	Location/Qualifiers	
REGION	1..110	
	note = chemically synthesized	
source	1..110	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 364		
LPVLTQPA SVGSPGQSITI SCTGTTSDIG GYDYVSWYQQ HPGKAPKLMI YDVSKRPSGV	60	
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSSTHV FGTGTLTVL	110	
SEQ ID NO: 365	moltype = AA length = 111	
FEATURE	Location/Qualifiers	
REGION	1..111	
	note = chemically synthesized	
source	1..111	
	mol_type = protein	

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SEQUENCE: 365          organism = synthetic construct
SEQ ID NO: 365          moltype = AA length = 110
FEATURE          Location/Qualifiers
REGION           1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 366          moltype = AA length = 110
SEQ ID NO: 366          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 366          moltype = AA length = 110
SEQ ID NO: 366          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 367          moltype = AA length = 110
SEQ ID NO: 367          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 367          moltype = AA length = 110
SEQ ID NO: 367          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 368          moltype = AA length = 110
SEQ ID NO: 368          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 368          moltype = AA length = 110
SEQ ID NO: 368          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 369          moltype = AA length = 112
SEQ ID NO: 369          Location/Qualifiers
FEATURE          REGION 1..112
source            note = chemically synthesized
                  1..112
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 369          moltype = AA length = 112
SEQ ID NO: 369          Location/Qualifiers
FEATURE          REGION 1..112
source            note = chemically synthesized
                  1..112
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 370          moltype = AA length = 110
SEQ ID NO: 370          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 370          moltype = AA length = 110
SEQ ID NO: 370          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 371          moltype = AA length = 110
SEQ ID NO: 371          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 371          moltype = AA length = 110
SEQ ID NO: 371          Location/Qualifiers
FEATURE          REGION 1..110
source            note = chemically synthesized
                  1..110
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 372          moltype = AA length = 112
SEQ ID NO: 372          Location/Qualifiers
FEATURE          REGION 1..112
source            note = chemically synthesized
                  1..112

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mol_type = protein
organism = synthetic construct
SEQUENCE: 372
QSVTQPPSV SAAPGQKVTI SCSGSSSNIG NNYVSWYQQL PGTAPKLLIY DNNKRPSGIP 60
DRFSGSKSGT SATLGITGLQ TGDEADYYCG TWDSSLSSAGS VVFGGGTKLT VL 112

SEQ ID NO: 373      moltype = AA length = 108
FEATURE           Location/Qualifiers
REGION            1..108
note = chemically synthesized
source             1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 373
SYELMQPPSV SVAPGKTATI ACGGENIGRK TVHWYQQKPG QAPVLVIYYD SDRPSGIPER 60
FSGSNNSGNTA TLTISRVEAG DEADYYCQLW DSSSDHRIFG GGTKLTVL 108

SEQ ID NO: 374      moltype = AA length = 108
FEATURE           Location/Qualifiers
REGION            1..108
note = chemically synthesized
source             1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 374
SYELMQPPSV SVAPGKTATI ACGGENIGRK TVHWYQQKPG QAPVLVIYYD SDRPSGIPER 60
FSGSNNSGNTA TLTISRVEAG DEADYYCQW DSSSDHRIFG GGTKLTVL 108

SEQ ID NO: 375      moltype = AA length = 108
FEATURE           Location/Qualifiers
REGION            1..108
note = chemically synthesized
source             1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 375
SYELMQPPSV SVAPGKTATI ACGGENIGRK TVHWYQQKPG QAPVLVIYYD SDRPSGIPER 60
FSGSNNSGNTA TLTISRVEAG DEADYYCQW DSSSDHRIFG GGTKLTVL 108

SEQ ID NO: 376      moltype = AA length = 108
FEATURE           Location/Qualifiers
REGION            1..108
note = chemically synthesized
source             1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 376
SYELMQPPSV SVAPGKTATI ACGGENIGRK TVHWYQQKPG QAPVLVIYYD SDRPSGIPER 60
FSGSNNSGNTA TLTISRVEAG DEADYYCQW DSSSDHRIFG GGTKLTVL 108

SEQ ID NO: 377      moltype = AA length = 122
FEATURE           Location/Qualifiers
REGION            1..122
note = chemically synthesized
source             1..122
mol_type = protein
organism = synthetic construct
SEQUENCE: 377
QVOLVQSGSE VKKSGSSVKV SCKTSGGTFS ITNYAINWVR QAPGQGLEWM GGILPIFGAA 60
KYAQKFDQDRV TITADESTNT AYLELSSLTS EDTAMYYCAR GKRWLQSDLQ YWGQGTLTV 120
SS 122

SEQ ID NO: 378      moltype = AA length = 110
FEATURE           Location/Qualifiers
REGION            1..110
note = chemically synthesized
source             1..110
mol_type = protein
organism = synthetic construct
SEQUENCE: 378
QPVLTQPAVS SGSPGQSQITI SCTGSSSDVG SYDLVSWYQQ SPGKVPKLLI YEGVKRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYAGTRNFF FGGGTQLTVL 110

