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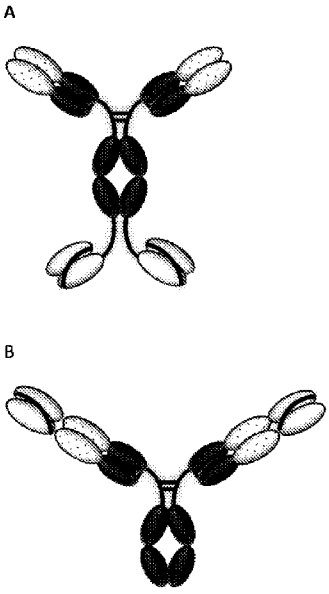
(54) Title: BISPECIFIC ANTIBODIES AND METHODS OF MAKING AND USING THEREOF

(57) Abstract: The disclosure provides bispecific antibodies having the binding specificity to at least two of human CTLA4, PD-1 or PD-L1. In one embodiment, the bispecific antibody comprises IgG domains having heavy chains and light chains, and two scFv components being connected to either C-terminal of the heavy chains or N-terminal of the light chains, wherein the IgG domains have the binding specificity to a first antigen, wherein the scFv components have the binding specificity to a second antigen, and wherein the first antigen and the second antigen are different and are independently selected from a-CTLA4, α-PD-1, and α-PD-L1.

Figure 1.



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BISPECIFIC ANTIBODIES AND METHODS OF MAKING AND USING THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 62580845 filed on November 2nd, 2017, titled "BISPECIFIC ANTIBODIES AND METHODS OF MAKING AND USING THEREOF", which are expressly incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] The present disclosure generally relates to the technical field of biologic therapeutics, and more particularly relates to making and using bispecific antibodies. All references are incorporated herein by its entirety.

BACKGROUND

[0003] Cancer cells develop various strategies to evade immunosurveillance. Absence of specific tumor antigens and loss of expression of major histocompatibility complex (MHC) molecules hinder the recognition of cancer cells by T lymphocytes. Immunosuppressive tumor microenvironment also contributes to the reduced recognition of tumor cells by the immune system. The tumor microenvironment is presented by immunosuppressive cellular populations composed of regulatory T cells, myeloid derived suppressor cells, tumor associated macrophages, suppressive B cells, immunosuppressive cytokines produced by tumor or stroma cells such as TGF-beta or IL-10, and immune checkpoint molecules that regulate T cell function [Marshall HT et al., Front Oncol 2018, 8:315].

[0004] Engaging a patient own immune system has been shown to be effective at controlling tumor growth and specific elimination of tumor cells while leaving normal tissue intact. Immunotherapy has provided an additional angle to treating cancer [Khalil DN et al., Adv Cancer Res 2015, 128:1-68].

[0005] Combining multiple modulators of the immune system is a new rapidly developing area of the immuno-oncology field. New therapeutic agents that can modulate immune response to tumor cells via multiple pathways can be greatly beneficial for cancer patient by increasing the patient response rate and in some cases decreasing toxicity.

[0006] Combination therapy with more than one monoclonal antibody targeting the immune system have been shown to be more efficacious in the treatment of cancer than treatments with single agents [Hellman MD et al., Adv Immunol 2016, 130: 251-77]. In addition to the increased efficacy and response rate, the combination therapy often has greater toxicity than a single agent treatment. Bispecific agents that modulate the immune system can be less toxic to patients and/or more potent, have additional

mechanisms of action than treatments comprised of a combination of monoclonal antibodies with identical specificities.

SUMMARY

[0007] The current disclosure relates to the bispecific antibodies, specifically, the bispecific antibodies that contain an IgG component therefore overcome fast clearance of BiTE molecule, having an advantage over CAR-T cell therapy as an off-the-shelf therapy that does not require *ex vivo* expansion of patients' immune cells. Another advantage of the bispecific antibodies is the enhanced ability to overcome suppressive tumor microenvironment by simultaneous engagement of two checkpoint receptors.

[0008] The bispecific antibodies in the current disclosure can be combined with other agents, for instance T-cell engagers, and further enhance their activity.

[0009] The present disclosure relates to bispecific antibodies that bind to two distinct targets expressed on immune and tumor cells. Both targets may be checkpoint antigens. In one embodiment, both targets may be checkpoint antigens on immune cells. In one embodiment, both targets may be checkpoint antigens on tumor cells. In one embodiment, one target is a checkpoint antigen on immune cells and another target is a checkpoint antigen on tumor cells. In one embodiment, the checkpoint antigen may be selected from PD-1, PD-L1 and CTLA4. In one embodiment, the targets may include any combination of PD-1, PD-L1 and CTLA4.

[0010] The disclosure further provides the composition of the bispecific agents and their therapeutic use for treatment of cancer and autoimmune deficiencies.

[0011] In one embodiment, the application discloses a bispecific antibody comprising IgG heavy chains and light chains, and two scFv components being connected to either C terminal of the heavy chains or N terminal of the light chains, wherein the IgG has the binding specificity to a first antigen, wherein the scFv components have the binding specificity to a second antigen, and wherein the first antigen and the second antigen are different and are independently selected from α-CTLA4, α-PD-1, and α-PD-L1.

[0012] In one embodiment, the bispecific antibody has the two scFv components connected to the C terminal of the heavy chain. In one embodiment, the first antigen comprises α-CTLA4 and the second antigen comprises α-PD-1 or α-PD-L1. In another embodiment, the first antigen comprises α-PD-1 or α-PD-L1 and the second antigen comprises α-CTLA4.

[0013] In one embodiment, the bispecific antibody has the two scFv components connected to the N terminal of the light chain. In one embodiment, the first antigen comprises α-PD-1 or α-PD-L1 and the

second antigen comprises α-CTLA4. In another embodiment, the first antigen comprises α-CTLA4 and the second antigen comprises α-PD-1 or α-PD-L1.

[0014] In one embodiment, the bispecific antibody is an isolated monoclonal antibody.

[0015] In one embodiment, the bispecific antibody comprises an antigenic peptide sequence having a sequence as disclosed herein. In one embodiment, the bispecific antibody may have an antigenic peptide sequence having at least 70%, 80%, 90%, 95%, 98%, or 99% similarity with the disclosed amino acid sequences.

[0016] In one embodiment, the bispecific antibody comprises an antigen-binding fragment having a sequence as disclosed herein. In one embodiment, the bispecific antibody may have an antigen-binding fragment having a sequence with at least 70%, 80%, 90%, 98%, or 99% similarity with the disclosed antibody sequences.

[0017] In one embodiment, the bispecific antibody may have a binding affinity to α-CTLA4, α-PD-1 or α-PD-L1 with a Kd not greater than 70nM, 50nM, 40nM, 30nM, 20nM, 10nM, or 5nM.

[0018] In one embodiment, the bispecific antibody may have a binding affinity to α-CTLA4 and α-PD-1 with a Kd not greater than 70nM, 50nM, 40nM, 30nM, 20nM, 10nM, or 5nM.

[0019] In one embodiment, the bispecific antibody may have a binding affinity to α-CTLA4 and α-PD-L1 with a Kd not greater than 70nM, 50nM, 40nM, 30nM, 20nM, 10nM, or 5nM.

[0020] In one embodiment, the bispecific antibody may have a binding affinity to two of α-CTLA4, α-PD-1, or α-PD-L1with a Kd not greater than 70nM, 50nM, 40nM, 30nM, 20nM, 10nM, or 5nM.

[0021] In one embodiment, the bispecific antibody may exhibit one or more functional properties selected from high affinity binding to α-CTLA4, α-PD-1, or α-PD-L1, inhibiting binding of PD-L1 to PD-1, enhancing T cell activation, the ability to stimulate antibody responses and/or the ability to reverse the suppressive function of immunosuppressive cells, such as T regulatory cells.

[0022] In one embodiment, enhancing T-cell activation comprises T-cell proliferation, IFN-γ and/or IL-2 secretion, or a combination thereof.

[0023] In one embodiment, the bispecific antibody comprising a human framework region.

[0024] In one embodiment, the bispecific antibody may be a humanized antibody, a chimeric antibody, or a recombinant antibody.

[0025] In one embodiment, the bispecific antibody comprises an IgG1 constant region to extend the circulating half-life of the bispecific molecules. In one embodiment, the IgG1 constant region of the bispecific antibody comprises an amino acid sequence having at least 98% similarity with SEQ ID No.136.

[0026] In one embodiment, the application discloses an isolated bispecific antibody selected from the group consisting of those clones described or having the described characteristics as disclosed herein.

[0027] In one embodiment, the application discloses an IgG1 heavy chains for the bispecific antibody, comprising an amino acid sequence selected from sequences as disclosed herein. In one embodiment, the IgG1 heavy chains may have an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 02, 06, 08, 10, 12, 14, 16, 18, 20, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 72, 92, 96, 100, 104,108, 112, 116, 120, 124, 128, or 132.

[0028] In one embodiment, the application discloses a kappa light chain for the bispecific antibody. In one embodiment, the kappa light chain may have an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 04, 28, 32, 36, 40, 44, 48, 52, 56, 60, and 64.

[0029] In one embodiment, the application discloses a variable light chain for the bispecific antibody, comprising an amino acid sequence as disclosed herein. In one embodiment, the variable light chain may have an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, or 134.

[0030] In one embodiment, the application discloses a variable heavy chain for the bispecific antibody, comprising an amino acid sequence as disclosed herein. In one embodiment, the variable heavy chain may have an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 92, 96, 100, 104,108, 112, 116, 120, 124, 128, or 132.

[0031] In one embodiment, the application discloses an isolated nucleic acid encoding the bispecific antibody, comprising the IgG1 heavy chain disclosed herein, the kappa light chain disclosed herein, the variable light chain disclosed herein, or the variable heavy chain disclosed herein. In one embodiment, the application discloses an isolated nucleic acid encoding the bispecific antibody, comprising the IgG1 heavy chain having an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 02, 06, 08, 10, 12, 14, 16, 18, 20, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 72, 92, 96, 100, 104,108, 112, 116, 120, 124, 128, or 132, the kappa light chain having an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 04, 28, 32, 36, 40, 44, 48, 52, 56, 60, and 64, the variable light chain having an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, or 134, or the variable heavy chain having an amino acid sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with SEQ ID NO. 92, 96, 100, 104,108, 112, 116, 120, 124, 128, or 132.

[0032] In one embodiment, the application discloses an expression vector comprising the isolated nucleic acid disclosed herein. In one embodiment, the expression vector comprises an isolated nucleic

acid having a sequence having at least 70%, 80%, 90%, 98%, or 99% similarity with the nucleic acid sequence disclosed herein.

[0033] In one embodiment, the expression vector is expressible in a cell.

[0034] In one embodiment, the application discloses a host cell comprising the nucleic acid of disclosed herein.

[0035] In one embodiment, the application discloses a host cell comprising the expression vector.

[0036] In some embodiments, the application discloses the host cell, wherein the host cell is a prokaryotic cell or a eukaryotic cell.

[0037] In some embodiments, the application discloses a method of producing an antibody comprising culturing the host cell provided thereof so that the antibody is produced.

[0038] In some embodiments, the application discloses an immunoconjugate comprising the bispecific antibody and a cytotoxic agent. In some embodiments, the cytotoxic agent is a chemotherapeutic agent, a growth inhibitory agent, a toxin, or a radioactive isotope.

[0039] In one embodiment, the application discloses a pharmaceutical composition, comprising the bispecific antibody and a pharmaceutically acceptable carrier. In one embodiment, the application discloses a pharmaceutical composition, comprising the immunoconjugate and a pharmaceutically acceptable carrier. In one embodiment, the pharmaceutical composition further comprises radioisotope, radionuclide, a toxin, a therapeutic agent, a chemotherapeutic agent or a combination thereof.

[0040] In one embodiment, the application discloses a method of treating a subject with a cancer, comprising administering to the subject an effective amount of the bispecific antibody disclosed herein. In one embodiment, the cancer comprises breast cancer, colorectal cancer, pancreatic cancer, head and neck cancer, melanoma, ovarian cancer, prostate cancer, non-small lung cell cancer, small cell lung cancer, glioma, esophageal cancer, nasopharyngeal cancer, kidney cancer, gastric cancer, liver cancer, bladder cancer, cervical cancer, brain cancer, lymphoma, leukaemia, myeloma.

[0041] In one embodiment, the application discloses the method of treating a subject with a cancer, wherein the cancer comprises cells expressing PD-L1.

[0042] In one embodiment, the application discloses the method of treating a subject with a cancer, further comprising co-administering an effective amount of a therapeutic agent. In some embodiments, the therapeutic agent comprises an antibody, a chemotherapy agent, an enzyme, or a combination thereof.

[0043] In some embodiments, the therapeutic agent comprises capecitabine, cisplatin, trastuzumab, fulvestrant, tamoxifen, letrozole, exemestane, anastrozole, aminoglutethimide, testolactone, vorozole, formestane, fadrozole, letrozole, erlotinib, lafatinib, dasatinib, gefitinib, imatinib, pazopinib, lapatinib, sunitinib, nilotinib, sorafenib, nab-palitaxel, a derivative or a combination thereof.

[0044] In one embodiment, the application discloses the method of treating a subject with a cancer, wherein the subject is a human.

[0045] In one embodiment, the application discloses a solution comprising an effective concentration of the bispecific antibody disclosed herein, wherein the solution is blood plasma in a subject.

[0046] Still other embodiments of the present application will become readily apparent to those skilled in the art from the following detailed description, wherein is described embodiments of the application by way of illustrating the best mode contemplated for carrying out the application. As will be realized, the application is capable of other and different embodiments and its several details are capable of modifications in various obvious respects, all without departing from the spirit and the scope of the present application. Accordingly, the drawings and detailed description are to be regarded as illustrative in nature and not as restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

[0047] The foregoing and other features of this disclosure may become more fully apparent from the following description and appended claims, taken in conjunction with the accompanying drawings. Understanding that these drawings depict only several embodiments arranged in accordance with the disclosure and are, therefore, not to be considered limiting of its scope, the disclosure may be described with additional specificity and detail through use of the accompanying drawings, in which:

[0048] Figure 1 shows a diagram of example bispecific antibodies targeting CTLA4, PD-1 and PD-L1 antigens;

[0049] Figure 2 shows binding of example anti-PD-1 antibodies to PD-1 antigen expressed on the surface of CHO cell line;

[0050] Figure 3 depicts results from a biochemical assay assessing the ability of the representative bispecific antibodies to block the interaction between CTLA4 and CD80;

[0051] Figure 4 shows stimulation of PBMC with super antigen SEB; Figure 4A shows the treatment with PD224D1 x CT4 IgG1 null and PL230C6 x CT4 IgG1 null; Figure 4B shows the treatment with CT4 x PD224D1 IgG1 null, CT4 x PL221G5 IgG1 and CT4 x PL221G5 IgG1 null;

[0052] Figure 5 shows results from a signaling assay for PD-1/PDL-1 pathway;

[0053] Figure 6 shows results from Dendritic Cell Mixed Lymphocytes Reaction study;

[0054] Figure 7 shows results from regulatory T cell suppression assay; Figure 7A shows the proliferation of CD8+ T cells; and Figure 7B shows IFNg production;

[0055] Figure 8 shows CD8 T cell degranulation in response to treatment with example bispecific antibodies;

[0056] Figure 9 shows results from MiXeno HCC287 mouse tumor model;

[0057] Figure 10 shows effect of example bispecific antibodies on proliferation of Flu-specific CD8 T cells;

[0058] Figure 11 shows results from PBMC memory response to CEFT peptide pool; and

[0059] Figure 12 shows enhancement of Redirected T Cell Cytotoxicity by example bispecific antibodies.

DETAILED DESCRIPTION

[0060] In the following detailed description of embodiments of the application, reference is made to the accompanying drawings in which like references indicates similar elements, and in which is shown by way of illustration, specific embodiments in which the application may be practiced. These embodiments are described in sufficient detail to enable those skilled in the art to practice the application. In other instances, well-known circuits, structures, and techniques have not been shown in detail in order not to obscure the understanding of this description. The following detailed description is, therefore, not to be taken in a limiting sense, and the scoop of the application is defined only by the appended claims.

[0061] The disclosure relates to bispecific antibodies that specifically bind to human CTLA4, PD-1 or PD-L1. In some embodiments, the bispecific antibody comprises of a first arm that binds to CTLA4 and a second arm that binds to PD-1 or PD-L1. In some embodiments, the bispecific antibody comprises of a first arm that binds to PD-1 or PD-L1 and a second arm that binds to CTLA4. Examples of domains that comprise the arms include, but are not limited to, Fab and scFv domains. Each arm contains two antigen-binding domains and is connected to another arm via Fc domain. The Fc domain can be of human IgG1, IgG2, IgG3, IgG4 or an engineered isotype.

[0062] The bispecific antibodies of this application (Figure 1) target human CTLA4, human PD-1 and human PD-L1. Each of these targeted bispecific antibodies carry an anti-CTLA4 (SEQ IDs 91, 93) and an anti-human PD-1 (SEQ IDs 95, 97, 131, 133) or PD-L1 binding domains (SEQ IDs 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129). Either one of the binding domains was converted to scFv (VH-VL orientation) for placement at the C-terminus, or scFv (VL-VH orientation) for placement at the N-terminus (Figure 1 A and B respectively).

[0063] In some embodiments, scFv molecules described herein contain a 20-amino acid flexible gly-gly-gly-gly-ser (G4S) X4 linker that operably links the VH and VL, regardless of the V-region orientation (LH or HL). The remaining positions in the bispecific antibody may be consist of a human IgG1 Fc or IgG1 null Fc heavy chain, VH-CH1-Hinge-CH2-CH3, and its corresponding kappa light chain, VL-CL. scFv domains were genetically linked through a 10-amino acid (G4S) x 2 linker to either N-terminal or C-terminal of IgG1 heavy chain, resulting in a contiguous ~ 100 kDa heavy chain monomer peptide. When co-transfected with the appropriate light chain, the final symmetric bispecific molecule may be purified through the human IgG1 Fc (Protein A) and assayed to assess functional activity.