SEQ ID NO: 379      moltype = AA length = 121
FEATURE           Location/Qualifiers
REGION            1..121

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source          note = chemically synthesized
               1..121
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 379
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IYSTGGATAY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKSS AGQSRRPGFDY WGQGTLVTVS 120
S                                         121

SEQ ID NO: 380      moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source          note = chemically synthesized
               1..121
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 380
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IYSTGGATAY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKSS AGQSWPFGFDY WGQGTLVTVS 120
S                                         121

SEQ ID NO: 381      moltype = AA  length = 121
FEATURE          Location/Qualifiers
REGION           1..121
source          note = chemically synthesized
               1..121
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 381
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IYSTGGATAY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKSS AGQSFPFGFDY WGQGTLVTVS 120
S                                         121

SEQ ID NO: 382      moltype = AA  length = 116
FEATURE          Location/Qualifiers
REGION           1..116
source          note = chemically synthesized
               1..116
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 382
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IYSTGGATAY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS AAFDYWGQGT LTVSS       116

SEQ ID NO: 383      moltype = AA  length = 116
FEATURE          Location/Qualifiers
REGION           1..116
source          note = chemically synthesized
               1..116
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 383
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IYSTGGATAY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS AGYDYWGQGT LTVSS       116

SEQ ID NO: 384      moltype = AA  length = 116
FEATURE          Location/Qualifiers
REGION           1..116
source          note = chemically synthesized
               1..116
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 384
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IYSTGGATAY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS KGFDYWGQGT LTVSS       116

SEQ ID NO: 385      moltype = AA  length = 113
FEATURE          Location/Qualifiers
REGION           1..113
source          note = chemically synthesized
               1..113
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 385
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWKQGIVTVY 60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQGTL VTV         113

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SEQ ID NO: 386      moltype = AA  length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 386
EVQLESAGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWRNGIVTVY 60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQQGTL VTVSS     115

SEQ ID NO: 387      moltype = AA  length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 387
EVQLESAGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSD IWKGGMVTY 60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQQGTL VTVSS     115

SEQ ID NO: 388      moltype = AA  length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 388
EVQLESAGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWRQGLATAY 60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQQGTL VTVSS     115

SEQ ID NO: 389      moltype = AA  length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 389
EVQLESAGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSE IVATGILTSY 60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQQGTL VTVSS     115

SEQ ID NO: 390      moltype = AA  length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 390
EVQLESAGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IGRQGLITVY 60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQQGTL VTVSS     115

SEQ ID NO: 391      moltype = AA  length = 115
FEATURE
REGION
1..115
note = chemically synthesized
source
1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 391
EVQLESAGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWYQGLVTY 60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQQGTL VTVSS     115

SEQ ID NO: 392      moltype = AA  length = 114
FEATURE
REGION
1..114
note = chemically synthesized
source
1..114
mol_type = protein
organism = synthetic construct
SEQUENCE: 392
EVQLESAGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSD IWKGQGFATAD 60

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SVKGRFTISR DNSKNTLYLQ MNSLRAEDTA VYYCAKSSAG FDYWGQGTLV TVSS	114
SEQ ID NO: 393	moltype = AA length = 115
FEATURE	Location/Qualifiers
REGION	1..115
	note = chemically synthesized
source	1..115
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 393	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWKQGIVTVY	60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQGTL VTVSS	115
SEQ ID NO: 394	moltype = AA length = 115
FEATURE	Location/Qualifiers
REGION	1..115
	note = chemically synthesized
source	1..115
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 394	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWRQGLATAY	60
DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKSSA GFDYWGQGTL VTVSS	115
SEQ ID NO: 395	moltype = AA length = 116
FEATURE	Location/Qualifiers
REGION	1..116
	note = chemically synthesized
source	1..116
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 395	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWRNGIVTVY	60
ADSVVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS AAFDYWGQGT LVTVSS	116
SEQ ID NO: 396	moltype = AA length = 116
FEATURE	Location/Qualifiers
REGION	1..116
	note = chemically synthesized
source	1..116
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 396	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWRNGIVTVY	60
ADSVVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS AGYDYWGQGT LVTVSS	116
SEQ ID NO: 397	moltype = AA length = 116
FEATURE	Location/Qualifiers
REGION	1..116
	note = chemically synthesized
source	1..116
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 397	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IWRNGIVTVY	60
ADSVVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS KGFDYWGQGT LVTVSS	116
SEQ ID NO: 398	moltype = AA length = 120
FEATURE	Location/Qualifiers
REGION	1..120
	note = chemically synthesized
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 398	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMETSWVRQA PGKGLEWVSS SSIWYQGLVT	60
YYADSVVKGRF TISRDNSKNT LYLMETNSL RAEDTAVYYC AKWSAAFDYW GQGTLTVSS	120
SEQ ID NO: 399	moltype = AA length = 116
FEATURE	Location/Qualifiers
REGION	1..116
	note = chemically synthesized
source	1..116
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 399	