[0064] Heavy and light chain gene "cassettes" were previously constructed such that V-regions could be cloned using either restriction enzyme sites (Figure 1A example: HindIII/NotI for the heavy chain and HindIII/BsiWI for the light chain). In one embodiment, "restriction-free cloning" NEBuilder (NEB, Ipswich, MA) was used.

[0065] Bispecific antibodies are produced through a process that involves design of the intact molecule, synthesis and cloning of the nucleotide sequences for each domain, expression in mammalian cells and purification of the final product. Nucleotide sequences were assembled using the Geneious 10.2.3 software package (Biomatters, Auckland, NZ) and broken up into their component domains for gene synthesis (Genewiz, South Plainsfield, NJ). In one example (Figure 1A), the heavy chain of CT4 x PD224D1 IgG1 null bispecific antibody (SEQ ID 2) consists of the anti-CTLA4 VH domain fused to the human IgG1 null Fc domain (hinge, CH1, and CH2), followed by a 10-amino acid (G4S) x 2 linker fused to the anti-PD-1 scFV domain (clone PD224D1). Using NEBuilder web-based tools, 5' and 3' nucleotides were appended to each of the domains so that each domain overlaps its flanking domains by 20-30 nucleotides, which direct site-specific recombination, thus genetically fusing each domain in a single gene assembly step.

[0066] The light chain of CT4 x PD224D1 IgG1 null consists of the anti-CTLA4 VL domain fused to the human C kappa domain. A synthesized gene fragment was digested with the restriction enzymes HindIII and BsiWI and was then ligated in-frame with the human C kappa domain. For both constructs, a small aliquot was transformed into *E.coli* DH10b (Invitrogen, Carlsbad, CA) and plated on TB + carbenicillin 100ug/ml plates (Teknova, Hollister, CA) and incubated at 37C overnight. Resultant colonies were selected and 2ml overnight cultures inoculated in TB + carbenicillin. DNA was prepared (Thermo-Fisher, Carlsbad, CA) from overnight cultures and subsequently sequenced (Genewiz, South Plainsfield, NJ) using sequencing primers (Sigma,St. Louis, MO) flanking each domain. All DNA sequences were assembled and analysed in Geneious.

EXAMPLES

[0067] **Example 1: Binding of anti-PD-L1 antibodies to PD-L1 antigen**

[0068] Binding affinities and kinetics of anti-PD-L1 antibodies to PD-L1 recombinant protein were assessed via Surface Plasmon Resonance on ForteBio Octet RED96 instrument. The antigen was immobilized on the sensor chip surface and the tested antibodies were flown over the immobilized antigens. All molecules showed strong binding to the antigen as shown in **Table 1** for examples.

[0069] **Table 1. Binding of Anti-PD-L1 Antibodies to PD-L1 Antigen**

	mAb			scFv-Fc			Fc-scFv		
Sample ID	KD (M)	kon(1/Ms)	kdis(1/s)	KD (M)	kon(1/Ms)	kdis(1/s)	KD (M)	kon(1/Ms)	kdis(1/s)
PL004B9	**1.37E-09**	5.08E+05	6.95E-04	**1.42E-09**	3.87E+05	5.50E-04	**1.54E-09**	3.07E+05	4.71E-04
PL221G5	**4.83E-10**	5.72E+05	2.76E-04	**5.97E-10**	5.08E+05	3.03E-04	**4.12E-10**	4.14E+05	1.71E-04
PL230C6	**7.69E-10**	6.09E+05	4.68E-04	**9.17E-10**	5.03E+05	4.61E-04	**8.68E-10**	4.18E+05	3.62E-04
PL231H2	**7.81E-10**	5.01E+05	3.91E-04	**9.99E-10**	4.20E+05	4.19E-04	**4.62E-10**	8.40E+05	3.89E-04

[0070] **Example 2: Binding of anti-PD-1 antibodies to PD-1 antigen**

Binding of the bispecific antibodies and their components to PD-1 antigen expressed on the surface of CHO cell line was assessed using FACS method. The bispecific antibodies were incubated with CHO cell line expressing PD-1 antigen and then detected with secondary anti-human antibodies directly conjugated to Alexa Fluor 647 fluorochrome. Cellular binding of the test antibodies was analyzed on a flow cytometer BD LSRFortessa. All tested antibodies bound to the antigen with a KD in a single digit nanomolar range (Figure 2).

[0071] **Example 3: Blockade of interaction between CTLA4 and CD80**

[0072] Ability of the bispecific antibodies to block the interaction between CTLA4 and its ligand CD80 was tested in a biochemical interaction assay (Cisbio). Briefly, a bispecific antibody was incubated with CTLA4 and CD80 proteins. Detection antibodies recognizing CTLA4 and CD80 proteins and labeled with HTRF donor/acceptor fluorescent pair then were added to the mixture. The interaction between CTLA4 and CD80 was assessed via FRET efficiency. All bispecific antibodies tested were able to block the interaction between CTLA4 and CD80 (Figure 3).

[0073] **Example 4: Stimulation of PBMC with superantigen SEB**

[0074] Ability of the bispecific antibodies to enhance cytokine release from human Peripheral Blood Mononuclear Cells (PBMC) after stimulation with superantigen SEB was assessed. All bispecific

molecules were able to significantly enhance the production of IL-2 by PBMC upon stimulation with SEB, as shown in Figure 4A and Figure 4B.

[0075] **Example 5: PD-1/PD-L1 pathway signaling**

[0076] The bispecific antibodies were tested for their ability to block PD-1/PD-L1 pathway. Briefly, the test molecules were incubated with Jurkat reporter cell line expressing PD-1 receptor and luciferase NFAT reporter and CHO-PD-L1 cell line (Promega). The ability of the test antibodies to block the signaling through the PD-1/PD-L1 pathway was assessed via an increase in NFAT signaling. The NFAT signaling in turn was monitored via activity of luciferase reporter gene. The assay was read on a plate reader (Clariostar, BMG). All tested bispecific antibodies and monoclonal antibody controls were able to block PD-1/PD-L1 signaling (Figure 5).

[0077] **Example 6: Dendritic cell Mixed Leukocyte Reaction**

[0078] The bispecific antibodies were tested for their ability to enhance Dendritic cell Mixed Leucocyte Reaction (MLR). The test molecules were incubated for 6 days with dendritic cells from one donor and T cells isolated from another donor. Dendritic cells were differentiated *in vitro* from monocytes in the presence of GM-CSF and IL-4. Monocytes and T cell populations were isolated from PBMC with StemCell isolation kits. The ability of the test molecules to enhance MLR was assessed via secreted IFNγ. All tested bispecific antibodies were able to augment production of IFNγ as shown on Figure 6.

[0079] **Example 7: Suppression of CD8 T cells by regulatory T cells**

[0080] The bispecific antibodies were tested for their ability to block suppressive effect of regulatory T cells on effector CD8 T cell proliferation and cytokine production. CD8 T cells were isolated with StemCell isolation kit and labeled with CellTrace dye (ThermoFisher). Dendritic cells were prepared as described earlier in the MLR study. Regulatory T cells were isolated from PBMC with StemCell isolation kit and expanded *in vitro*. The bispecific antibody was incubated with effector CD8 T cells, dendritic cells and regulatory T cells for 4 days. The ability of the bispecific antibody to rescue effector CD8 T cell function in the presence of regulatory T cells was assessed via proliferation of effector CD8 T cells (Figure 7A) and secreted IFNγ (Figure 7 B).

[0081] **Example 8: CD8 T cell degranulation**

[0082] Ability of bispecific molecules to have an effect on cytotoxic CD8 T cells was assessed in this study. Briefly, CD8 T cells were purified with StemCell isolation kit and stimulated with CEFT peptide pool (JPT Peptide Technologies) in the presence of the bispecific test molecules. The media was supplemented with IL-7 and IL-21. On day 11 CD8 T cells were re-stimulated with the peptides in the presence of Brefeldin and Monensin and anti-CD107a antibody directly labeled with a fluorochrome. 24

hours later CD8 T cells were stained with anti-IFNγ antibodies directly conjugated to a fluorochrome and assessed on a flow cytometer BD LSRFortessa. As shown on Figure 8, all tested bispecific antibodies were able to increase the number of cytotoxic IFNγ positive T cells.

[0083] **Example 9: MiXeno mouse tumor model**

[0084] Humanized mouse model was used to assess the ability of bispecific antibodies of this class to inhibit tumor growth *in vivo*. Briefly, NOG mice were reconstituted with human PBMC ($5x10^6$ cells per mouse). On day 3 the animals were subcutaneously inoculated with a human lung cancer cell line HCC827 (0.5E6 cells/animal) and started on a biweekly treatment with a bispecific antibody and control antibodies. Tumor volumes were measured every 2-3 days. Animal weight was monitored. The tested bispecific antibody was able to inhibit tumor growth better than the control antibodies (Figure 9).

[0085] **Example 10: Proliferation of Flu-specific T cells**

[0086] Ability of the bispecific antibodies to augment proliferation of antigen specific CD8 T cells was assessed in this study. CD8 T cells were purified from PBMC with StemCell isolation kit, pulsed with influenza specific peptides (JPT Peptide Technologies) and incubated in the presence of the bispecific antibodies for 14 days. The media was supplemented with IL-7 and IL-21. On day 15 the cells were stained with a peptide specific MHC dextramers (Immudex) and assessed on a flow cytometer BD LSRFortessa. All tested bispecific antibodies were able to increase the number of antigen specific CD8 T cells (Figure 10).

[0087] **Example 11: PBMC memory response to CEFT peptide pool**

[0088] Ability of the bispecific antibodies to augment T cell memory response was assessed. Briefly, PBMC were incubated for 4-5 days in the presence of peptides specific for CMV, EBV, Influenza and Tetanus (JPT Peptide Technologies). The amount of secreted IFNγ was quantified. The bispecific CT4 x PD224D1, shown on Figure 11, was able to enhance production of IFNγ several fold over the control treatment.

[0089] **Example 12: Enhancement of Redirected T cell Cytotoxicity**

[0090] The bispecific antibodies were tested for their ability to enhance Redirected T cell Cytotoxicity (RTCC) against a tumor cell line target. The tumor cell line was stably expressing nucleus-localized Red Fluorescent Protein (RFP) delivered via lentiviral transduction (Sartorius). The tumor cells were co-cultured with PBMC and a T cell engager molecule specific for the given tumor cell line. The bispecific antibodies were added to the co-cultures. Lysis of tumor cells was assessed by counting RFP labeled tumor cell nuclei. Images were acquired on live cell imager IncuCyte (Sartorius). Activity of the antibodies were assessed after 96 hours of incubation. Four PBMC donors were tested in this study. All

bispecific antibodies tested were able to enhance RTCC activity in at least one PBMC donor tested (Figure 12).

[0091] While the present disclosure has been described with reference to particular embodiments or examples, it may be understood that the embodiments are illustrative and that the disclosure scope is not so limited. Alternative embodiments of the present disclosure may become apparent to those having ordinary skill in the art to which the present disclosure pertains. Such alternate embodiments are considered to be encompassed within the scope of the present disclosure. Accordingly, the scope of the present disclosure is defined by the appended claims and is supported by the foregoing description. All references cited or referred to in this disclosure are hereby incorporated by reference in their entireties.

SEQUENCE LISTING

SEQ ID	Description
1	CT4 x PD224D1 nucleotide
2	CT4 x PD224D1 amino acid
3	CT4 Light Chain nucleotide
4	CT4 Light Chain amino acid
5	CT4 x PL230C6 nucleotide
6	CT4 x PL230C6 amino acid
7	CT4 x PL221G5 nucleotide
8	CT4 x PL221G5 amino acid
9	CT4 x PL231H2 nucleotide
10	CT4 x PL231H2 amino acid
11	CT4 x PL004B5 nucleotide
12	CT4 x PL004B5 amino acid
13	CT4 x PL004B9 nucleotide
14	CT4 x PL004B9 amino acid
15	CT4 x PD206F12 nucleotide
16	CT4 x PD206F12 amino acid
17	CT4 x PD215A1 nucleotide
18	CT4 x PD215A1 amino acid
19	CT4 x PD220F6 nucleotide
20	CT4 x PD220F6 amino acid
21	CT4 x PD225G11 nucleotide
22	CT4 x PD225G11 amino acid
23	Gly 4 Ser x 4 nucleotide

24	Gly 4 Ser x 4 amino acid
25	PL230C6 x CT4 nucleotide
26	PL230C6 x CT4 amino acid
27	PL230C6 Light Chain nucleotide
28	PL230C6 Light Chain amino acid
29	PD224D1 x CT4 nucleotide
30	PD224D1 x CT4 amino acid
31	PD224D1 Light Chain nucleotide
32	PD224D1 Light Chain amino acid
33	PL221G5 x CT4
34	PL221G5 x CT4
35	PL221G5 Light Chain
36	PL221G5 Light Chain
37	PL231H2 x CT4 nucleotide
38	PL231H2 x CT4 amino acid
39	PL231H2 Light Chain nucleotide
40	PL231H2 Light Chain amino acid
41	PL004B5 x CT4 nucleotide
42	PL004B5 x CT4 amino acid
43	PL004B5 Light Chain nucleotide
44	PL004B5 Light Chain amino acid
45	PL004B9 x CT4 nucleotide
46	PL004B9 x CT4 amino acid
47	PL004B9 Light Chain nucleotide
48	PL004B9 Light Chain amino acid

49	PD206F12 x CT4 nucleotide
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55	PD215A1Light Chain nucleotide
56	PD215A1 Light Chain amino acid
57	PD220F6 x CT4 nucleotide
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59	PD220F6Light Chain nucleotide
60	PD220F6 Light Chain amino acid
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63	PD225G11 Light Chain nucleotide
64	PD225G11 Light Chain amino acid
65	CT4 signal peptide nucleotide
66	CT4 signal peptide amino acid
67	Heavy Chain signal peptide nucleotide
68	Heavy Chain signal peptide amino acid
69	Light Chain signal peptide nucleotide
70	Light Chain signal peptide amino acid
71	CT4 scFv nucleotide
72	CT4 scFv amino acid
73	PD224D1 scFv nucleotide

74	PD224D1 scFv amino acid
75	PD206F12 scFv nucleotide
76	PD206F12 scFv amino acid
77	PD215A1 scFv nucleotide
78	PD215A1 scFv amino acid
79	PD225G11 scFv nucleotide
80	PD225G11 scFv amino acid
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83	PL231H2 scFv nucleotide
84	PL231H2 scFv amino acid
85	PL221G5 scFv nucleotide
86	PL221G5 scFv amino acid
87	PL004B5 scFv nucleotide
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89	PL004B9 scFv nucleotide
90	PL004B9 scFv amino acid
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103	PD215A1 VH nucleotide
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118	PL231H2 VL amino acid
119	PL221G5 VH nucleotide
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121	PL221G5 VL nucleotide
122	PL221G5 VL amino acid
123	PL004B5 VH nucleotide

124	PL004B5 VH amino acid
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126	PL004B5 VL amino acid
127	PL004B9 VH nucleotide
128	PL004B9 VH amino acid
129	PL004B9 VL nucleotide
130	PL004B9 VL amino acid
131	PD220F6 VH nucleotide
132	PD220F6 VH amino acid
133	PD220F6 VL nucleotide
134	PD220F6 VL amino acid
135	Human IgG1 Constant Domain nucleotide
136	Human IgG1 Constant Domain amino acid
137	Human IgG1 Constant Domain null nucleotide
138	Human IgG1 Constant Domain null amino acid
139	PD220F6 scFv nucleotide
140	PD220F6 scFv amino acid

SEQ ID 01: CT4 x PD224D1 nucleotide sequence (nt)

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SEQ ID 02: CT4 x PD224D1 amino acid sequence (aa)

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SEQ ID 03: CT4 kappa light chain nt

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SEQ ID 04: CT4 kappa light chain aa

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SEQ ID 05: CT4 x PL230C6 nt

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SEQ ID 06: CT4 x PL230C6 aa

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SEQ ID 07: CT4 x PL221G5 null2 Fc nt

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SEQ ID 08: CT4 x PL221G5 null Fc aa

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SEQ ID 09: CT4 x PL231H2 nt

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ATGATCTGGGTCCGCCAGGCTCCAGGCAAGGGGCTAGAGTGGGTGGGAATCATTAGTTATGTTGGTAACA
CATACTACGCGAGCTGGGCGAAAGGCCGATTCACCCTCTCCAAAGACAATACCTCGACCACGGTGGATCT
GCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAGAGATTTTATTAGTGGTTCC
CACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCG
GCGGTGGCGGCTCCGGTGGAGGCGGTTCTGCCTATGATATGACCCAGTCTCCATCTTCCGTGTCTGCATC
TGTAGGAGACAGAGTCACCATCAATTGTCAGGCCAGTGAGAGCATTAGTAGCTTCTTATCCTGGTATCAG
CAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTTTTCTGCATCCACTCTGGCATCTGGGGTCCCATCAA
GGTTCAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGC
AACTTACTATTGTCAACAGGGTTATAGTAAAAGTAATGTGGATAATGCTTTCGGCGGAGGGACCAAGGTG
GAGATCAAA

SEQ ID 10: CT4 x PL231H2 aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGLVQPGGSLRLSCTTSGIDLSTYD
MIWVRQAPGKGLEWVGIISYVGNTYYASWAKGRFTLSKDNTSTTVDLQMNSLRAEDTAVYYCARDFISGS
HLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSAYDMTQSPSSVSASVGDRVTINCQASESISSFLSWYQ
QKPGKAPKLLIFSASTLASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGYSKSNVDNAFGGGTKV
EIK

SEQ ID 11: CT4 x PL004B5 nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCTTCAGTAGCTATACTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG
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TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATAT
ATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTC
CTCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA
GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCC
TGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT
GACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
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AAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGAC
CCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG
GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGG
TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
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CGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG
GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCC
TGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCAGAGGTGCAGCTGGTGGAGTCTGGGGGAGG
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ATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGGAGTCATTGATACTAATGTTTATA
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TTATCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGGTGCATCCACTCTGGCAT
CTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAATTCACTCTCACCATCAGCAGCCTGCA
GCCTGATGATTTTGCAACTTATTACTGCCTAGGCAGTTATACTAGTAGTACTGAGAACTCTTTCGGCGGA
GGGACCAAGGTGGAGATCAAA