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EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWSS IWYQGLVTVY	60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS AGYDYWGQGT LTVSS	116
SEQ ID NO: 400	moltype = AA length = 116
FEATURE	Location/Qualifiers
REGION	1..116
	note = chemically synthesized
source	1..116
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 400	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWSS IWYQGLVTVY	60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKWS KGFDYWQGT LTVSS	116
SEQ ID NO: 401	moltype = AA length = 108
FEATURE	Location/Qualifiers
REGION	1..108
	note = chemically synthesized
source	1..108
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 401	
DIQMTQSPSS LSASVGDRV TITCRASQSI SYLNWYQQKP GKAPKLLIYY ASTLQSGVPS	60
RFGSGSGSTD FTLTISSSLQP EDFATYYCQQ DNGYPSTFGQ GTKVEIKR	108
SEQ ID NO: 402	moltype = AA length = 108
FEATURE	Location/Qualifiers
REGION	1..108
	note = chemically synthesized
source	1..108
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 402	
DIQMTQSPSS LSASVGDRV TITCRASQSI SYLNWYQQKP GKAPKLLIYY ASTLQSGVPS	60
RFGSGSGSTD FTLTISSSLQP EDFATYYCQQ DNGYPSTFGQ GTKVEIKR	108
SEQ ID NO: 403	moltype = AA length = 108
FEATURE	Location/Qualifiers
REGION	1..108
	note = chemically synthesized
source	1..108
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 403	
DIQMTQSPSS LSASVGDRV TITCRASQSI SYLNWYQQKP GKAPKLLIYA ASSLQSGVPS	60
RFGSGSGSTD FTLTISSSLQP EDFATYYCQQ DNGYPSTFGQ GTKVEIKR	108
SEQ ID NO: 404	moltype = AA length = 240
FEATURE	Location/Qualifiers
REGION	1..240
	note = chemically synthesized
source	1..240
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 404	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWSD ITASGQRTTY	60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARSK IAFDYWGQGT LTVVSSGGG	120
SGGGGSGGG STDIQMTQSP SSLSASVGDR VTITCRASQ ISSYLNWYQQ KPGKAPKLLI	180
YKASRLQSGV PSRFSGSGSG TDFTLTISSL QPEDFATYYC QQRALKPVTF GQGTKVEIKR	240
SEQ ID NO: 405	moltype = AA length = 240
FEATURE	Location/Qualifiers
REGION	1..240
	note = chemically synthesized
source	1..240
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 405	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWSS INKDGHYTSY	60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKNL DEFDYWGQGT LTVVSSGGG	120
SGGGGSGGG STDIQMTQSP SSLSASVGDR VTITCRASQ ISSYLNWYQQ KPGKAPKLLI	180
YAASSLQSGV PSRFSGSGSG TDFTLTISSL QPEDFATYYC QQSystPNTF GQGTKVEIKR	240
SEQ ID NO: 406	moltype = AA length = 240
FEATURE	Location/Qualifiers
REGION	1..240

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source          note = chemically synthesized
               1..240
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 406
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IMATGAGTLY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKDG AGFDYWGQGT LVTVSSGGGG 120
SGGGGSGGG STDIQMTQSP SSLSASVGDR VTITCRASQS ISSYLNWYQQ KPGKAPKLLI 180
YSASQLQSGV PSRFSGSGSG TDFTLTISL QPEDFATYYC QQANSRPSTF GQGTKVEIKR 240

SEQ ID NO: 407      moltype = AA length = 240
FEATURE          Location/Qualifiers
REGION           1..240
source          note = chemically synthesized
               1..240
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 407
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLQWVST ITSSGAATYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKMY TGFDYWGQGT LVTVSSGGGG 120
SGGGGSGGG STDIQMTQSP SSLSASVGDR VTITCRASQS ISSYLNWYQQ KPGKAPKLLI 180
YNASSLQSGV PSRFSGSGSG TDFTLTISL QPEDFATYYC QQYTYGPGTF GQGTKVEIKR 240

SEQ ID NO: 408      moltype = AA length = 240
FEATURE          Location/Qualifiers
REGION           1..240
source          note = chemically synthesized
               1..240
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 408
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSS IYSTGGATAY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKSS AGFDYWGQGT LVTVSSGGGG 120
SGGGGSGGG STDIQMTQSP SSLSASVGDR VTITCRASQS ISSYLNWYQQ KPGKAPKLLI 180
YYASTLQSGV PSRFSGSGSG TDFTLTISL QPEDFATYYC QQDNGYPSTF GQGTKVEIKR 240