SEQ ID 12: CT4 x PL004B5 aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFSLSSYW
MSWVRQAPGKGLEWIGVIDTNVYIYYANWAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYVGNND
DYINLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSTLSASVGDRVTITCQSSQSVYNGYW

LSWYQQKPGKAPKLLIYGASTLASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGSYTSSTENSFGG
GTKVEIK

SEQ ID 13: CT4 x PL004B9 nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG
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TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATAT
ATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTC
CTCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA
GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCC
TGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT
GACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
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AAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGAC
CCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG
GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGG
TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
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GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCC
TGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCAGAGGTGCAGCTGGTGGAGTCTGGGGGAGG
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CATATTACGCGAGCTGGGCGAAAGGCAGATTCACCATCTCCAAAACCTCGACCACGGTGGATCTTAAAAT
CACCAGTCCGACAACCGAGGACACGGCTGTGTATTACTGTGCGAGAGAATCTGGTACTATTTATTACAGT
TACTTTAACTTGTGGGGCCAAGGGACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTG
GTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGCATTCGAATTGACCCAGTCTCCATCCTCCCTGTC
TGCATCTGTAGGAGACAGAGTCACCATCAAGTGCCAGGCCAGTGAAAGCATTAGCAACTACTTATCCTGG
TATCAGCAGATTCCAGGGAAAGTTCCTAAGCTCCTGATCTATTATGCATCCAATCTGGCATCTGGGGTCC
CATCTCGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA
TGTTGCAACTTATTACTGTCAAAGCTATTATGGTGGTGGTAGTGCCTATACTTTCGGCGGAGGGACCAAG
GTGGAGATCAAA

SEQ ID 14: CT4 x PL004B9 aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCTVSGIDLSVIN
MGWVRQAPGKGLEWIGTITYVGNTYYASWAKGRFTISKTSTTVDLKITSPTTEDTAVYYCARESGTIYYS

YFNLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSAFELTQSPSSLSASVGDRVTIKCQASESISNYLSW
YQQIPGKVPKLLIYYASNLASGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQSYYGGGSAYTFGGGTK
VEIK

SEQ ID 15: CT4 x PD206F12 nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG
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GGTGACATTTATATCATATGATGGAAACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATC
TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATAT
ATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTC
CTCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA
GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCC
TGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT
GACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
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AAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGAC
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GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGG
TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
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ATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCC
CGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG
GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCC
TGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCAGAGGTGCAGCTGGTGGAGTCTGGGGGAGG
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TGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTTGATCGCATGCATTTATGCTGGTACTA
GTGGTAGTACTTCCTACGCGAGCTGGGCGAGAGGCAGATTCACCATCTCCGAAACCTCCAAGAACACGGT
GACTCTTCAAATGAACAGCCTGAGAGCCGAGGACTCGGCTGTGTATTACTGTGCGAGAAATCTTTACACT
TACAATAGCTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTG
GTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGACATCCAGATGACCCAGTCTCCTTCCACCCTGTC
TGCATCTGTAGGAGACAGAGTCACCATCACTTGCCAGTCCAGTCAGAGTGTTTATGATAACAACTGGTTA
GCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATACAGTATCCACTCTGGCATCTG
GGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAATTCACTCTCACCATCAGCAGCCTGCAGCC
TGATGATTTTGCAACTTATTACTGCCAAGGCACTTATTATAGTAGTGGTTGGAACTTTGCTTTCGGCGGA
GGGACCAAGGTGGAGATCAAA

SEQ ID 16: CT4 x PD206F12 aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
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AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFDFSSGY

WICWVRQAPGKGLELIACIYAGTSGSTSYASWARGRFTISETSKNTVTLQMNSLRAEDSAVYYCARNLYT
YNSLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSTLSASVGDRVTITCQSSQSVYDNNWL
AWYQQKPGKAPKLLIYTVSTLASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQGTYYSSGWNFAFGG
GTKVEIK

SEQ ID 17: CT4 x PD215A1 nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG
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GGTGACATTTATATCATATGATGGAAACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATC
TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATAT
ATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTC
CTCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA
GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCC
TGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT
GACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
AAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTG
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TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
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GCACTTACTACGCGAGCTGGGCGAAGCGCCGGTTCACCATCTCCAAAGACAATTCCAAGAACACGGTGAC
TCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTACGAGAGCATTTGACTTGTGG
GGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCG
GCTCCGGTGGAGGCGGCTCTGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGA
CAGAGTCACCATCACTTGCCAGGCCAGTCAGAGCATTTACAGCTACTTAAACTGGTATCAGCAGAAACCA
GGGAAAGCCCCTAAGCTCCTGATCTATGGTGCATCCAATCTGGCATCTGGGGTCCCATCAAGGTTCAGTG
GCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTA
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SEQ ID 18: CT4 x PD215A1 aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQEQLLESGGGLVQPGGSLRLSCTASGFSFSSYW

MCWVRQAPGKGLEWIGCITTGSGSTYYASWAKRRFTISKDNSKNTVTLQMNSLRAEDTAVYYCTRAFDLW
GQGTLVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCQASQSIYSYLNWYQQKP
GKAPKLLIYGASNLASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQSSWLSGAVGNAFGGGTKVEIK

SEQ ID 19: CT4 x PD220F6 nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG
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TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATAT
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TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
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GGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCG
GCTCCGGTGGAGGCGGCTCTGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGA
CAGAGTCACCATCACTTGCCAGTCCAGTCCGAGTGTTTATAGTAACTACTTATCCTGGTATCAGCAGAAA
CCAGGGAAAGTTCCTAAGCTCCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCCCATCTCGGTTCA
GTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTA
TTACTGTGCAGGCGGTTATAGTAGTAGTACTCGTGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 20: CT4 x PD220F6 aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
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AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQEQVKETGGGLVQPGGSLRLSCAASGFTISSYG
VSWVRQAPGKGLEWVALIFPGIGFKDYASWVNGRFTLSSDNAQNTVELQMNSLRAEDTAVYYCARDLDLW

GQGTLVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCQSSPSVYSNYLSWYQQK
PGKVPKLLIYYASTLASGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCAGGYSSSTRAFGGGTKVEIK

SEQ ID 21: CT4 x PD225G11 nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCTTCAGTAGCTATACTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG
GGTGACATTTATATCATATGATGGAAACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATC
TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATAT
ATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTC
CTCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA
GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCC
TGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT
GACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
AAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTG
AAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGAC
CCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG
GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGG
TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
ACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCT
ATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCC
CGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG
GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCC
TGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCAGAGGTGCAGCTGTTGGAGTCTGGGGGAGG
CTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCAGCAGCCAC
TGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGCATGCATTTATACTGGTAGTA
TTGATGTCTTTTACTACGCGAGCTGGGCGAAAGGCCGGTTCACCATCTCCAGAGACAATTCCAAGAACAC
GCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAGAGCCGCTAAT
ACTGATACTACCTACTTTAACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGAT
CTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGCCTATGATATGACCCAGTCTCC
ATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCAATTGCCAGGCCAGTCAGAGCATTAACAAC
CAACTATCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCTGATCTATGGTGCATCCACTCTGG
CATCTGGGGTCCCATCTCGGTTCACCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCT
GCAGCCTGAAGATGTTGCAACTTATTACTGTCATGTTCATTATTGCAGTGGTGGTAGTTGTTTTTGGGCT
TTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 22: CT4 x PD225G11 aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSSSH
WICWVRQAPGKGLEWIACIYTGSIDVFYYASWAKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARAAN

TDTTYFNLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSAYDMTQSPSSLSASVGDRVTINCQASQSINN
QLSWYQQKPGKVPKLLIYGASTLASGVPSRFTGSGSGTDFTLTISSLQPEDVATYYCHVHYCSGGSCFWA
FGGGTKVEIK

SEQ ID 23: G4S x 4 nt

GGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCT

SEQ ID 24: G4S x 4 aa

GGGGSGGGGSGGGGSGGGGS

SEQ ID 25: PL230C6 x CT4 nt

CAGTCGGTGGAGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACCGCCT
CTGGAATCGACCTTAATACCTACGACATGATCTGGGTCCGCCAGGCTCCAGGCAAGGGGCTAGAGTGGGT
TGGAATCATTACTTATAGTGGTAGTAGATACTACGCGAACTGGGCGAAAGGCCGATTCACCATCTCCAAA
GACAATACCAAGAACACGGTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACT
GTGCGAGAGATTATATGAGTGGTTCCCACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGCTAG
CACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTG
GGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCG
GCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCC
CTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGAC
AAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAAGCCGCGG
GGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGT
CACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTG
GAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCC
TCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAAAGCCCTCCC
AGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCC
CCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCG
ACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGA
CTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTC
TTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG
GTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGGAGGCGTGGTCCA
GCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATACTATGCACTGG
GTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAAACAATAAATACT
ACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAAT
GAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGAC
TACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGTTCAGGCGGAGGTGGAAGTGGTG
GTGGCGGCTCTGGAGGCGGCGGATCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCC
AGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCCTGGTACCAG
CAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTGGCATCCCAGACA
GGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGC
AGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA

SEQ ID 26: PL230C6 x CT4 aa

QSVEESGGGLVQPGGSLRLSCTASGIDLNTYDMIWVRQAPGKGLEWVGIITYSGSRYYANWAKGRFTISK
DNTKNTVYLQMNSLRAEDTAVYYCARDYMSGSHLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAAL
GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHW
VRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFD
YWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQ
QKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

SEQ ID 27: PL230C6 kappa light chain nt

GCCTATGATATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGTCACCATCAAGTGTC
AGGCCAGTGAGGACATTTATAGCTTCTTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCCATTCTGCATCCTCTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGGTTATGGTA
AAAATAATGTTGATAATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA
CGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCT
CTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCT
CCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGC
ACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCC
TGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT

SEQ ID 28: PL230C6 kappa light chain aa

AYDMTQSPSSVSASVGDRVTIKCQASEDIYSFLAWYQQKPGKAPKLLIHSASSLASGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQQGYGKNNVDNAFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN
NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTK
SFNRGEC

SEQ ID 29: PD224D1 x CT4 nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
CCTCTGGATTCTCCCTCAGTAGCTATGCAATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTA
CATCGGCTACATTGGTGATACTACTGGCATAGCCTACGCGAGCTGGGCGAATGGCAGATTCACCATCTCC
AAAGACAATACCAAGAACACGGTGGATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATT
ACTGTGCGAGAGGCTGGTCCTACTTAGACATCTGGGGCCAAGGGACCCTGGTCACCGTCTCGAGCGCTAG
CACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTG
GGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCG
GCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCC
CTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGAC
AAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAAGCCGCGG
GGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGT
CACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTG
GAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCC
TCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAAAGCCCTCCC

AGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCC
CCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCG
ACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGA
CTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTC
TTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG
GTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGGAGGCGTGGTCCA
GCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATACTATGCACTGG
GTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAAACAATAAATACT
ACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAAT
GAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGAC
TACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCG
GTGGCGGCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCC
AGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCCTGGTACCAG
CAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTGGCATCCCAGACA
GGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGC
AGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA

SEQ ID 30: PD224D1 x CT4 aa

EVQLVESGGGLVQPGGSLRLSCTASGFSLSSYAMSWVRQAPGKGLEYIGYIGDTTGIAYASWANGRFTIS
KDNTKNTVDLQMNSLRAEDTAVYYCARGWSYLDIWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAAL
GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHW
VRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFD
YWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQ
QKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

SEQ ID 31: PD224 light chain nt

GCCCTTGTGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGGCCAGTCAGAACATTTACAGCAATTTAGCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCT
GATCTATCAGGCCTCCACTCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATATGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAGGCGGTTATTATA
GTGCTGCCCTTAATACTTTCGGCGGAGGGACCAAGGTGGAGATCAAA
CGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCT
CTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCT
CCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGC
ACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCC
TGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT

SEQ ID 32: PD224 light chain aa

ALVMTQSPSSLSASVGDRVTITCQASQNIYSNLAWYQQKPGKVPKLLIYQASTLASGVPSRFSGSGYGTD
FTLTISSLQPEDVATYYCQGGYYSAALNTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNN

FYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS
FNRGEC

SEQ ID 33: PL221G5 x CT4 null Fc nt

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCTCCTTCAGTAGCGGGTACGACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTGGATCGCATGCATTGCTGCTGGTAGTGCTGGTATCACTTACGACGCGAACTGGGCGAAAGGCCGGTTC
ACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGG
CCGTATATTACTGTGCGAGATCGGCGTTTTCGTTCGACTACGCCATGGACCTCTGGGGCCAGGGAACCCT
GGTCACCGTCTCGAGCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACC
TCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGA
ACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCT
CAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAG
CCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGT
GCCCAGCACCTGAAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCAT
GATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTC
AACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCA
CGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGC
GGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAA
CCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGG
TCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAA
GACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGC
AGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGA
AGAGCCTCTCCCTGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGA
GTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTC
AGTAGCTATACTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCAT
ATGATGGAAACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAA
GAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACC
GGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGAT
CTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCC
AGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGC
AGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCA
GGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAG
ACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAA
GGGACCAAGGTGGAAATCAAA

SEQ ID 34: PL221G5 x CT4 null Fc aa

EVQLLESGGGLVQPGGSLRLSCAASGFSFSSGYDMCWVRQAPGKGLEWIACIAAGSAGITYDANWAKGRF
TISRDNSKNTLYLQMNSLRAEDTAVYYCARSAFSFDYAMDLWGQGTLVTVSSASTKGPSVFPLAPSSKST
SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHK
PSNTKVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF
NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTF

SSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCART
GWLGPFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGS
SYLAWYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQ
GTKVEIK

SEQ ID 35: PL221G5 Light Chain nt

GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGGCCAGTCAGAGCATTAGTTCCCACTTAAACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCTATAAGGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAA
TTTACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAACAGGGTTATAGTT
GGGGTAATGTTGATAATGTTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGCACCATC
TGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAAT
AACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGG
AGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGC
AGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAG
AGCTTCAACAGGGGAGAGTGT

SEQ ID 36: PL221G5 Light Chain aa

DIQMTQSPSTLSASVGDRVTITCQASQSISSHLNWYQQKPGKAPKLLIYKASTLASGVPSRFSGSGSGTE
FTLTISSLQPDDFATYYCQQGYSWGNVDNVFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN
NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTK
SFNRGEC

SEQ ID 37: PL231H2 x CT4 null Fc nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCCTGGTCCAGCCTGGGGGCTCCCTGAGACTCTCCTGTACAA
CTTCTGGAATCGACCTTAGTACCTACGACATGATCTGGGTCCGCCAGGCTCCAGGCAAGGGGCTAGAGTG
GGTGGGAATCATTAGTTATGTTGGTAACACATACTACGCGAGCTGGGCGAAAGGCCGATTCACCCTCTCC
AAAGACAATACCTCGACCACGGTGGATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATT
ACTGTGCGAGAGATTTTATTAGTGGTTCCCACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGC
TAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCC
CTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCA
GCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGT
GCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTG
GACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAAGCCG
CGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGA
GGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGC
GTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCG
TCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAAAGCCCT
CCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG
CCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCA
GCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCT
GGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAAC
GTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTC
CGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGGAGGCGTGGT

CCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATACTATGCAC
TGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAAACAATAAAT
ACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCA
AATGAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTT
GACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCG
GCGGTGGCGGCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTC
TCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCCTGGTAC
CAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTGGCATCCCAG
ACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTT
TGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTGGAAATC
AAA

SEQ ID 38: PL231H2 x CT4 null Fc aa

QVQLVESGGGLVQPGGSLRLSCTTSGIDLSTYDMIWVRQAPGKGLEWVGIISYVGNTYYASWAKGRFTLS
KDNTSTTVDLQMNSLRAEDTAVYYCARDFISGSHLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAA
LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMH
WVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPF
DYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWY
QQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEI
K

SEQ ID 39: PL231H2 Light Chain nt

GCCTATGATATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGTCACCATCAATTGTC
AGGCCAGTGAGAGCATTAGTAGCTTCTTATCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCTTTTCTGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGGTTATAGTA
AAAGTAATGTGGATAATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGCACCATC
TGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAAT
AACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGG
AGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGC
AGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAG
AGCTTCAACAGGGGAGAGTGT

SEQ ID 40: PL231H2 Light Chain aa

AYDMTQSPSSVSASVGDRVTINCQASESISSFLSWYQQKPGKAPKLLIFSASTLASGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQQGYSKSNVDNAFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN
NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTK
SFNRGEC

SEQ ID 41: PL004B5 x CT4 nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCTCCCTCAGTAGCTACTGGATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGAGTCATTGATACTAATGTTTATATATACTACGCGAACTGGGCAAAAGGCAGATTCACCATCTCC
AGAGACAATTCCAAGAACACGCTGTATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATT
ACTGTGCGAGATATGTGGGTAATAATGATGATTATATTAACTTGTGGGGCCAGGGAACCCTGGTCACCGT
CTCGAGCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGC
ACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCG
CCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGT
GGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAAC
ACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCAC
CTGAAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCG
GACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC
GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTG
TGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAA
CAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTG
TACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCT
TCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCC
TCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG
CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT
CCCTGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGG
AGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTAT
ACTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAA
ACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTG
GGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAG
GTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCT
GTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTA
GCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTG
GCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCC
TGAAGATTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAG
GTGGAAATCAAA

SEQ ID 42: PL004B5 x CT4 aa

EVQLVESGGGLVQPGGSLRLSCAASGFSLSSYWMSWVRQAPGKGLEWIGVIDTNVYIYYANWAKGRFTIS
RDNSKNTLYLQMNSLRAEDTAVYYCARYVGNNDDYINLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGG
TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN
TKVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSY
TMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWL
GPFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYL
AWYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTK
VEIK