SEQ ID NO: 409      moltype = AA length = 122
FEATURE          Location/Qualifiers
REGION           1..122
source          note = chemically synthesized
               1..122
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 409
QLQLQESGGG LVQAGGSLRL SCAASGIMFY ISDMGWYRQA PGKQREFVAT ITSGGTTNYA 60
DSVEGRFSIS RDNAKNTVYL QMNSLEPEDT AVYYCTAHGP TYGSTWDDLW GQGTQVTVKP 120
GG 122

SEQ ID NO: 410      moltype = AA length = 8
FEATURE          Location/Qualifiers
REGION           1..8
source          note = chemically synthesized
               1..8
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 410
GIMFYISD 8

SEQ ID NO: 411      moltype = AA length = 10
FEATURE          Location/Qualifiers
REGION           1..10
source          note = chemically synthesized
               1..10
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 411
TITSGGTTNY 10

SEQ ID NO: 412      moltype = AA length = 14
FEATURE          Location/Qualifiers
REGION           1..14
source          note = chemically synthesized
               1..14
               mol_type = protein
               organism = synthetic construct

SEQUENCE: 412

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TAHGPTYGST WDDL	14
SEQ ID NO: 413	moltype = AA length = 113
FEATURE	Location/Qualifiers
REGION	1..113
	note = chemically synthesized
source	1..113
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 413	
QVQLQESGGG LVQAGGSLRL SCAASETFCGV VFTLGWYRQTA PGKQREFVAR VTGTDVDY	60
DSVKGRFTIS SDFARNTVYL QMNNLKPEDT AVYYCNTGAY WGQGTQVTVK PGG	113
SEQ ID NO: 414	moltype = AA length = 7
FEATURE	Location/Qualifiers
REGION	1..7
	note = chemically synthesized
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 414	
TFGVVF	7
SEQ ID NO: 415	moltype = AA length = 7
FEATURE	Location/Qualifiers
REGION	1..7
	note = chemically synthesized
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 415	
VTGTDV	7
SEQ ID NO: 416	moltype = AA length = 5
FEATURE	Location/Qualifiers
REGION	1..5
	note = chemically synthesized
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 416	
NTGAY	5
SEQ ID NO: 417	moltype = AA length = 119
FEATURE	Location/Qualifiers
REGION	1..119
	note = chemically synthesized
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 417	
QVQLVQSGGG LVQTGGSLRL SCAASGRTAS TYSMGWFRQA PGKERQFVAR IIWSTGSTYY	60
TNSVEGRFTI SRDIAKNTLY LQMNSLEPED TAVYYCTARE PTGYDYWGQQ TQVTVKPGG	119
SEQ ID NO: 418	moltype = AA length = 8
FEATURE	Location/Qualifiers
REGION	1..8
	note = chemically synthesized
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 418	
GRTASTYS	8
SEQ ID NO: 419	moltype = AA length = 7
FEATURE	Location/Qualifiers
REGION	1..7
	note = chemically synthesized
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 419	
IWSTGST	7
SEQ ID NO: 420	moltype = AA length = 10
FEATURE	Location/Qualifiers

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REGION	1..10
source	note = chemically synthesized
	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 420	
TAREPTGYDY	10
SEQ ID NO: 421	moltype = AA length = 122
FEATURE	Location/Qualifiers
REGION	1..122
source	note = chemically synthesized
	1..122
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 421	
QLQLQESGGG LVQAGGSLGL SCAASGSIFR FGARGWYRQA PGKQRELVAI ITSGGSTNYA	60
DSVQGRFTIS RDNAKNMVYL QMNGLKSGDT AVYYCAADRS DAVGVGWDYW GQGTQVTVKP	120
GG	122
SEQ ID NO: 422	moltype = AA length = 8
FEATURE	Location/Qualifiers
REGION	1..8
source	note = chemically synthesized
	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 422	
GSIFRFGA	8
SEQ ID NO: 423	moltype = AA length = 7
FEATURE	Location/Qualifiers
REGION	1..7
source	note = chemically synthesized
	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 423	
ITSGGST	7
SEQ ID NO: 424	moltype = AA length = 14
FEATURE	Location/Qualifiers
REGION	1..14
source	note = chemically synthesized
	1..14
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 424	
AADRSDAVGV GWDY	14
SEQ ID NO: 425	moltype = AA length = 119
FEATURE	Location/Qualifiers
REGION	1..119
source	note = chemically synthesized
	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 425	
QVQLQQSGGG LVQTGGSLRL SCAASGRATAS TYSMGWFRQA PGKERQFVAR IIWSTGSTYY	60
TNSVEGRFTI SRDIAKNTLY LQMNSLEPED TAVYYCTARD PTGYDYGQG TQVTVKPGG	119
SEQ ID NO: 426	moltype = AA length = 8
FEATURE	Location/Qualifiers
REGION	1..8
source	note = chemically synthesized
	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 426	
IIWSTGST	8
SEQ ID NO: 427	moltype = AA length = 10
FEATURE	Location/Qualifiers
REGION	1..10
source	note = chemically synthesized
	1..10

-continued

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mol_type = protein
organism = synthetic construct
SEQUENCE: 427
TARDPTGYDY                                         10

SEQ ID NO: 428          moltype = AA length = 121
FEATURE           Location/Qualifiers
REGION            1..121
source             note = chemically synthesized
                  1..121
mol_type = protein
organism = synthetic construct
SEQUENCE: 428
QLQLQESGGG LVQAGGSLRL SCAASGSIFS IDATAWYRQA PGKQRELVAI ITSSGSTNYP 60
DSVKGRFTIS RDNAKNTVYL QMNSLNPEDT ALYSCNAITR MGGSTYDFWG QGTQVTVKPG 120
G                                         121

SEQ ID NO: 429          moltype = AA length = 8
FEATURE           Location/Qualifiers
REGION            1..8
source             note = chemically synthesized
                  1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 429
GSIFSIDA                                         8

SEQ ID NO: 430          moltype = AA length = 7
FEATURE           Location/Qualifiers
REGION            1..7
source             note = chemically synthesized
                  1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 430
ITSSGST                                         7

SEQ ID NO: 431          moltype = AA length = 13
FEATURE           Location/Qualifiers
REGION            1..13
source             note = chemically synthesized
                  1..13
mol_type = protein
organism = synthetic construct
SEQUENCE: 431
NAITRMGGST YDF                                         13

SEQ ID NO: 432          moltype = AA length = 117
FEATURE           Location/Qualifiers
REGION            1..117
source             note = chemically synthesized
                  1..117
mol_type = protein
organism = synthetic construct
SEQUENCE: 432
QVQLVQSGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA IPAGDGSTKY 60
ADSVKGRFTI SRDNAKNTVY LQMDSLKPED TAVYFCAKSRSR GWSTVDDMDY WGKGQTQV 117

SEQ ID NO: 433          moltype = AA length = 8
FEATURE           Location/Qualifiers
REGION            1..8
source             note = chemically synthesized
                  1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 433
GFTFSSYA                                         8

SEQ ID NO: 434          moltype = AA length = 8
FEATURE           Location/Qualifiers
REGION            1..8
source             note = chemically synthesized
                  1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 434

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-continued

IPAGDGST

8

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SEQ ID NO: 435      moltype = AA length = 14
FEATURE
REGION
1..14
note = chemically synthesized
1..14
mol_type = protein
organism = synthetic construct

SEQUENCE: 435
AKSRGWSTVD DMDY                                         14

SEQ ID NO: 436      moltype = AA length = 117
FEATURE
REGION
1..117
note = chemically synthesized
1..117
mol_type = protein
organism = synthetic construct

SEQUENCE: 436
QVQLVQSGGG LVQPGGSLRL SCVVS GFTFR SYAMSWVRQA PGKGLEWVST INSGESSTKY 60
ADSVKGRFTI SRDDAKNTLY LQMSDLKPED TAVYFCAKHR GWSTVDDINY WGKGQTQV    117

SEQ ID NO: 437      moltype = AA length = 8
FEATURE
REGION
1..8
note = chemically synthesized
1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 437
GFTFRSYA                                         8

SEQ ID NO: 438      moltype = AA length = 8
FEATURE
REGION
1..8
note = chemically synthesized
1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 438
INSGESST                                         8

SEQ ID NO: 439      moltype = AA length = 14
FEATURE
REGION
1..14
note = chemically synthesized
1..14
mol_type = protein
organism = synthetic construct

SEQUENCE: 439
AKHRGWSTVD DINY                                         14

SEQ ID NO: 440      moltype = AA length = 119
FEATURE
REGION
1..119
note = chemically synthesized
1..119
mol_type = protein
organism = synthetic construct

SEQUENCE: 440
QVQLVQSGGG LVQPGGSLRL SCAAS GFTFD DHAMSWVRQA PGKGLEWVSA ISWNNGHYTYY 60
AESMKGRFAI SRDNAKNTLY LQMNSLKSED TAVYYCVKGW RGSYTRDRPF ASWGQGTQV    119

SEQ ID NO: 441      moltype = AA length = 8
FEATURE
REGION
1..8
note = chemically synthesized
1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 441
GFTFDDHA                                         8

SEQ ID NO: 442      moltype = AA length = 8
FEATURE

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-continued

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REGION          1..8
source          note = chemically synthesized
                1..8
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 442 ISWNNGHYT                                         8

SEQ ID NO: 443      moltype = AA  length = 16
FEATURE          Location/Qualifiers
REGION           1..16
source          note = chemically synthesized
                1..16
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 443 VKGWRGSYTR DRPFAS                                         16

SEQ ID NO: 444      moltype = AA  length = 118
FEATURE          Location/Qualifiers
REGION           1..118
source          note = chemically synthesized
                1..118
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 444 EVQLVQSGGG LVQPGGSLRL SCAASGFTFS SYYMSWRQQA PGKGLEWVST ISTNTGGGST 60
YYAYADSVKG RFTISRDNAK NTLYLEMNSL KPEDTAQYYC VRTRWEGVYD YWGLGTQV 118