SEQ ID 43: PL004B5 Light Chain nt

GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGTCCAGTCAGAGTGTTTATAATGGCTACTGGTTATCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA
GCTCCTGATCTATGGTGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGG
ACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCTAGGCAGTT
ATACTAGTAGTACTGAGAACTCTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGCACC
ATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTG
AATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCC
AGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAA
AGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACA
AAGAGCTTCAACAGGGGAGAGTGT

SEQ ID 44: PL004B5 Light Chain aa

DIQMTQSPSTLSASVGDRVTITCQSSQSVYNGYWLSWYQQKPGKAPKLLIYGASTLASGVPSRFSGSGSG
TEFTLTISSLQPDDFATYYCLGSYTSSTENSFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC

SEQ ID 45: PL004B9 x CT4 nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
TGTCTGGAATCGACCTCAGTGTCATCAATATGGGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGAACCATTACTTATGTTGGTAACACATATTACGCGAGCTGGGCGAAAGGCAGATTCACCATCTCC
AAAACCTCGACCACGGTGGATCTTAAAATCACCAGTCCGACAACCGAGGACACGGCTGTGTATTACTGTG
CGAGAGAATCTGGTACTATTTATTACAGTTACTTTAACTTGTGGGGCCAAGGGACCCTGGTCACCGTCTC
GAGCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA
GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCC
TGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT
GACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
AAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTG
AAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGAC
CCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG
GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGG
TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
ACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCT
ATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCC
CGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG
GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCC
TGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGGAGG
CGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATACT
ATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAAACA
ATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTA
TCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGG
CCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTG

GTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTC
TTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCC
TGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTGGCA
TCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGA
AGATTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTG
GAAATCAAA

SEQ ID 46: PL004B9 x CT4 aa

EVQLVESGGGLVQPGGSLRLSCTVSGIDLSVINMGWVRQAPGKGLEWIGTITYVGNTYYASWAKGRFTIS
KTSTTVDLKITSPTTEDTAVYYCARESGTIYYSYFNLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYT
MHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLG
PFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLA
WYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKV
EIK

SEQ ID 47: PL004B9 Light Chain nt

GCATTCGAATTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCAAGTGCC
AGGCCAGTGAAAGCATTAGCAACTACTTATCCTGGTATCAGCAGATTCCAGGGAAAGTTCCTAAGCTCCT
GATCTATTATGCATCCAATCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAAGCTATTATGGTG
GTGGTAGTGCCTATACTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGCACCATCTGT
CTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAAC
TTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGA
GTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGA
CTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGC
TTCAACAGGGGAGAGTGT

SEQ ID 48: PL004B9 Light Chain aa

AFELTQSPSSLSASVGDRVTIKCQASESISNYLSWYQQIPGKVPKLLIYYASNLASGVPSRFSGSGSGTD
FTLTISSLQPEDVATYYCQSYYGGGSAYTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNN
FYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS
FNRGEC

SEQ ID 49: PD206F12 x CT4 nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCGACTTCAGTAGCGGCTACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTTGATCGCATGCATTTATGCTGGTACTAGTGGTAGTACTTCCTACGCGAGCTGGGCGAGAGGCAGATTC
ACCATCTCCGAAACCTCCAAGAACACGGTGACTCTTCAAATGAACAGCCTGAGAGCCGAGGACTCGGCTG

TGTATTACTGTGCGAGAAATCTTTACACTTACAATAGCTTGTGGGGCCAGGGAACCCTGGTCACCGTCTC
GAGCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA
GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCC
TGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT
GACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
AAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTG
AAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGAC
CCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG
GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGG
TCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAA
AGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC
ACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCT
ATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCC
CGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG
GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCC
TGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGGAGG
CGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATACT
ATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAAACA
ATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTA
TCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGG
CCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTG
GTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTC
TTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCC
TGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTGGCA
TCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGA
AGATTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTG
GAAATCAAA

SEQ ID 50: PD206F12 x CT4 aa

EVQLVESGGGLVQPGGSLRLSCAASGFDFSSGYWICWVRQAPGKGLELIACIYAGTSGSTSYASWARGRF
TISETSKNTVTLQMNSLRAEDSAVYYCARNLYTYNSLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYT
MHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLG
PFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLA
WYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKV
EIK

SEQ ID 51: PD206F12 Light Chain nt

GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGTCCAGTCAGAGTGTTTATGATAACAACTGGTTAGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA

GCTCCTGATCTATACAGTATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGG
ACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAAGGCACTT
ATTATAGTAGTGGTTGGAACTTTGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGC
ACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTG
CTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACT
CCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAG
CAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTC
ACAAAGAGCTTCAACAGGGGAGAGTGT

SEQ ID 52: PD206F12 Light Chain aa

DIQMTQSPSTLSASVGDRVTITCQSSQSVYDNNWLAWYQQKPGKAPKLLIYTVSTLASGVPSRFSGSGSG
TEFTLTISSLQPDDFATYYCQGTYYSSGWNFAFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL
LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPV
TKSFNRGEC

SEQ ID 53: PD215A1 x CT4 nt

CAGGAGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
CCTCTGGATTCTCCTTTAGCAGCTACTGGATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGATGCATTACGACTGGTAGTGGTAGCACTTACTACGCGAGCTGGGCGAAGCGCCGGTTCACCATC
TCCAAAGACAATTCCAAGAACACGGTGACTCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTAT
ATTACTGTACGAGAGCATTTGACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGCTAGCACCAA
GGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGC
CTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGC
ACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG
CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAGA
GTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAAGCCGCGGGGGCAC
CGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATG
CGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTG
CATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCG
TCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAAAGCCCTCCCAGCCCC
CATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCC
CGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCG
CCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA
CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCA
TGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTGGCG
GTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGG
GAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATACTATGCACTGGGTCCGC
CAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAAACAATAAATACTACGCAG
ACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAG
CCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGG
GGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCG
GCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGA
AAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCCTGGTACCAGCAGAAA
CCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTGGCATCCCAGACAGGTTCA

GTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTA
TTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA

SEQ ID 54: PD215A1 x CT4 aa

QEQLLESGGGLVQPGGSLRLSCTASGFSFSSYWMCWVRQAPGKGLEWIGCITTGSGSTYYASWAKRRFTI
SKDNSKNTVTLQMNSLRAEDTAVYYCTRAFDLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC
LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPS
RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVR
QAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYW
GQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQQK
PGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

SEQ ID 55: PD215A1 Light Chain nt

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGGCCAGTCAGAGCATTTACAGCTACTTAAACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCTATGGTGCATCCAATCTGGCATCTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAAAGCAGTTGGTTGA
GTGGTGCTGTTGGTAATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGCACCATC
TGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAAT
AACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGG
AGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGC
AGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAG
AGCTTCAACAGGGGAGAGTGT

SEQ IF 56: PD215A1 Light Chain aa

DIQMTQSPSSLSASVGDRVTITCQASQSIYSYLNWYQQKPGKAPKLLIYGASNLASGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQSSWLSGAVGNAFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN
NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTK
SFNRGEC

SEQ ID 57: PD220F6 x CT4 nt

CAGGAGCAGGTGAAGGAGACCGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCATCAGCAGCTATGGAGTGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GGTCGCATTGATTTTTCCCGGGATTGGTTTCAAAGACTACGCGAGCTGGGTGAATGGCCGGTTCACCCTC
TCCAGCGACAACGCCCAGAACACTGTGGAACTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTAT
ATTACTGTGCGAGAGATTTGGACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGCTAGCACCAA
GGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGC
CTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGC
ACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG
CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAGA

GTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAAGCCGCGGGGGCAC
CGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATG
CGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTG
CATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCG
TCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAAAGCCCTCCCAGCCCC
CATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCC
CGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCG
CCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA
CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCA
TGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTGGCG
GTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGG
GAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATACTATGCACTGGGTCCGC
CAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGATGGAAACAATAAATACTACGCAG
ACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAG
CCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGG
GGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCG
GCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGA
AAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCCTGGTACCAGCAGAAA
CCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCAGGGCCACTGGCATCCCAGACAGGTTCA
GTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTA
TTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA

SEQ ID 58: PD220F6 x CT4 aa

QEQVKETGGGLVQPGGSLRLSCAASGFTISSYGVSWVRQAPGKGLEWVALIFPGIGFKDYASWVNGRFTL
SSDNAQNTVELQMNSLRAEDTAVYYCARDLDLWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC
LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPS
RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVR
QAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYW
GQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQQK
PGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

SEQ ID 59: PD220F6 Light Chain nt

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGTCCAGTCCGAGTGTTTATAGTAACTACTTATCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCT
CCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACA
GATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTGCAGGCGGTTATA
GTAGTAGTACTCGTGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGCACCATCTGT
CTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAAC
TTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGA
GTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGA

CTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGC
TTCAACAGGGGAGAGTGT

SEQ ID 60: PD220F6 Light Chain aa

DIQMTQSPSSLSASVGDRVTITCQSSPSVYSNYLSWYQQKPGKVPKLLIYYASTLASGVPSRFSGSGSGT
DFTLTISSLQPEDVATYYCAGGYSSSTRAFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNN
FYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS
FNRGEC

SEQ ID 61: PD225G11 x CT4 nt

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCTTTAGCAGCAGCCACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTGGATCGCATGCATTTATACTGGTAGTATTGATGTCTTTTACTACGCGAGCTGGGCGAAAGGCCGGTTC
ACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGG
CCGTATATTACTGTGCGAGAGCCGCTAATACTGATACTACCTACTTTAACTTGTGGGGCCAGGGAACCCT
GGTCACCGTCTCGAGCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACC
TCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGA
ACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCT
CAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAG
CCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGT
GCCCAGCACCTGAAGCCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCAT
GATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTC
AACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCA
CGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGC
GGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAA
CCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGG
TCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAA
GACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGC
AGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGA
AGAGCCTCTCCCTGTCTCCGGGTGGCGGTGGAGGGTCCGGCGGTGGTGGATCCCAGGTGCAATTGGTGGA
GTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTC
AGTAGCTATACTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCAT
ATGATGGAAACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAA
GAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACC
GGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGAT
CTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGTTCTGAAATTGTGTTGACGCAGTCTCC
AGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTGGCAGC
AGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATTCAGCA
GGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAG
ACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACCGTGGACGTTCGGCCAA
GGGACCAAGGTGGAAATCAAA

SEQ ID 62: PD225G11 x CT4 aa

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSSHWICWVRQAPGKGLEWIACIYTGSIDVFYYASWAKGRF
TISRDNSKNTLYLQMNSLRAEDTAVYYCARAANTDTTYFNLWGQGTLVTVSSASTKGPSVFPLAPSSKST
SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHK
PSNTKVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF
NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTF
SSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCART
GWLGPFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGS
SYLAWYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQ
GTKVEIK

SEQ ID 63: PD225G11 Light Chain nt
GCCTATGATATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCAATTGCC
AGGCCAGTCAGAGCATTAACAACCAACTATCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCT
GATCTATGGTGCATCCACTCTGGCATCTGGGGTCCCATCTCGGTTCACCGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCATGTTCATTATTGCA
GTGGTGGTAGTTGTTTTTGGGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGTACGGTGGCTGCACC
ATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTG
AATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCC
AGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAA
AGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACA
AAGAGCTTCAACAGGGGAGAGTGT

SEQ ID 64: PD225G11 Light Chain aa
AYDMTQSPSSLSASVGDRVTINCQASQSINNQLSWYQQKPGKVPKLLIYGASTLASGVPSRFTGSGSGTD
FTLTISSLQPEDVATYYCHVHYCSGGSCFWAFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC

SEQ ID 65: CT4 heavy chain signal peptide nucleotide sequence nt
ATGAAACACCTGTGGTTCTTCCTCCTCCTGGTGGCAGCTCCCAGATGGGTCCTGTCC

SEQ ID 66: CT4 heavy chain signal peptide nucleotide sequence aa
MKHLWFFLLLVAAPRWVLS

SEQ ID 67: PL230/PD224 Heavy chain signal peptide nt
ATGGCTGTCTTGGGGCTGCTCTTCTGCCTGGTGACATTCCCAAGCTGTGTCCTATCC

SEQ ID 68: PL230/PD224 Heavy chain signal peptide aa
MAVLGLLFCLVTFPSCVLS

SEQ ID 69: PL230/PD224 Light chain signal peptide nt
ATGAGGGCCCCTGCTCAGTTTCTTGGCTTCTTGCTTTTCTGGATTCCAGCCTCCAGAAGT

SEQ ID 70: PL230/PD224 Light chain signal peptide aa

MRAPAQFLGFLLFWIPASRS

SEQ ID 71: CT4 scFv nt

CAGGTGCAATTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCTTCAGTAGCTATACTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTG
GGTGACATTTATATCATATGATGGAAACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATC
TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATAT
ATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTC
GAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGTTCTGAAATT
GTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCA
GTCAGAGTGTTGGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCAT
CTATGGTGCATTCAGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTC
ACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCAC
CGTGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA

SEQ ID 72: CT4 scFv aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEI
VLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDF
TLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

SEQ ID73: PD224D1 scFv nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAGC
CTCTGGATTCTCCCTCAGTAGCTATGCAATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTACATCGGCTACA
TTGGTGATACTACTGGCATAGCCTACGCGAGCTGGGCGAATGGCAGATTCACCATCTCCAAAGACAATACCAAGAACACG
GTGGATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGGCTGGTCCTACTTAGACAT
CTGGGGCCAAGGGACCCTGGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCG
GTGGAGGCGGCTCTGCCCTTGTGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACT
TGCCAGGCCAGTCAGAACATTTACAGCAATTTAGCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCTGATCTA
TCAGGCCTCCACTCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATATGGGACAGATTTCACTCTCACCATCA
GCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAGGCGGTTATTATAGTGCTGCCCTTAATACTTTCGGCGGA
GGGACCAAGGTGGAGATCAAA

SEQ ID 74: PD224D1 scFv aa

EVQLVESGGGLVQPGGSLRLSCTASGFSLSSYAMSWVRQAPGKGLEYIGYIGDTTGIAYASWANGRFTISKDNTKNTVDLQMNS
LRAEDTAVYYCARGWSYLDIWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSALVMTQSPSSLSASVGDRVTITCQASQNIYSN
LAWYQQKPGKVPKLLIYQASTLASGVPSRFSGSGYGTDFTLTISSLQPEDVATYYCQGGYYSAALNTFGGGTKVEIK

SEQ ID 75: PD206F12 scFv nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCGACTTCAGTAGCGGCTACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTTGATCGCATGCATTTATGCTGGTACTAGTGGTAGTACTTCCTACGCGAGCTGGGCGAGAGGCAGATTC
ACCATCTCCGAAACCTCCAAGAACACGGTGACTCTTCAAATGAACAGCCTGAGAGCCGAGGACTCGGCTG
TGTATTACTGTGCGAGAAATCTTTACACTTACAATAGCTTGTGGGGCCAGGGAACCCTGGTCACCGTCTC

GAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGACATC
CAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCAGTCCA
GTCAGAGTGTTTATGATAACAACTGGTTAGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCTATACAGTATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAA
TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAAGGCACTTATTATA
GTAGTGGTTGGAACTTTGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 76: PD206F12 scFv aa

EVQLVESGGGLVQPGGSLRLSCAASGFDFSSGYWICWVRQAPGKGLELIACIYAGTSGSTSYASWARGRF
TISETSKNTVTLQMNSLRAEDSAVYYCARNLYTYNSLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSDI
QMTQSPSTLSASVGDRVTITCQSSQSVYDNNWLAWYQQKPGKAPKLLIYTVSTLASGVPSRFSGSGSGTE
FTLTISSLQPDDFATYYCQGTYYSSGWNFAFGGGTKVEIK

SEQ ID 77: PD215A1 scFv nt

CAGGAGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
CCTCTGGATTCTCCTTTAGCAGCTACTGGATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGATGCATTACGACTGGTAGTGGTAGCACTTACTACGCGAGCTGGGCGAAGCGCCGGTTCACCATC
TCCAAAGACAATTCCAAGAACACGGTGACTCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTAT
ATTACTGTACGAGAGCATTTGACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGG
ATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGACATCCAGATGACCCAGTCT
CCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCAGGCCAGTCAGAGCATTTACA
GCTACTTAAACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGGTGCATCCAATCT
GGCATCTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGT
CTGCAACCTGAAGATTTTGCAACTTACTACTGTCAAAGCAGTTGGTTGAGTGGTGCTGTTGGTAATGCTT
TCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 78: PD215A1 scFv aa

QEQLLESGGGLVQPGGSLRLSCTASGFSFSSYWMCWVRQAPGKGLEWIGCITTGSGSTYYASWAKRRFTI
SKDNSKNTVTLQMNSLRAEDTAVYYCTRAFDLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQS
PSSLSASVGDRVTITCQASQSIYSYLNWYQQKPGKAPKLLIYGASNLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQSSWLSGAVGNAFGGGTKVEIK

SEQ ID 79: PD225G11 scFv nt

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCTTTAGCAGCAGCCACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTGGATCGCATGCATTTATACTGGTAGTATTGATGTCTTTTACTACGCGAGCTGGGCGAAAGGCCGGTTC
ACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGG
CCGTATATTACTGTGCGAGAGCCGCTAATACTGATACTACCTACTTTAACTTGTGGGGCCAGGGAACCCT
GGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGC
GGCTCTGCCTATGATATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCA
ATTGCCAGGCCAGTCAGAGCATTAACAACCAACTATCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAA
GCTCCTGATCTATGGTGCATCCACTCTGGCATCTGGGGTCCCATCTCGGTTCACCGGCAGTGGATCTGGG

ACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCATGTTCATT
ATTGCAGTGGTGGTAGTTGTTTTTGGGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 80: PD225G11 scFv aa

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSSHWICWVRQAPGKGLEWIACIYTGSIDVFYYASWAKGRF
TISRDNSKNTLYLQMNSLRAEDTAVYYCARAANTDTTYFNLWGQGTLVTVSSGGGGSGGGGSGGGGSGGG
GSAYDMTQSPSSLSASVGDRVTINCQASQSINNQLSWYQQKPGKVPKLLIYGASTLASGVPSRFTGSGSG
TDFTLTISSLQPEDVATYYCHVHYCSGGSCFWAFGGGTKVEIK

SEQ ID 81: PL230C6 scFv nt

CAGTCGGTGGAGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACCGCCT
CTGGAATCGACCTTAATACCTACGACATGATCTGGGTCCGCCAGGCTCCAGGCAAGGGGCTAGAGTGGGT
TGGAATCATTACTTATAGTGGTAGTAGATACTACGCGAACTGGGCGAAAGGCCGATTCACCATCTCCAAA
GACAATACCAAGAACACGGTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACT
GTGCGAGAGATTATATGAGTGGTTCCCACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCTTCCGGTGG
AGGCGGTTCAGGCGGAGGTGGAAGTGGTGGTGGCGGCTCTGGAGGCGGCGGATCTGCCTATGATATGACC
CAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGTCACCATCAAGTGTCAGGCCAGTGAGGACA
TTTATAGCTTCTTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCCATTCTGCATC
CTCTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC
AGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGGTTATGGTAAAAATAATGTTGATA
ATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 82: PL230C6 scFv aa

QSVEESGGGLVQPGGSLRLSCTASGIDLNTYDMIWVRQAPGKGLEWVGIITYSGSRYYANWAKGRFTISK
DNTKNTVYLQMNSLRAEDTAVYYCARDYMSGSHLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSAYDMT
QSPSSVSASVGDRVTIKCQASEDIYSFLAWYQQKPGKAPKLLIHSASSLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCQQGYGKNNVDNAFGGGTKVEIK

SEQ ID 83: PL231H2 scFv nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCCTGGTCCAGCCTGGGGGCTCCCTGAGACTCTCCTGTACAA
CTTCTGGAATCGACCTTAGTACCTACGACATGATCTGGGTCCGCCAGGCTCCAGGCAAGGGGCTAGAGTG
GGTGGGAATCATTAGTTATGTTGGTAACACATACTACGCGAGCTGGGCGAAAGGCCGATTCACCCTCTCC
AAAGACAATACCTCGACCACGGTGGATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATT
ACTGTGCGAGAGATTTTATTAGTGGTTCCCACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGG
TGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGTTCTGCCTATGATATG
ACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGTCACCATCAATTGTCAGGCCAGTGAGA
GCATTAGTAGCTTCTTATCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTTTTCTGC
ATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACC
ATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGGTTATAGTAAAAGTAATGTGG
ATAATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 84: PL231H2 scFv aa

QVQLVESGGGLVQPGGSLRLSCTTSGIDLSTYDMIWVRQAPGKGLEWVGIISYVGNTYYASWAKGRFTLS
KDNTSTTVDLQMNSLRAEDTAVYYCARDFISGSHLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSAYDM

TQSPSSVSASVGDRVTINCQASESISSFLSWYQQKPGKAPKLLIFSASTLASGVPSRFSGSGSGTDFTLT
ISSLQPEDFATYYCQQGYSKSNVDNAFGGGTKVEIK

SEQ ID 85: PL221G5 scFv nt

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCTCCTTCAGTAGCGGGTACGACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTGGATCGCATGCATTGCTGCTGGTAGTGCTGGTATCACTTACGACGCGAACTGGGCGAAAGGCCGGTTC
ACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGG
CCGTATATTACTGTGCGAGATCGGCGTTTTCGTTCGACTACGCCATGGACCTCTGGGGCCAGGGAACCCT
GGTCACCGTCTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGC
GGCTCTGACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCA
CTTGCCAGGCCAGTCAGAGCATTAGTTCCCACTTAAACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA
GCTCCTGATCTATAAGGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGG
ACAGAATTTACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAACAGGGTT
ATAGTTGGGGTAATGTTGATAATGTTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 86: PL221G5 scFv aa

EVQLLESGGGLVQPGGSLRLSCAASGFSFSSGYDMCWVRQAPGKGLEWIACIAAGSAGITYDANWAKGRF
TISRDNSKNTLYLQMNSLRAEDTAVYYCARSAFSFDYAMDLWGQGTLVTVSSGGGGSGGGGSGGGGSGGG
GSDIQMTQSPSTLSASVGDRVTITCQASQSISSHLNWYQQKPGKAPKLLIYKASTLASGVPSRFSGSGSG
TEFTLTISSLQPDDFATYYCQQGYSWGNVDNVFGGGTKVEIK

SEQ ID 87: PL004B5 scFv nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCTCCCTCAGTAGCTACTGGATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGAGTCATTGATACTAATGTTTATATATACTACGCGAACTGGGCAAAAGGCAGATTCACCATCTCC
AGAGACAATTCCAAGAACACGCTGTATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATT
ACTGTGCGAGATATGTGGGTAATAATGATGATTATATTAACTTGTGGGGCCAGGGAACCCTGGTCACCGT
CTCGAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGAC
ATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCAGT
CCAGTCAGAGTGTTTATAATGGCTACTGGTTATCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCT
CCTGATCTATGGTGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACA
GAATTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCTAGGCAGTTATA
CTAGTAGTACTGAGAACTCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 88: PL004B5 scFv aa

EVQLVESGGGLVQPGGSLRLSCAASGFSLSSYWMSWVRQAPGKGLEWIGVIDTNVYIYYANWAKGRFTIS
RDNSKNTLYLQMNSLRAEDTAVYYCARYVGNNDDYINLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSD
IQMTQSPSTLSASVGDRVTITCQSSQSVYNGYWLSWYQQKPGKAPKLLIYGASTLASGVPSRFSGSGSGT
EFTLTISSLQPDDFATYYCLGSYTSSTENSFGGGTKVEIK

SEQ ID 89: PL004B9 scFv nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
TGTCTGGAATCGACCTCAGTGTCATCAATATGGGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG

GATCGGAACCATTACTTATGTTGGTAACACATATTACGCGAGCTGGGCGAAAGGCAGATTCACCATCTCC
AAAACCTCGACCACGGTGGATCTTAAAATCACCAGTCCGACAACCGAGGACACGGCTGTGTATTACTGTG
CGAGAGAATCTGGTACTATTTATTACAGTTACTTTAACTTGTGGGGCCAAGGGACCCTGGTCACCGTCTC
GAGCGGTGGAGGCGGATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGCATTC
GAATTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCAAGTGCCAGGCCA
GTGAAAGCATTAGCAACTACTTATCCTGGTATCAGCAGATTCCAGGGAAAGTTCCTAAGCTCCTGATCTA
TTATGCATCCAATCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACT
CTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAAGCTATTATGGTGGTGGTA
GTGCCTATACTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 90: PL004B9 scFv aa

EVQLVESGGGLVQPGGSLRLSCTVSGIDLSVINMGWVRQAPGKGLEWIGTITYVGNTYYASWAKGRFTIS
KTSTTVDLKITSPTTEDTAVYYCARESGTIYYSYFNLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSAF
ELTQSPSSLSASVGDRVTIKCQASESISNYLSWYQQIPGKVPKLLIYYASNLASGVPSRFSGSGSGTDFT
LTISSLQPEDVATYYCQSYYGGGSAYTFGGGTKVEIK

SEQ ID 91: CT4 VH nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCA
CCTTCAGTAGCTATACTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGACATTTATATCATATGAT
GGAAACAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCT
GCAAATGAACAGCCTGAGAGCTGAGGACACGGCTATATATTACTGTGCGAGGACCGGCTGGCTGGGGCCCTTTGACTACT
GGGGCCAGGGAACCCTGGTCACCGTCTCCTCA

SEQ ID 92: CT4 VH aa

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSS

SEQ ID 93: CT4 VL nt

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCA
GGGCCAGTCAGAGTGTTGGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCT
CCTCATCTATGGTGCATTCAGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACA
GACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGTATGGTA
GCTCACCGTGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA

SEQ ID 94: CT4 VL aa

EIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGT
DFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

SEQ ID 95: PD224D1 VH nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
CCTCTGGATTCTCCCTCAGTAGCTATGCAATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTA
CATCGGCTACATTGGTGATACTACTGGCATAGCCTACGCGAGCTGGGCGAATGGCAGATTCACCATCTCC
AAAGACAATACCAAGAACACGGTGGATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATT
ACTGTGCGAGAGGCTGGTCCTACTTAGACATCTGGGGCCAAGGGACCCTGGTCACCGTCTCGAGC

SEQ ID 96: PD224D1 VH aa

EVQLVESGGGLVQPGGSLRLSCTASGFSLSSYAMSWVRQAPGKGLEYIGYIGDTTGIAYASWANGRFTIS
KDNTKNTVDL
QMNSLRAEDTAVYYCARGWSYLDIWGQGTLVTVSS

SEQ ID 97: PD224D1 VL nt
GCCCTTGTGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGGCCAGTCAGAACATTTACAGCAATTTAGCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCT
GATCTATCAGGCCTCCACTCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATATGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAGGCGGTTATTATA
GTGCTGCCCTTAATACTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 98: PD224D1 VL aa
ALVMTQSPSSLSASVGDRVTITCQASQNIYSNLAWYQQKPGKVPKLLIYQASTLASGVPSRFSGSGYGTD
FTLTISSLQP
EDVATYYCQGGYYSAALNTFGGGTKVEIK

SEQ ID 99: PD206F12 VH nt
GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCGACTTCAGTAGCGGCTACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTTGATCGCATGCATTTATGCTGGTACTAGTGGTAGTACTTCCTACGCGAGCTGGGCGAGAGGCAGATTC
ACCATCTCCGAAACCTCCAAGAACACGGTGACTCTTCAAATGAACAGCCTGAGAGCCGAGGACTCGGCTG
TGTATTACTGTGCGAGAAATCTTTACACTTACAATAGCTTGTGGGGCCAGGGAACCCTGGTCACCGTCTC
GAGC

SEQ ID 100: PD206F12 VH aa
EVQLVESGGGLVQPGGSLRLSCAASGFDFSSGYWICWVRQAPGKGLELIACIYAGTSGSTSYASWARGRF
TISETSKNTVTLQMNSLRAEDSAVYYCARNLYTYNSLWGQGTLVTVSS

SEQ ID 101: PD206F12 VL nt
GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGTCCAGTCAGAGTGTTTATGATAACAACTGGTTAGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA
GCTCCTGATCTATACAGTATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGG
ACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAAGGCACTT
ATTATAGTAGTGGTTGGAACTTTGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 102: PD206F12 VL aa
DIQMTQSPSTLSASVGDRVTITCQSSQSVYDNNWLAWYQQKPGKAPKLLIYTVSTLASGVPSRFSGSGSG
TEFTLTISSLQPDDFATYYCQGTYYSSGWNFAFGGGTKVEIK

SEQ ID 103: PD215A1 VH nt
CAGGAGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
CCTCTGGATTCTCCTTTAGCAGCTACTGGATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGATGCATTACGACTGGTAGTGGTAGCACTTACTACGCGAGCTGGGCGAAGCGCCGGTTCACCATC
TCCAAAGACAATTCCAAGAACACGGTGACTCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTAT
ATTACTGTACGAGAGCATTTGACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC

SEQ ID 104: PD215A1 VH aa
QEQLLESGGGLVQPGGSLRLSCTASGFSFSSYWMCWVRQAPGKGLEWIGCITTGSGSTYYASWAKRRFTI
SKDNSKNTVTLQMNSLRAEDTAVYYCTRAFDLWGQGTLVTVSS

SEQ ID 105: PD215A1 VL nt
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGGCCAGTCAGAGCATTTACAGCTACTTAAACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCTATGGTGCATCCAATCTGGCATCTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAAAGCAGTTGGTTGA
GTGGTGCTGTTGGTAATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 106: PD215A1 VL aa
DIQMTQSPSSLSASVGDRVTITCQASQSIYSYLNWYQQKPGKAPKLLIYGASNLASGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQSSWLSGAVGNAFGGGTKVEIK

SEQ ID 107: PD225G11 VH nt
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCTTTAGCAGCAGCCACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTGGATCGCATGCATTTATACTGGTAGTATTGATGTCTTTTACTACGCGAGCTGGGCGAAAGGCCGGTTC
ACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGG
CCGTATATTACTGTGCGAGAGCCGCTAATACTGATACTACCTACTTTAACTTGTGGGGCCAGGGAACCCT
GGTCACCGTCTCGAGC

SEQ ID 108: PD225G11 VH aa
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSSHWICWVRQAPGKGLEWIACIYTGSIDVFYYASWAKGRF
TISRDNSKNTLYLQMNSLRAEDTAVYYCARAANTDTTYFNLWGQGTLVTVSS

SEQ ID 109: PD225G11 VL nt
GCCTATGATATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCAATTGCC
AGGCCAGTCAGAGCATTAACAACCAACTATCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCT
GATCTATGGTGCATCCACTCTGGCATCTGGGGTCCCATCTCGGTTCACCGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCATGTTCATTATTGCA
GTGGTGGTAGTTGTTTTTGGGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 110: PD225G11 VL aa
AYDMTQSPSSLSASVGDRVTINCQASQSINNQLSWYQQKPGKVPKLLIYGASTLASGVPSRFTGSGSGTD
FTLTISSLQPEDVATYYCHVHYCSGGSCFWAFGGGTKVEIK

SEQ ID 111: PL230C6 VH nt
CAGTCGGTGGAGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACCGCCT
CTGGAATCGACCTTAATACCTACGACATGATCTGGGTCCGCCAGGCTCCAGGCAAGGGGCTAGAGTGGGT
TGGAATCATTACTTATAGTGGTAGTAGATACTACGCGAACTGGGCGAAAGGCCGATTCACCATCTCCAAA
GACAATACCAAGAACACGGTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACT
GTGCGAGAGATTATATGAGTGGTTCCCACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCTTCC

SEQ ID 112: PL230C6 VH aa
QSVEESGGGLVQPGGSLRLSCTASGIDLNTYDMIWVRQAPGKGLEWVGIITYSGSRYYANWAKGRFTISK
DNTKNTVYLQMNSLRAEDTAVYYCARDYMSGSHLWGQGTLVTVSS

SEQ ID 113: PL230C6 VL nt

GCCTATGATATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGTCACCATCAAGTGTC
AGGCCAGTGAGGACATTTATAGCTTCTTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCCATTCTGCATCCTCTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGGTTATGGTA
AAAATAATGTTGATAATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 114: PL230C6 VL aa

AYDMTQSPSSVSASVGDRVTIKCQASEDIYSFLAWYQQKPGKAPKLLIHSASSLASGVPSRFSGSGSGTD
FTLTISSLQP
EDFATYYCQQGYGKNNVDNAFGGGTKVEIK

SEQ ID 115: PL231H2 VH nt

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCCTGGTCCAGCCTGGGGGCTCCCTGAGACTCTCCTGTACAA
CTTCTGGAATCGACCTTAGTACCTACGACATGATCTGGGTCCGCCAGGCTCCAGGCAAGGGGCTAGAGTG
GGTGGGAATCATTAGTTATGTTGGTAACACATACTACGCGAGCTGGGCGAAAGGCCGATTCACCCTCTCC
AAAGACAATACCTCGACCACGGTGGATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATT
ACTGTGCGAGAGATTTTATTAGTGGTTCCCACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC

SEQ ID 116: PL231H2 VH aa

QVQLVESGGGLVQPGGSLRLSCTTSGIDLSTYDMIWVRQAPGKGLEWVGIISYVGNTYYASWAKGRFTLS
KDNTSTTVDLQMNSLRAEDTAVYYCARDFISGSHLWGQGTLVTVSS

SEA ID 117: PL231H2 VL nt

GCCTATGATATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGTCACCATCAATTGTC
AGGCCAGTGAGAGCATTAGTAGCTTCTTATCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCTTTTCTGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGGTTATAGTA
AAAGTAATGTGGATAATGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 118: PL231H2 VL aa

AYDMTQSPSSVSASVGDRVTINCQASESISSFLSWYQQKPGKAPKLLIFSASTLASGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQQGYSKSNVDNAFGGGTKVEIK

SEQ ID 119: PL221G5 VH nt

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCTCCTTCAGTAGCGGGTACGACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
GTGGATCGCATGCATTGCTGCTGGTAGTGCTGGTATCACTTACGACGCGAACTGGGCGAAAGGCCGGTTC
ACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGG
CCGTATATTACTGTGCGAGATCGGCGTTTTCGTTCGACTACGCCATGGACCTCTGGGGCCAGGGAACCCT
GGTCACCGTCTCGAGC

SEA ID 120: PL221G5 VH aa

EVQLLESGGGLVQPGGSLRLSCAASGFSFSSGYDMCWVRQAPGKGLEWIACIAAGSAGITYDANWAKGRF
TISRDNSKNTLYLQMNSLRAEDTAVYYCARSAFSFDYAMDLWGQGTLVTVSS

SEQ ID 121: PL221G5 VL nt

GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGGCCAGTCAGAGCATTAGTTCCCACTTAAACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCT
GATCTATAAGGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAA
TTTACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAACAGGGTTATAGTT
GGGGTAATGTTGATAATGTTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEA ID 122: PL221G5 VL aa

DIQMTQSPSTLSASVGDRVTITCQASQSISSHLNWYQQKPGKAPKLLIYKASTLASGVPSRFSGSGSGTE
FTLTISSLQPDDFATYYCQQGYSWGNVDNVFGGGTKVEIK

SEA ID 123: PL004B5 VH nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCTCCCTCAGTAGCTACTGGATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGAGTCATTGATACTAATGTTTATATATACTACGCGAACTGGGCAAAAGGCAGATTCACCATCTCC
AGAGACAATTCCAAGAACACGCTGTATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATT
ACTGTGCGAGATATGTGGGTAATAATGATGATTATATTAACTTGTGGGGCCAGGGAACCCTGGTCACCGT
CTCGAGC