SEQ ID NO: 445      moltype = AA  length = 8
FEATURE          Location/Qualifiers
REGION           1..8
source          note = chemically synthesized
                1..8
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 445 GFTFSSYY                                         8

SEQ ID NO: 446      moltype = AA  length = 10
FEATURE          Location/Qualifiers
REGION           1..10
source          note = chemically synthesized
                1..10
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 446 ISTNTGGGST                                         10

SEQ ID NO: 447      moltype = AA  length = 11
FEATURE          Location/Qualifiers
REGION           1..11
source          note = chemically synthesized
                1..11
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 447 VRTRWEGVYD Y                                         11

SEQ ID NO: 448      moltype = AA  length = 482
FEATURE          Location/Qualifiers
REGION           1..482
source          note = chemically synthesized
                1..482
                mol_type = protein
                organism = synthetic construct
SEQUENCE: 448 EVOLLESGGG EVQPGGSLRL SCAASGFSFS INAMGWYRQQA PGKRREFVAA IESGRNTVVA 60
ESVKGRFTIS RDNAKNTVYL QMSSLRAEDT AVYYCGLLKQ NRVVSPSVAY WGQGTLTVK 120
PGGGGDKTHT CPPCPAPGGP SVFLFPKP DKTMISRTPE VTCVVVDVSH EDPEVKFNWY 180
VDGVEVHNAK TKPREEQYNS TYRVVSVLTW LHQDWLNCKE YKCKVSNKAL PAPIEKTISK 240
AKGQPREPVQ YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESENQPE NNYKTPPVVL 300
DSDGGSFFLYS KLTVDKSRWQ QGNVFSCSVN HEALHNHYTQ KSLSLSPGSG GGGSGGGSE 360
VQLLESGGGE VQPGGSLRLS CAASGFSFSI NAMGWYRQAP GKRREFVAAI ESGRNTVYAE 420
SVKGRFTISR DNAKNTVYLQ MSSLRAEDTA VYYCGLLKGN RVVSPSVAYW GQGTLTVK 480
GG                                         482

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-continued

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SEQ ID NO: 449      moltype = AA length = 466
FEATURE          Location/Qualifiers
REGION           1..466
note = chemically synthesized
source            1..466
mol_type = protein
organism = synthetic construct

SEQUENCE: 449
EVOLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PKGQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ PGGSLRLSCA ASGFSSFSINA MGWYRQAPGK RREFVAAIYS GRNTVYAESV 180
KGRTFISRDN AKNTVYLQMS SLRAEDTAVY YCGLLKGNRV VSPSVAYWGQ GTLVTVKPGG 240
GGDKTHTCPP CPAPGGPSVF LFPPPKDCTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG 300
VEVHNNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG 360
QPREPVQVTL PPSRDELTN QVSLTCLVKG FYPSDIAVEW ESNQGPENNY KTPPPVLDSD 420
GSFFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPKG               466

SEQ ID NO: 450      moltype = AA length = 466
FEATURE          Location/Qualifiers
REGION           1..466
note = chemically synthesized
source            1..466
mol_type = protein
organism = synthetic construct

SEQUENCE: 450
EVOLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PKGQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ PGGSLRLSCA ASGFSSFSINA MGWYRQAPGK RREFVAAIYS GRNTVYAESV 180
KGRTFISRDN AKNTVYLQMS SLRAEDTAVY YCGLLKGNRV VSPSVAYWGQ GTLVTVKPGG 240
GGDKTHTCPP CPAPGGPSVF LFPPPKDCTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG 300
VEVHNNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG 360
QPREPVQVTL PPSRDELTN QVSLTCLVKG FYPSDIAVEW ESNQGPENNY KTPPPVLDSD 420
GSFFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPKG               466

SEQ ID NO: 451      moltype = AA length = 466
FEATURE          Location/Qualifiers
REGION           1..466
note = chemically synthesized
source            1..466
mol_type = protein
organism = synthetic construct

SEQUENCE: 451
EVOLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PKGQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ PGGSLRLSCA ASGFSSFSINA MGWYRQAPGK RREFVAAIYS GSSTVYAESV 180
KGRTFISRDN AKNTVYLQMS SLRAEDTAVY YCGLLKGNRV VSPSVAYWGQ GTLVTVKPGG 240
GGDKTHTCPP CPAPGGPSVF LFPPPKDCTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG 300
VEVHNNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG 360
QPREPVQVTL PPSRDELTN QVSLTCLVKG FYPSDIAVEW ESNQGPENNY KTPPPVLDSD 420
GSFFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPKG               466