SEQ ID 124: PL004B5 VH aa

EVQLVESGGGLVQPGGSLRLSCAASGFSLSSYWMSWVRQAPGKGLEWIGVIDTNVYIYYANWAKGRFTIS
RDNSKNTLYLQMNSLRAEDTAVYYCARYVGNNDDYINLWGQGTLVTVSS

SEQ ID 125: PL004B5 VL nt

GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGTCCAGTCAGAGTGTTTATAATGGCTACTGGTTATCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA
GCTCCTGATCTATGGTGCATCCACTCTGGCATCTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGG
ACAGAATTCACTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCTAGGCAGTT
ATACTAGTAGTACTGAGAACTCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 126: PL004B5 VL aa

DIQMTQSPSTLSASVGDRVTITCQSSQSVYNGYWLSWYQQKPGKAPKLLIYGASTLASGVPSRFSGSGSG
TEFTLTISSLQPDDFATYYCLGSYTSSTENSFGGGTKVEIK

SEA ID 127: PL004B9 VH nt

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTACAG
TGTCTGGAATCGACCTCAGTGTCATCAATATGGGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGAACCATTACTTATGTTGGTAACACATATTACGCGAGCTGGGCGAAAGGCAGATTCACCATCTCC
AAAACCTCGACCACGGTGGATCTTAAAATCACCAGTCCGACAACCGAGGACACGGCTGTGTATTACTGTG
CGAGAGAATCTGGTACTATTTATTACAGTTACTTTAACTTGTGGGGCCAAGGGACCCTGGTCACCGTCTC
GAGC

SEQ ID 128: PL004B9 VH aa

EVQLVESGGGLVQPGGSLRLSCTVSGIDLSVINMGWVRQAPGKGLEWIGTITYVGNTYYASWAKGRFTIS
KTSTTVDLKITSPTTEDTAVYYCARESGTIYYSYFNLWGQGTLVTVSS

SEQ ID 129: PL004B9 VL nt

GCATTCGAATTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCAAGTGCC
AGGCCAGTGAAAGCATTAGCAACTACTTATCCTGGTATCAGCAGATTCCAGGGAAAGTTCCTAAGCTCCT
GATCTATTATGCATCCAATCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACAGAT
TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAAGCTATTATGGTG
GTGGTAGTGCCTATACTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 130: PL004B9 VL aa

AFELTQSPSSLSASVGDRVTIKCQASESISNYLSWYQQIPGKVPKLLIYYASNLASGVPSRFSGSGSGTD
FTLTISSLQPEDVATYYCQSYYGGGSAYTFGGGTKVEIK

SEQ ID 131: PD220F6 VH nt

CAGGAGCAGGTGAAGGAGACCGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCATCAGCAGCTATGGAGTGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GGTCGCATTGATTTTTCCCGGGATTGGTTTCAAAGACTACGCGAGCTGGGTGAATGGCCGGTTCACCCTC
TCCAGCGACAACGCCCAGAACACTGTGGAACTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTAT
ATTACTGTGCGAGAGATTTGGACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC

SEQ ID 132: PD220F6 VH aa

QEQVKETGGGLVQPGGSLRLSCAASGFTISSYGVSWVRQAPGKGLEWVALIFPGIGFKDYASWVNGRFTL
SSDNAQNTVELQMNSLRAEDTAVYYCARDLDLWGQGTLVTVSS

SEQ ID 133: PD220F6 VL nt

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC
AGTCCAGTCCGAGTGTTTATAGTAACTACTTATCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCT
CCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACA
GATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTGCAGGCGGTTATA
GTAGTAGTACTCGTGCTTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 134: PD220F6 VL aa

DIQMTQSPSSLSASVGDRVTITCQSSPSVYSNYLSWYQQKPGKVPKLLIYYASTLASGVPSRFSGSGSGT
DFTLTISSLQPEDVATYYCAGGYSSSTRAFGGGTKVEIK

SEQ ID 135: human IgG1 constant region nt

GCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGG
CCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGAC
CAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACC
GTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGG
TGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACT
CCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT
GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG
CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCC
CTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCC

TGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCC
CAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTG
CTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGA
ACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTC
TCCGGGT

SEQ ID 136: human IgG1 constant region aa

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT
VPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

SEQ ID 137: human IgG1 effector null nt

GCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGG
CCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGAC
CAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACC
GTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGG
TGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAAGC
CGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT
GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG
CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCGCGGTCTCCAACAAAGCC
CTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCC
TGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCC
CAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTG
CTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGA
ACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTC
TCCGGGT

SEQ ID 138: human IgG1 effector null aa

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT
VPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCAVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

SEQ ID 139: PD220F6 scFv nt

CAGGAGCAGGTGAAGGAGACCGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGATTCACCATCAGCAGCTATGGAGTGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GGTCGCATTGATTTTTCCCGGGATTGGTTTCAAAGACTACGCGAGCTGGGTGAATGGCCGGTTCACCCTC
TCCAGCGACAACGCCCAGAACACTGTGGAACTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTAT
ATTACTGTGCGAGAGATTTGGACTTGTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGCGGTGGAGGCGG
ATCTGGCGGAGGTGGTTCCGGCGGTGGCGGCTCCGGTGGAGGCGGCTCTGACATCCAGATGACCCAGTCT
CCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCAGTCCAGTCCGAGTGTTTATA

GTAACTACTTATCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCTGATCTATTATGCATCCAC
TCTGGCATCTGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC
AGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTGCAGGCGGTTATAGTAGTAGTACTCGTGCTTTCG
GCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID 140: PD220F6 scFv aa
QEQVKETGGGLVQPGGSLRLSCAASGFTISSYGVSWVRQAPGKGLEWVALIFPGIGFKDYASWVNGRFTL
SSDNAQNTVELQMNSLRAEDTAVYYCARDLDLWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQS
PSSLSASVGDRVTITCQSSPSVYSNYLSWYQQKPGKVPKLLIYYASTLASGVPSRFSGSGSGTDFTLTIS
SLQPEDVATYYCAGGYSSSTRAFGGGTKVEIK

SEQ ID 141: CT4 VH CDR1 aa
SSYTMH

SEQ ID 142: CT4 VH CDR2 aa
FISYDGNNKYYADSVKG

SEQ ID 143: CT4 VH CDR3 aa
TGWLGPFDY

SEQ ID 144: CT4 VL CDR1 aa
RASQSVGSSYLA

SEQ ID 145: CT4 VL CDR2 aa
GAFSRAT

SEQ ID 146: CT4 VL CDR3 aa
QQYGSSPWT

SEQ ID 147: PL230C6 VH CDR1 aa
NTYDMI

SEQ ID 148: PL230C6VH CDR2 aa
IITYSGSRYYANWAKG

SEQ ID 149: PL230C6VH CDR3 aa
DYMSGSHL

SEQ ID 150: PL230C6VL CDR1 aa
QASEDIYSFLA

SEQ ID 151: PL230C6VL CDR2 aa
SASSLAS

SEQ ID 152: PL230C6VL CDR3 aa
QQGYGKNNVDNA

SEQ ID 153: PD224D1 VH CDR1 aa
NTYDMI

SEQ ID 154: PD224D1 CDR2 aa
IITYSGSRYYANWAKG

SEQ ID 155: PD224D1 CDR3 aa
DYMSGSHL

SEQ ID 156: PD224D1 CDR1 aa
QASEDIYSFLA

SEQ ID 157: PD224D1 CDR2 aa
SASSLAS

SEQ ID 158: PD224D1 CDR3 aa
QQGYGKNNVDNA

SEQ ID 159: PL221G5 VH CDR1 aa
SGYDMC

SEQ ID 160: PL221G5 CDR2 aa
CIAAGSAGITYDANWAKG

SEQ ID 161: PL221G5 CDR3 aa
SAFSFDYAMDL

SEQ ID 162: PL221G5 CDR1 aa
QASQSISSHLN

SEQ ID 163: PL221G5 CDR2 aa
KASTLAS

SEQ ID 164: PL221G5 CDR3 aa
QQGYSWGNVDNV

SEQ ID 165: PL231H2 VH CDR1 aa
STYDMI

SEQ ID 166: PL231H2 VH CDR2 aa
IISYVGNTYYASWAKG

SEQ ID 167: PL231H2 VH CDR3 aa
DFISGSHL

SEQ ID 168: PL231H2 VL CDR1 aa
QASESISSFLS

SEQ ID 169: PL231H2 VL CDR2 aa
SASTLAS

SEQ ID 170: PL231H2 VL CDR3 aa

QQGYSKSNVDNA

SEQ ID 171: PL004B5 VH CDR1 aa
SSYWMS

SEQ ID 172: PL004B5 VH CDR2 aa
VIDTNVYIYYANWAKG

SEQ ID 173: PL004B5 VH CDR3 aa
YVGNNDDYINL

SEQ ID 174: PL004B5 VL CDR1 aa
QSSQSVYNGWLS

SEQ ID 175: PL004B5 VL CDR2 aa
GASTLAS

SEQ ID 176: PL004B5 VL CDR3 aa
LGSYTSSTENS

SEQ ID 177: PL004B9 VH CDR1 aa
SVINMG

SEQ ID 178: PL004B9 VH CDR2 aa
TITYVGNTYYASWAKG

SEQ ID 179: PL004B9 VH CDR3 aa
ESGTIYYSYFNL

SEQ ID 180: PL004B9 VL CDR1 aa
QASESISNYLS

SEQ ID 181: PL004B9 VL CDR2 aa
YASNLAS

SEQ ID 182: PL004B9 VL CDR3 aa
QSYYGGGSAYT

SEQ ID 183: PD206F12 VH CDR1 aa
SGYWIC

SEQ ID 184: PD206F12 VH CDR2 aa
CIYAGTSGSTSYASWARG

SEQ ID 185: PD206F12 VH CDR3 aa
NLYTYNSL

SEQ ID 186: PD206F12 VL CDR1 aa
QSSQSVYDNNWLA

SEQ ID 187: PD206F12 VL CDR2 aa

TVSTLAS

SEQ ID 188: PD206F12 VL CDR3 aa
QGTYYSSGWNFA

SEQ ID 189: PD215A1 VH CDR1 aa
SSYWMC

SEQ ID 190: PD215A1 VH CDR2 aa
CITTGSGSTYYASWAKR

SEQ ID 191: PD215A1 VH CDR3 aa
AFDL

SEQ ID 192: PD215A1 VL CDR1 aa
QASQSIYSYLN

SEQ ID 193: PD215A1 VL CDR2 aa
GASNLAS

SEQ ID 194: PD215A1 VL CDR3 aa
QSSWLSGAVGNA

SEQ ID 195: PD220F6 VH CDR1 aa
SSYGVS

SEQ ID 196: PD220F6 VH CDR2 aa
LIFPGIGFKDYASWVNG

SEQ ID 197: PD220F6 VH CDR3 aa
DLDL

SEQ ID 198: PD220F6 VL CDR1 aa
QSSPSVYSNYLS

SEQ ID 199: PD220F6 VL CDR2 aa
YASTLAS

SEQ ID 200: PD220F6 VL CDR3 aa
AGGYSSSTRA

SEQ ID 201: PD225G11 VH CDR1 aa
SSHWIC

SEQ ID 202: PD225G11 VH CDR2 aa
CIYTGSIDVFYYASWAKG

SEQ ID 203: PD225G11 VH CDR3 aa
AANTDTTYFNL

SEQ ID 204: PD225G11 VL CDR1 aa
QASQSINNQLS

SEQ ID 205: PD225G11 VL CDR2 aa
GASTLAS

SEQ ID 206: PD225G11 VL CDR3 aa
HVHYCSGGSCFWA

		CDR Sequences for anti-CTLA4, anti-PD-1 and anti-PD-L1					
mAb	**Target**	**VH**			**VL**		
		CDR 1	CDR 2	CDR 3	CDR 1	CDR 2	CDR 3
CT4	CTLA4	SSYTMH Seq ID 141	FISYDGNNKYYADSVKG Seq ID 142	TGWLGPFDY Seq ID 143	RASQSVGSSYLA Seq ID 144	GAFSRAT Seq ID 145	QQYGSSPWT Seq ID 146
PL230C6	PD-L1	NTYDMI Seq ID 147	IITYSGSRYYANWAKG Seq ID148	DYMSGSHL Seq ID149	QASEDIYSFLA Seq ID 150	SASSLAS Seq ID 151	QQGYGKNNVDNA Seq ID 152
PD224D1	PD-1	SSYAMS Seq ID 153	YIGDTTGIAYASWANG Seq ID 154	GWSYLDI Seq ID 155	QASQNIYSNLA Seq ID 156	QASTLAS Seq ID 157	QGGYYSAALNT Seq ID 158
PL221G5	PD-L1	SGYDMC Seq ID 159	CIAAGSAGITYDANWAKG Seq ID 160	SAFSFDYAMDL Seq ID 161	QASQSISSHLN Seq ID 162	KASTLAS Seq ID 163	QQGYSWGNVDNV Seq ID 164
PL231H2	PD-L1	STYDMI Seq ID 165	IISYVGNTYYASWAKG Seq ID 166	DFISGSHL Seq ID 167	QASESISSFLS Seq ID 168	SASTLAS Seq ID 169	QQGYSKSNVDNA Seq ID 170
PL004B5	PD-L1	SSYWMS Seq ID 171	VIDTNVYIYYANWAKG Seq ID 172	YVGNNDDYINL Seq ID 173	QSSQSVYNGWLS Seq ID 174	GASTLAS Seq ID 175	LGSYTSSTENS Seq ID 176
PL004B9	PD-L1	SVINMG Seq ID 177	TITYVGNTYYASWAKG Seq ID 178	ESGTIYYSYFNL Seq ID 179	QASESISNYLS Seq ID 180	YASNLAS Seq ID 181	QSYYGGGSAYT Seq ID 182
PD206F12	PD-1	SGYWIC Seq ID 183	CIYAGTSGSTSYASWARG Seq ID 184	NLYTYNSL Seq ID 185	QSSQSVYDNNWLA Seq ID 186	TVSTLAS Seq ID 187	QGTYYSSGWNFA Seq ID 188
PD215A1	PD-1	SSYWMC Seq ID 189	CITTGSGSTYYASWAKR Seq ID 190	AFDL Seq ID 191	QASQSIYSYLN Seq ID 192	GASNLAS Seq ID 193	QSSWLSGAVGNA Seq ID 194
PD220F6	PD-1	SSYGVS Seq ID 195	LIFPGIGFKDYASWVNG Seq ID 196	DLDL Seq ID 197	QSSPSVYSNYLS Seq ID 198	YASTLAS Seq ID 199	AGGYSSSTRA Seq ID 200
PD225G11	PD-1	SSHWIC Seq ID 201	CIYTGSIDVFYYASWAKG Seq ID 202	AANTDTTYFNL Seq ID 203	QASQSINNQLS Seq ID 204	GASTLAS Seq ID 205	HVHYCSGGSCFWA Seq ID 206

CLAIMS

What is claimed is:

1. A bispecific antibody, comprising IgG domains having heavy chains and light chains, and two scFv components being connected to either C terminal of the heavy chains or N terminal of the light chains, wherein the IgG domains have a first binding specificity to a first antigen, wherein the scFv components have a second binding specificity to a second antigen, and wherein the first antigen and the second antigen are different and are independently selected from α-CTLA4, α-PD-1, and α-PD-L1.

2. The bispecific antibody of Claim 1, wherein the two scFv components are connected to the C terminal of the heavy chain.

3. The bispecific antibody of Claim 2, wherein the first antigen comprises α-CTLA4 and the second antigen comprises α-PD-1 or α-PD-L1.

4. The bispecific antibody of Claim 2, wherein the first antigen comprises α-PD-1 or α-PD-L1 and the second antigen comprises α-CTLA4.

5. The bispecific antibody of Claim 1, wherein the two scFv components are connected to the N terminal of the light chain.

6. The bispecific antibody of Claim 5, wherein the first antigen comprises α-PD-1 or α-PD-L1 and the second antigen comprises α-CTLA4.

7. The bispecific antibody of Claim 5, wherein the first antigen comprises α-CTLA4 and the second antigen comprises α-PD-1 or α-PD-L1.

8. The bispecific antibody of Claim 1, wherein the bispecific antibody is an isolated monoclonal antibody.

9. The bispecific antibody of Claim 1, comprising an antigen-binding fragment having a sequence having at least 98% similarity with SEQ ID No. 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, or 134.

10. The bispecific antibody of Claim 1, having a first binding specificity to α-CTLA4 and a second binding specificity to α-PD-1 or α-PD-L1, wherein neither the first nor the second has a Kd greater than 70nM.

11. The bispecific antibody of Claim 1, having a first binding specificity to α-CTLA4 and a second specificity to α-PD-1, wherein neither the first nor the second has a Kd greater than 70nM.

12. The bispecific antibody of Claim 1, having a first binding specificity to α-CTLA4 and a second binding specificity to α-PD-L1, wherein neither the first nor the second has a Kd greater than 70nM.

13. The bispecific antibody of Claim 1, comprising a human framework region.

14. The bispecific antibody of Claim 1, wherein the antibody is a humanized antibody, a chimeric antibody, or a recombinant antibody.

15. The bispecific antibody of Claim 1, wherein the IgG domain comprises an IgG1 constant region, wherein the IgG1 constant region comprises an amino acid sequence having at least 98% similarity with SEQ ID No. 136.

16. An IgG1 heavy chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 02, 06, 08, 10, 12, 14, 16, 18, 20, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 72, 92, 96, 100, 104,108, 112, 116, 120, 124, 128, or 132.

17. A kappa light chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 04, 28, 32, 36, 40, 44, 48, 52, 56, 60, and 64.

18. A variable light chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, or 134.

19. A variable heavy chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 92, 96, 100, 104,108, 112, 116, 120, 124, 128, or 132.

20. An isolated nucleic acid encoding the bispecific antibody of Claim 1, the IgG1 heavy chain of Claim 16, the kappa light chain of Claim 17, the variable light chain of Claim 18, or the variable heavy chain of Claim 19.

21. An expression vector comprising the isolated nucleic acid of Claim 20.

22. The expression vector of Claim 21, wherein the vector is expressible in a cell.

23. A host cell comprising the nucleic acid of Claim 20.

24. A host cell comprising the expression vector of Claim 21.

25. The host cell of Claim 23 or 24, wherein the host cell is a prokaryotic cell or a eukaryotic cell.

26. A method of producing a bispecific antibody, comprising culturing the host cell of one of Claims 23-25 so that the bispecific antibody is produced.

27. An immunoconjugate comprising the bispecific antibody of Claim 1 and a cytotoxic agent.

28. The immunoconjugate according to claim 27, wherein the cytotoxic agent comprises a chemotherapeutic agent, a growth inhibitory agent, a toxin, or a radioactive isotope.

29. A pharmaceutical composition, comprising the bispecific antibody of Claim 1 and a pharmaceutically acceptable carrier.

30. The pharmaceutical composition of Claim 29, further comprising radioisotope, radionuclide, a toxin, a therapeutic agent, a chemotherapeutic agent or a combination thereof.

31. A pharmaceutical composition, comprising the immunoconjugate of Claim 30 and a pharmaceutically acceptable carrier.

32. A method of treating a subject with a cancer, comprising administering to the subject an effective amount of the bispecific antibody of Claim 1

33. The method of Claim 32, wherein the cancer comprises cells expressing PD-L1.

34. The method of Claim 32, wherein the cancer comprises breast cancer, colorectal cancer, pancreatic cancer, head and neck cancer, melanoma, ovarian cancer, prostate cancer, non-small lung cell cancer, small cell lung cancer, glioma, esophageal cancer, nasopharyngeal cancer, kidney cancer, gastric cancer, liver cancer, bladder cancer, cervical cancer, brain cancer, lymphoma, leukaemia, myeloma.

35. The method of Claim 32, further comprising co-administering an effective amount of a therapeutic agent.

36. The method of Claim 35, wherein the therapeutic agent comprises an antibody, a chemotherapy agent, an enzyme, or a combination thereof.

37. The method of Claim 36, wherein the therapeutic agent comprises capecitabine, cisplatin, trastuzumab, fulvestrant, tamoxifen, letrozole, exemestane, anastrozole, aminoglutethimide, testolactone, vorozole, formestane, fadrozole, letrozole, erlotinib, lafatinib, dasatinib, gefitinib, imatinib, pazopinib, lapatinib, sunitinib, nilotinib, sorafenib, nab-palitaxel, a derivative or a combination thereof.

38. The method of Claim 32, wherein the subject is a human.

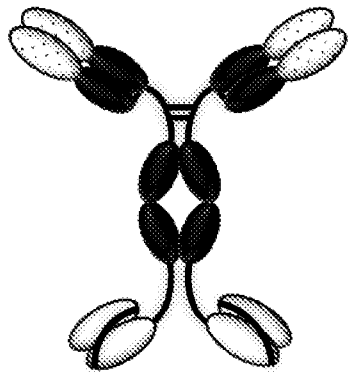
39. A solution comprising an effective concentration of the bispecific antibody of Claim 1, wherein the solution is blood plasma in a subject.

40. A bispecific antibody, having a first binding specificity to a first antigen and a second binding specificity to a second antigen, wherein both the first and the second antigen are check point antigens, and wherein neither the first specificity nor the second specificity has a Kd greater than 70nM.

41. A bispecific antibody, comprising IgG domains having heavy chains and light chains, and two scFv components being connected to either C terminal of the heavy chains or N terminal of the light chains, wherein the IgG domains have a first binding specificity to a first antigen, wherein the scFv components have a second binding specificity to a second antigen, and wherein both the first antigen and the second antigen are checkpoint antigens and wherein the first antigen differs from the second antigen.

Figure 1.

A



B

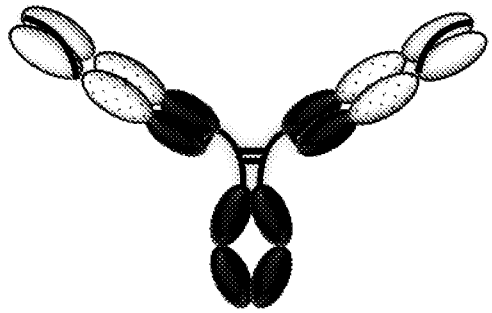


Figure 2.

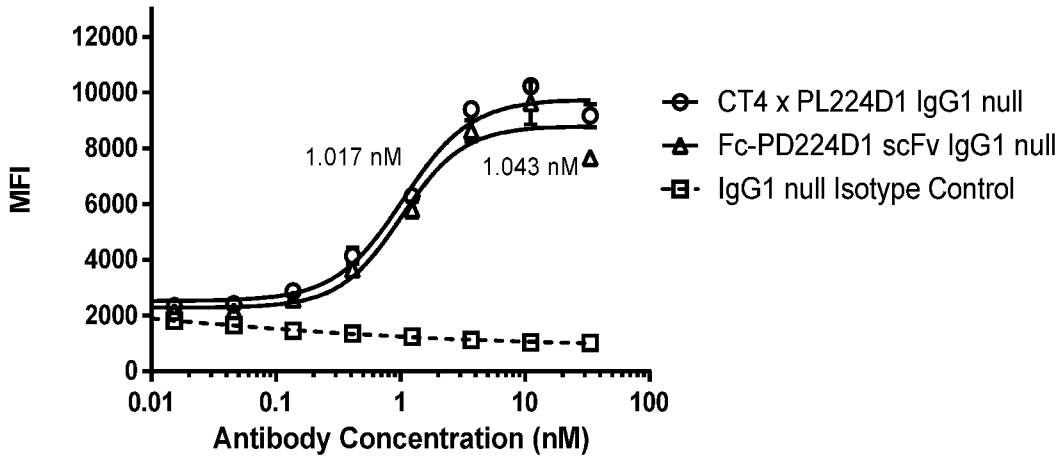

12000
10000
8000
6000
4000
2000
0
MFI
1.017 nM
1.043 nM
0.01
0.1
1
10
100
Antibody Concentration (nM)
CT4 x PL224D1 IgG1 null
Fc-PD224D1 scFv IgG1 null
IgG1 null Isotype Control

Figure 3.

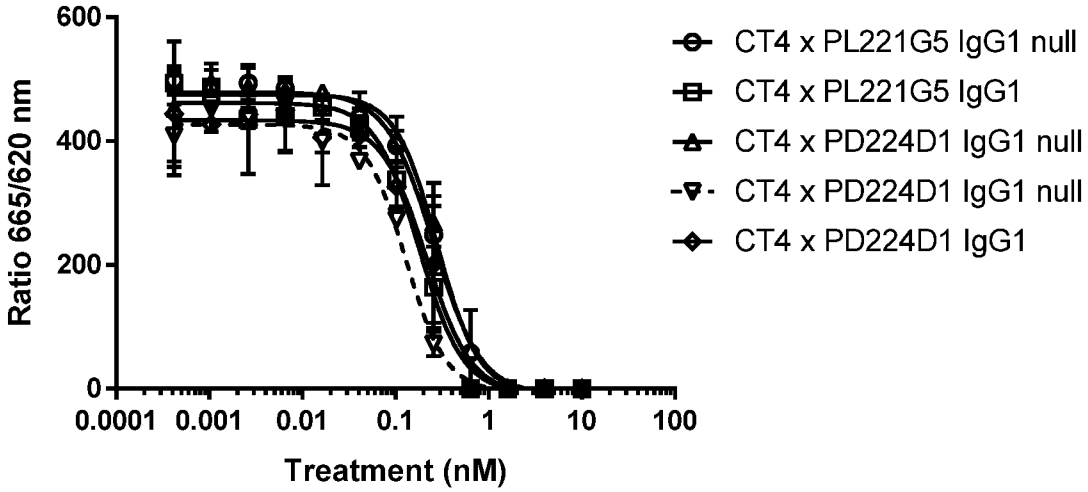
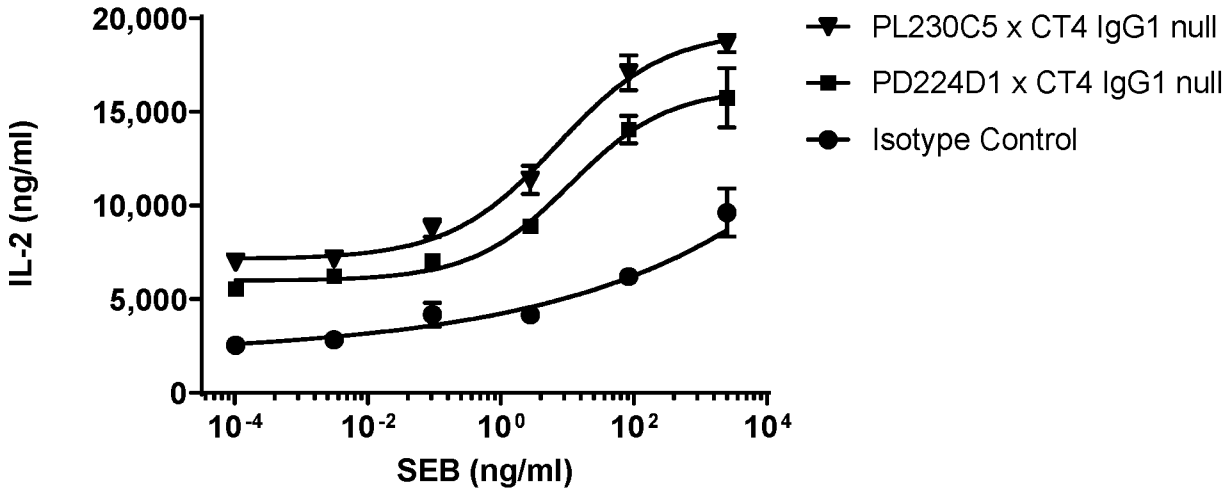

600
400
200
0
Ratio 665/620 nm
0.0001
0.001
0.01
0.1
1
10
100
Treatment (nM)
CT4 x PL221G5 IgG1 null
CT4 x PL221G5 IgG1
CT4 x PD224D1 IgG1 null
CT4 x PD224D1 IgG1 null
CT4 x PD224D1 IgG1

Figure 4.

A


20,000
15,000
10,000
5,000
0
IL-2 (ng/ml)
10-4
10-2
100
102
104
SEB (ng/ml)
PL230C5 x CT4 IgG1 null
PD224D1 x CT4 IgG1 null
Isotype Control

B

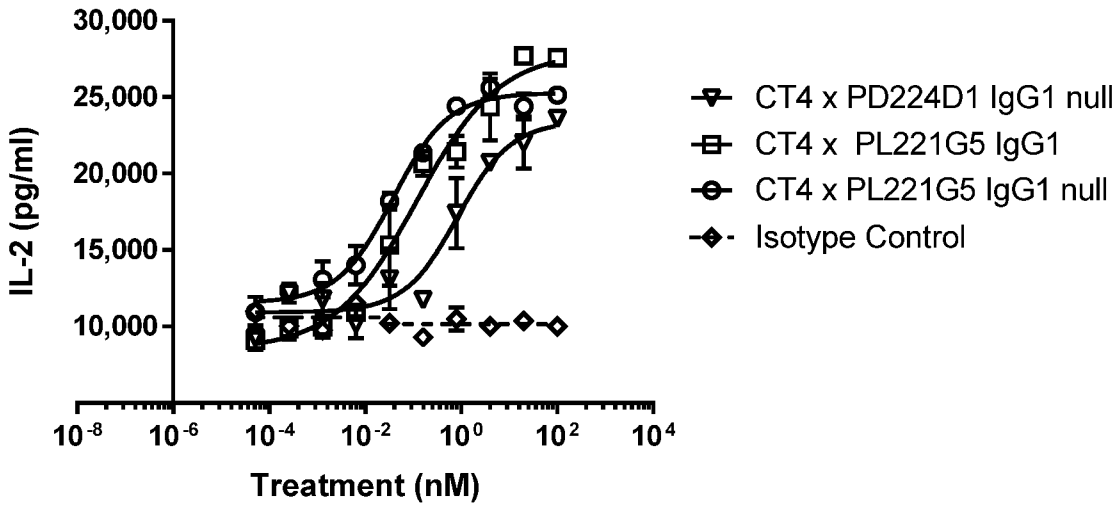

30,000
25,000
20,000
15,000
10,000
IL-2 (pg/ml)
10-8
10-6
10-4
10-2
100
102
104
Treatment (nM)
CT4 x PD224D1 IgG1 null
CT4 x PL221G5 IgG1
CT4 x PL221G5 IgG1 null
Isotype Control

Figure 5.

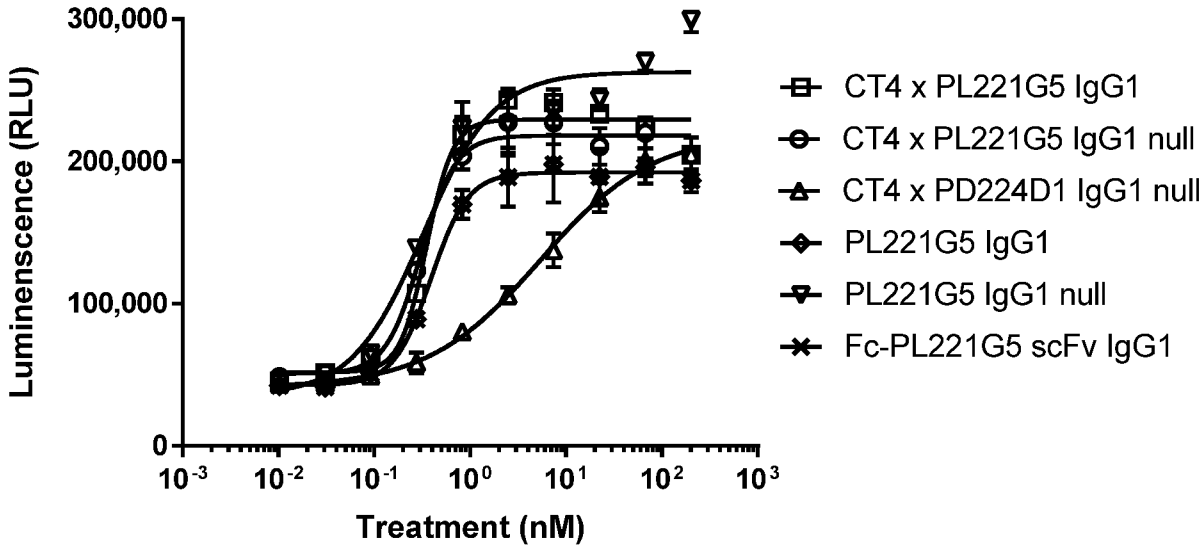

300,000
200,000
100,000
0
Luminenscence (RLU)
10-3
10-2
10-1
100
101
102
103
Treatment (nM)
CT4 x PL221G5 IgG1
CT4 x PL221G5 IgG1 null
CT4 x PD224D1 IgG1 null
PL221G5 IgG1
PL221G5 IgG1 null
Fc-PL221G5 scFv IgG1

Figure 6.

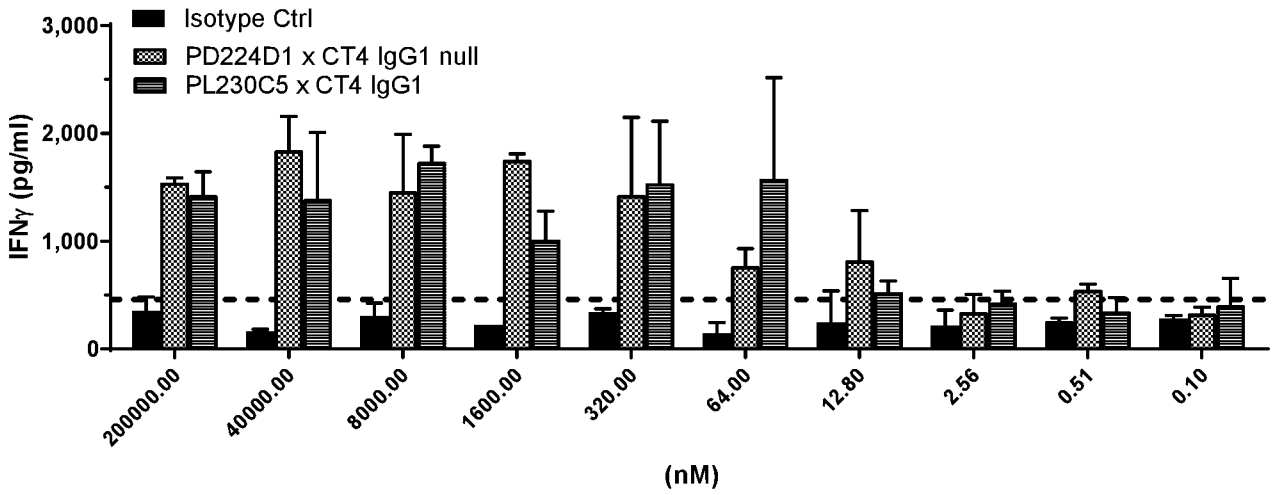
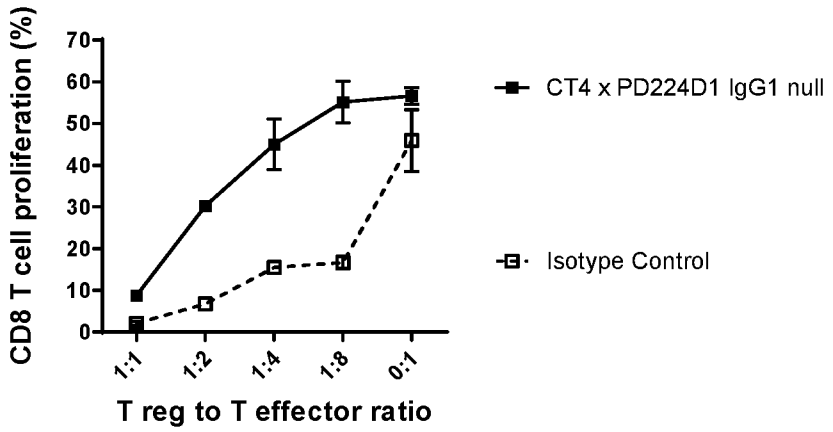

Isotype Ctrl
PD224D1 x CT4 IgG1 null
PL230C5 x CT4 IgG1
IFNγ (pg/ml)
3,000
2,000
1,000
0
200000.00
40000.00
8000.00
1600.00
320.00
64.00
12.80
2.56
0.51
0.10
(nM)

Figure 7.