SEQ ID NO: 452      moltype = AA length = 481
FEATURE          Location/Qualifiers
REGION           1..481
note = chemically synthesized
source            1..481
mol_type = protein
organism = synthetic construct

SEQUENCE: 452
EVOLLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PKGQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNVFEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ LLESGGGGEVQ PGGSLRLSCA ASGWAFGNYG MAWFQAPGK EREFVSLRAW 180
QCGSTDYVES VKGRFTISRD NAKNTLYLQM SSLRAEDTAV YYCARQRSYS RYDIRTPQTY 240
DYWGQGTLVT VPKGGGGDKT HTCPCCPAPG GPSVFLFPKK PKDTLMISRT PEVTCVVVDV 300
SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYCKVSNK 360
ALPAPIEKTI SKAKGQPREP QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ 420
PENNYKTPPP VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG 480
K                                         481

SEQ ID NO: 453      moltype = AA length = 481
FEATURE          Location/Qualifiers
REGION           1..481
note = chemically synthesized
source            1..481
mol_type = protein

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-continued

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organism = synthetic construct
SEQUENCE: 453
EVQPLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNFVEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ LLESGGGGEVQ PGGSRLSCA ASGWAFGNYG MAWFQRQAPGK EREFVSLRAW 180
GGGSTDYVES VKGRFTISRD NAKNTLYLQM SSLRAEDTAV YYCARQRSYS RYDIRTPQTY 240
DYWGQGTLVT VKPGGGGDKT HTCPCPAPG GPSVFLFPKK PKDTLMISRT PEVTCVVVDV 300
SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK 360
ALPAPIEKTI SKAKGQPREP QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ 420
PENNYKTTPP VLDSDGSSFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSSLSPG 480
K 481

SEQ ID NO: 454      moltype = AA length = 481
FEATURE           Location/Qualifiers
REGION            1..481
note = chemically synthesized
source             1..481
mol_type = protein
organism = synthetic construct
SEQUENCE: 454
EVQPLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNFVEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ LLESGGGGEVQ PGGSRLSCA ASGWAFGNYG MAWFQRQAPGK EREFVSLRAW 180
GGGSTDYVES VKGRFTISRD NAKNTLYLQM SSLRAEDTAV YYCARQRSYS RYDIRTPQTY 240
DYWGQGTLVT VKPGGGGDKT HTCPCPAPG GPSVFLFPKK PKDTLMISRT PEVTCVVVDV 300
SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK 360
ALPAPIEKTI SKAKGQPREP QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ 420
PENNYKTTPP VLDSDGSSFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSSLSPG 480
K 481

SEQ ID NO: 455      moltype = AA length = 481
FEATURE           Location/Qualifiers
REGION            1..481
note = chemically synthesized
source             1..481
mol_type = protein
organism = synthetic construct
SEQUENCE: 455
EVQPLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNFVEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ LLESGGGGEVQ PGGSRLSCA ASGWAFGNYG MAWFQRQAPGK EREFVSLRAW 180
GGGSTDYVES VKGRFTISRD NAKNTLYLQM SSLRAEDTAV YYCARQRSYS RYDIRTPQTY 240
DYWGQGTLVT VKPGGGGDKT HTCPCPAPG GPSVFLFPKK PKDTLMISRT PEVTCVVVDV 300
SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK 360
ALPAPIEKTI SKAKGQPREP QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ 420
PENNYKTTPP VLDSDGSSFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSSLSPG 480
K 481

SEQ ID NO: 456      moltype = AA length = 481
FEATURE           Location/Qualifiers
REGION            1..481
note = chemically synthesized
source             1..481
mol_type = protein
organism = synthetic construct
SEQUENCE: 456
EVQPLESGGG EVQPGGSLRL SCAASGGIFA IKPISWYRQA PGKQREWVST TTSSGATNYA 60
ESVKGRFTIS RDNAKNTLYL QMSSLRAEDT AVYYCNFVEY WGQGTLVTVK PGGSGGSEVQ 120
LLESGGGGEVQ LLESGGGGEVQ PGGSRLSCA ASGWAFGNYG MAWFQRQAPGK EREFVSLRAW 180
GGGSTDYVES VKGRFTISRD NAKNTLYLQM SSLRAEDTAV YYCARQRSYS RYDIRTPQTY 240
DYWGQGTLVT VKPGGGGDKT HTCPCPAPG GPSVFLFPKK PKDTLMISRT PEVTCVVVDV 300
SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK 360
ALPAPIEKTI SKAKGQPREP QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ 420
PENNYKTTPP VLDSDGSSFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSSLSPG 480
K 481

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1-47. (canceled)

48. A method of treating cancer comprising administering to a human subject with cancer a polypeptide comprising at least one VHH domain that binds human programmed death ligand 1 (PDL1), wherein at least one VHH domain that binds PDL1 comprises:

- (i) a CDR1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence

of SEQ ID NO: 102, and a CDR3 comprising an amino acid sequence of SEQ ID NO: 103;

- (ii) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 105, a CDR2 comprising an amino acid sequence of SEQ ID NO: 106, and a CDR comprising an amino acid sequence of SEQ ID NO: 107;
- (iii) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 109, a CDR2 comprising an amino acid

sequence of SEQ ID NO: 110, and a CDR comprising an amino acid sequence of SEQ ID NO: 111;
(iv) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence of SEQ ID NO: 110, and a CDR comprising an amino acid sequence of SEQ ID NO: 113;
(v) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence of SEQ ID NO: 110, and a CDR comprising an amino acid sequence of SEQ ID NO: 115; or
(vi) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence of SEQ ID NO: 117, and a CDR comprising an amino acid sequence of SEQ ID NO: 118.

49. The method of claim **48**, wherein at least one VHH domain that binds PDL1 comprises a CDR1 comprising the amino acid sequence of SEQ ID NO: 105, a CDR2 comprising the amino acid sequence of SEQ ID NO: 106, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 107.

50. The method of claim **48**, wherein each VHH domain that binds PDL1 is humanized.

51. The method of claim **48**, wherein the polypeptide is monospecific.

52. The method of claim **48**, wherein at least one VHH domain that binds PDL1 comprises an amino acid sequence that is at least 95% identical to an amino acid sequence selected from SEQ ID NOS: 100, 104, 108, 112, 114, 116, and 119-124.

54. The method of claim **48**, wherein at least one VHH domain that binds PDL1 comprises an amino acid sequence selected from SEQ ID NOS: 100, 104, 108, 112, 114, 116, and 119-124.

55. The method of claim **48**, wherein at least one VHH domain that binds PDL1 comprises the amino acid sequence of SEQ ID NO: 124.

56. The method of claim **48**, wherein each VHH domain that binds PDL1 comprises the amino acid sequence of SEQ ID NO: 124.

57. The method of claim **48**, wherein the isolated polypeptide comprises an Fc region.

58. The method of claim **57**, wherein the Fc region comprises an amino acid sequence that is at least 97% or 100% identical to an amino acid sequence selected from SEQ ID NOS: 1-6.

59. The method of claim **48**, wherein the cancer is selected from carcinoma, sarcoma, lymphoma, and leukemia.

60. A method of increasing T cell activation and/or proliferation comprising contacting T cells with a polypeptide of claim comprising at least one VHH domain that binds human programmed death ligand 1 (PDL1), wherein at least one VHH domain that binds PDL1 comprises:

(i) a CDR1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence

of SEQ ID NO: 102, and a CDR3 comprising an amino acid sequence of SEQ ID NO: 103;

(ii) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 105, a CDR2 comprising an amino acid sequence of SEQ ID NO: 106, and a CDR comprising an amino acid sequence of SEQ ID NO: 107;

(iii) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 109, a CDR2 comprising an amino acid sequence of SEQ ID NO: 110, and a CDR comprising an amino acid sequence of SEQ ID NO: 111;

(iv) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence of SEQ ID NO: 110, and a CDR comprising an amino acid sequence of SEQ ID NO: 113;

(v) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence of SEQ ID NO: 110, and a CDR comprising an amino acid sequence of SEQ ID NO: 115; or

(vi) a CDR 1 comprising an amino acid sequence of SEQ ID NO: 101, a CDR2 comprising an amino acid sequence of SEQ ID NO: 117, and a CDR comprising an amino acid sequence of SEQ ID NO: 118.

61. The method of claim **60**, wherein the T cells are CD4⁺ T cells and/or CD8⁺ T cells.

62. The method of claim **60**, wherein at least one VHH domain that binds PDL1 comprises a CDR1 comprising the amino acid sequence of SEQ ID NO: 105, a CDR2 comprising the amino acid sequence of SEQ ID NO: 106, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 107.

63. The method of claim **60**, wherein each VHH domain that binds PDL1 is humanized.

64. The method of claim **60**, wherein the polypeptide is monospecific.

65. The method of claim **60**, wherein at least one VHH domain that binds PDL1 comprises an amino acid sequence that is at least 95% identical to an amino acid sequence selected from SEQ ID NOS: 100, 104, 108, 112, 114, 116, and 119-124.

66. The method of claim **60**, wherein at least one VHH domain that binds PDL1 comprises an amino acid sequence selected from SEQ ID NOS: 100, 104, 108, 112, 114, 116, and 119-124.

67. The method of claim **60**, wherein at least one VHH domain that binds PDL1 comprises the amino acid sequence of SEQ ID NO: 124.

68. The method of claim **60**, wherein each VHH domain that binds PDL1 comprises the amino acid sequence of SEQ ID NO: 124.

69. The method of claim **60**, wherein the isolated polypeptide comprises an Fc region.

70. The method of claim **69**, wherein the Fc region comprises an amino acid sequence that is at least 97% or 100% identical to an amino acid sequence selected from SEQ ID NOS: 1-6.