A


CD8 T cell proliferation (%)
70
60
50
40
30
20
10
0
1:1
1:2
1:4
1:8
0:1
T reg to T effector ratio
CT4 x PD224D1 IgG1 null
Isotype Control

B

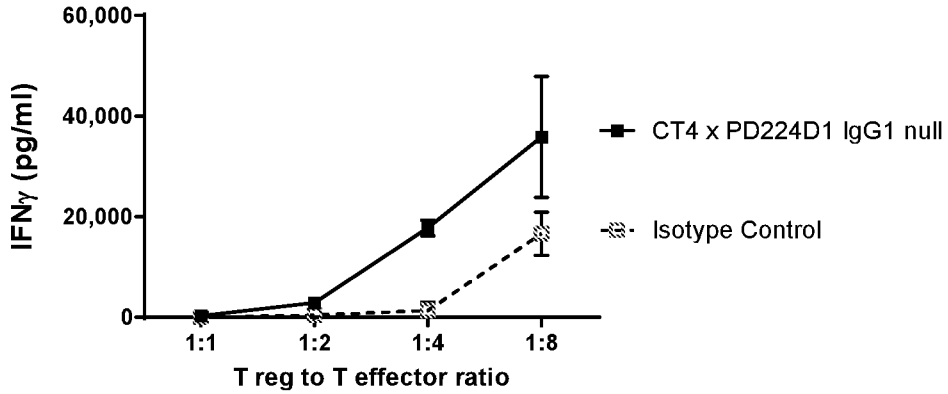

IFNγ (pg/ml)
60,000
40,000
20,000
0
1:1
1:2
1:4
1:8
T reg to T effector ratio
CT4 x PD224D1 IgG1 null
Isotype Control

Figure 8.

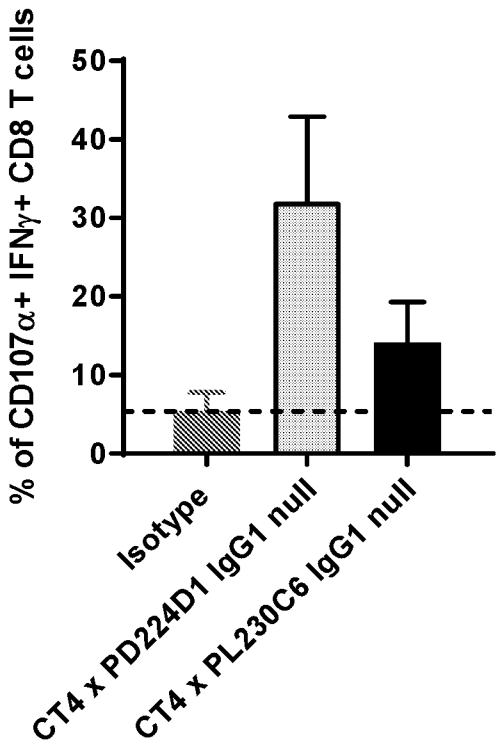

% of CD107α+ IFNγ+ CD8 T cells
50
40
30
20
10
0
Isotype
CT4 x PD224D1 IgG1 null
CT4 x PL230C6 IgG1 null

Figure 9.

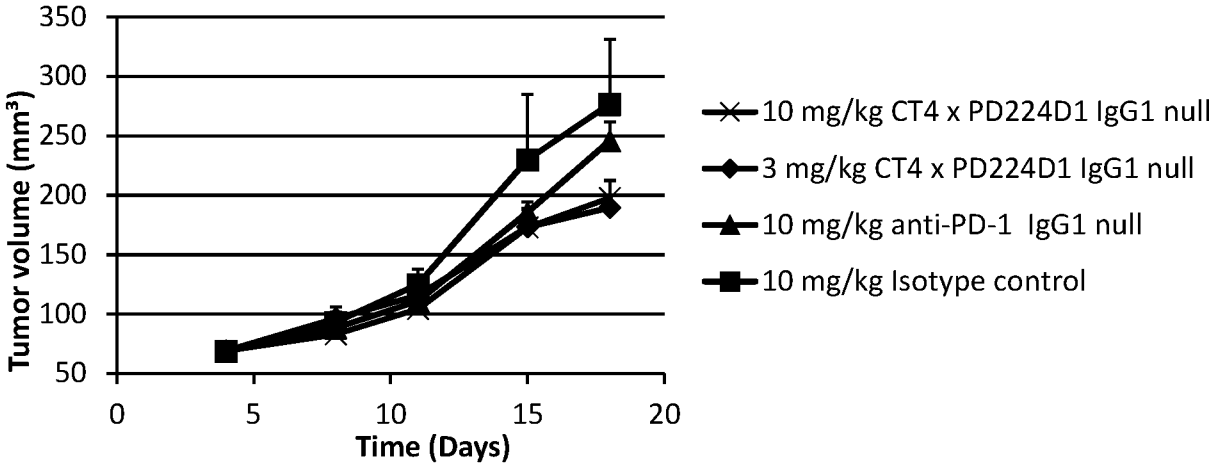

350
300
250
200
150
100
50
Tumor volume (mm³)
0
5
10
15
20
Time (Days)
10 mg/kg CT4 x PD224D1 IgG1 null
3 mg/kg CT4 x PD224D1 IgG1 null
10 mg/kg anti-PD-1 IgG1 null
10 mg/kg Isotype control

Figure 10.

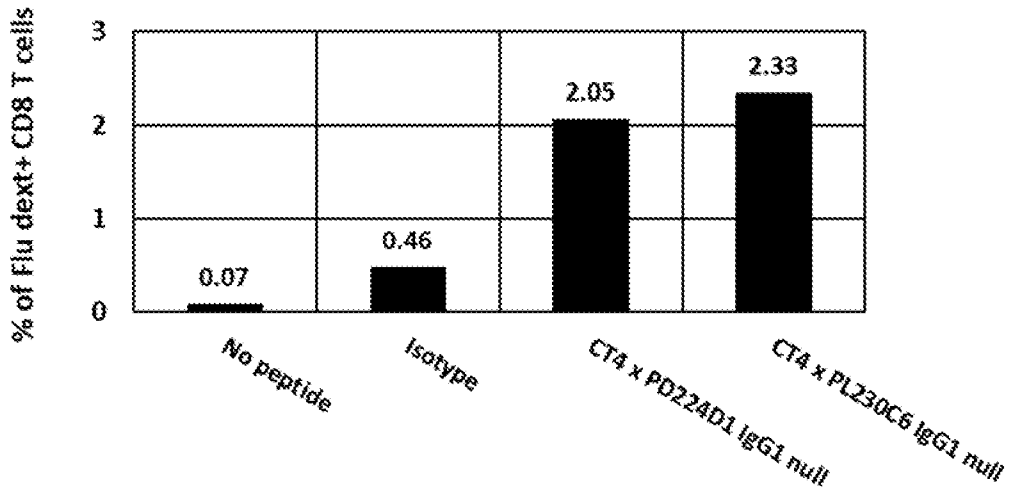

% of Flu dext+ CD8 T cells
3
2
1
0
0.07
0.46
2.05
2.33
No peptide
Isotype
CT4 x PD224D1 IgG1 null
CT4 x PL230C6 IgG1 null

Figure 11.

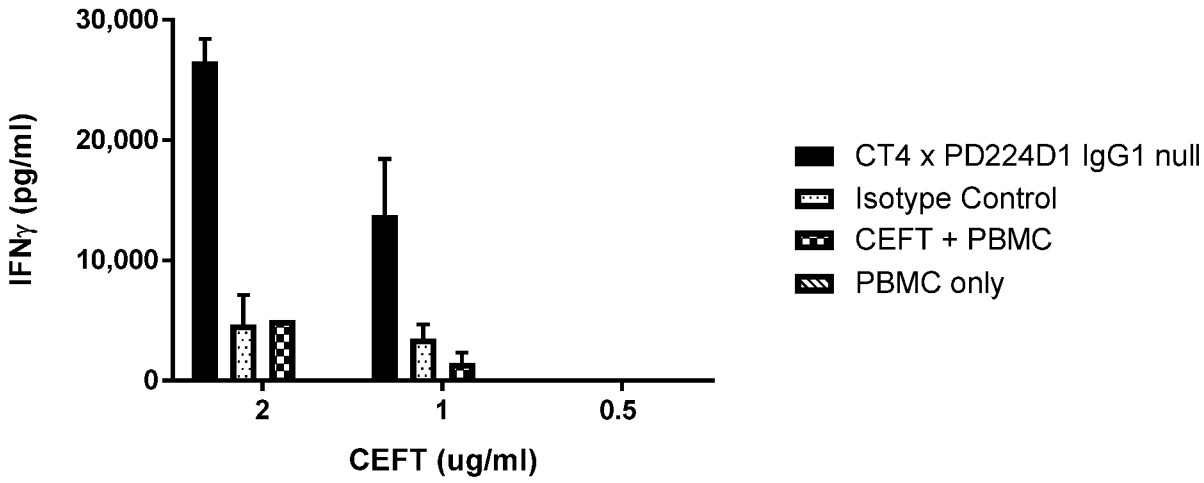
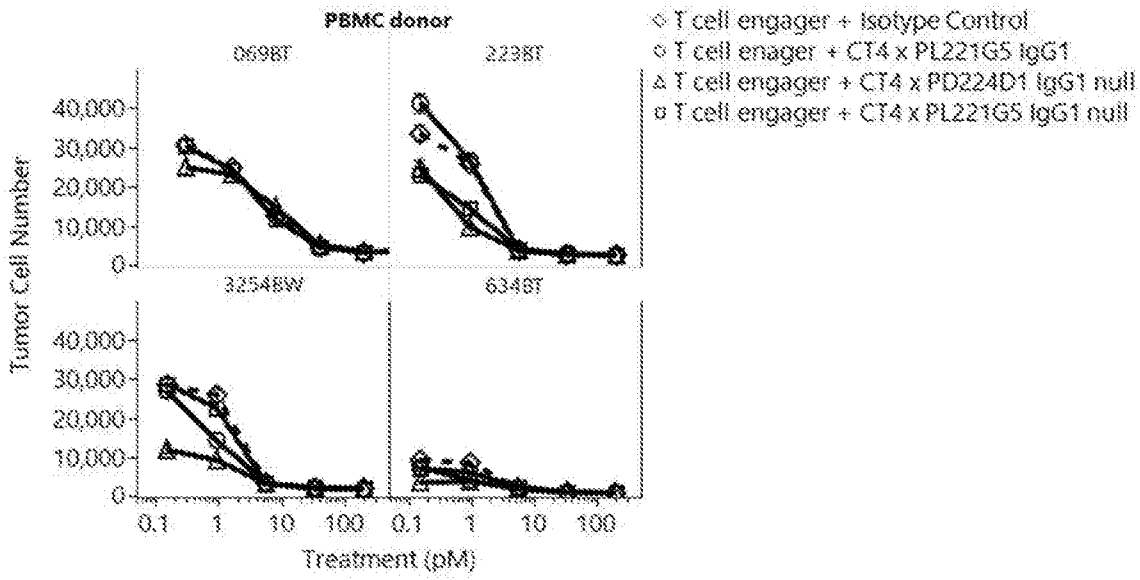

30,000
20,000
10,000
0
IFNγ (pg/ml)
2
1
0.5
CEFT (ug/ml)
CT4 x PD224D1 IgG1 null
Isotype Control
CEFT + PBMC
PBMC only

Figure 12.


PBMC donor
0698T
2238T
32548W
6348T
Tumor Cell Number
40,000
30,000
20,000
10,000
0
0.1
1
10
100
Treatment (pM)
◇ T cell engager + Isotype Control
○ T cell enager + CT4 x PL221G5 IgG1
△ T cell engager + CT4 x PD224D1 IgG1 null
▫ T cell engager + CT4 x PL221G5 IgG1 null

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/58810

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/00, C07K 16/28, C07K 16/30 (2018.01)
CPC - C07K 2317/622, C07K 2317/35, C07K 2317/626, C07K 2317/76, C07K 2317/92

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	WO 2006/105338 A2 (XENCOR, INC.) 5 October 2006 (05.10.2006) para [20]; para [49]; para [183]; page 30, page 32; Fig. 24E; Fig. 24F; Fig. 26B; SEQ ID NO: 5; SEQ ID NO: 6 ; SEQ ID NO: 13	16-19 --- 9
X --- Y	US 2016/0145355 A1 (BIOMED VALLEY DISCOVERIES, INC) 26 May 2016 (26.05.2016) Abstract; para [0021]; para [0026]; para [0028]; para [0056]; para [0070]-[0071]; para [0083]; para [0090]-[0091]; para [0100]; para [0104]; para [107], para [0134], claim 36	41 --- 1-15, 27-31, 39-40
Y	LUSSIER et al. "Combination immunotherapy with alpha-CTLA-4 and alpha-PD-L1 antibody blockade prevents immune escape and leads to complete control of metastatic osteosarcoma". J Immunother Cancer, 19 May 2015, Vol. 3, page 21 (pp 1-11). Especially, Abstract	1-15, 27-31, 39
Y	US 2017/0073418 A1 (SYSTIMMUNE INC) 16 March 2017 (16.03.2017) Abstract; para [0043]; para [0049]; para [0053], para [0072]; claim 1; claim 11 claim 12; claim 14 claim 38, claim 51	4-7, 10-12, 27-28, 31, 39-40
Y	US 2007/0281334 A1 (HORWITZ) 6 December 2007 (06.12.2007) para [0171], [0173], SEQ ID NO: 23	15

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 February 2019	06 MAR 2019

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/58810

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 25-26
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I: Claims 1-19, 27-31 and 39-41, directed a bispecific antibody composition, comprising polypeptides with IgG domains, heavy and light chains, and two scFv domains connected to the N- or C- termini, the bisprcific antibodies having first and second binding specificities to two antigens, the antigens being independently selected from a-CTLA4, a-PD-1, and a-PD-LI.

Group II: Claims 20-24, directed to an isolated nucleic acid encoding a bi specific antibody with IgG antibody domanis linked to ScFv domains, having first and second binding specificities to two antigens, the antigens being independently selected from a-CTLA4, a-PD-1, and a-PD-LI.

----------continued on supplemental sheet----------

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-19, 27-31, 39-41

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/58810

Continuation of Box III: Obbervations where unity of invention is lacking:

Group III: Claims 32-38, directed to a method of treating a subject with a cancer, by administering an effective amount of a bi specific antibody with IgG antibody domanis linked to ScFv domains, having first and second binding specificities to two antigens, the antigens being independently selected from a-CTLA4, a-PD-1, and a-PD-LI.

The inventions listed as Groups I - III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

Groups II and III do not require isolated antibody compositions, as required by group I.

Groups I and III do not require isolated nucleic acid constructs, as required by group II.

Group I and II do not require a method of treating cancer, as required by group III.

Common Technical Features

The common technical feature shared by Groups I through III that would otherwise unify the groups, is abispecific antibody, comprising IgG domains having heavy chains and light chains, and two scFv components being connected to either C terminal of the heavy chains or N terminal of the light chains, wherein the IgG domains have a first binding specificity to a first antigen, wherein the scFv components have a second binding specificity to a second antigen, and wherein the first antigen and the second antigen are different and are independently selected from a-CTLA4, a-PD-1, and a-PD-LI.

However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is made obvious by US 2016/0145355 A1 to Biomed Valley Discoveries Inc (hereinafter 'Biomed') in view of an article entitled "Combination immunotherapy with alpha-CTLA-4 and alpha-PD-L1 antibody blockade prevents immune escape and leads to complete control of metastatic osteosarcoma" by Lussier et al. (hereinafter 'Lussier') (J Immunother Cancer (19 May 2015); vol 3: article 21, pp 1-11 doi:10.1186/s40425-015-0067-z); Biomed discloses a bispecific antibody (Abstract- "bispecific antibodies") , comprising IgG domains having heavy chains and light chains (para [0090]- "each antigen binding moiety is independently selected from... IgG"; para [0091]- "the bispecific antibody is... IgG-scFv,"; para [0104]- " the first antigen binding moiety comprises a heavy chain and a light chain"; claim 1), and
two scFv components being connected to either C terminal of the heavy chains or N terminal of the light chains (para [0070]- "two distinct scFvs to heterodimerizable Fc domains... IgG-scFv and scFv-IgG... have scFvs linked to their C-termini and N-termini, respectively"; para [0071]- "a single dAb specific for another epitope linked... C-termini of the heavy chains"), wherein the IgG domains have a first binding specificity to a first antigen (para [0090]- "each antigen binding moiety is independently selected"; para [0083]- "humanized IgG1 anti-PD1"), wherein the scFv components have a second binding specificity to a second antigen (para [0028]- "scFvs that recognize CTLA-4"), and wherein the first antigen and the second antigen are different and are independently selected from CTLA4, PD-1, and PD-LI (Abstract- "bispecific antibodies containing a first antigen binding moiety that specifically binds an epitope on human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and a second antigen binding moiety that specifically binds an epitope on a human programmed death 1 (PD-1)"; para [0026]- 'binding moiety of which specifically binds human CTLA-4 and the other antigen binding moiety of which binds to human PD-L1"), but does not teach alpha-CTLA4, alpha-PD-1, and alpha-PD-LI.
Lussier teaches a combination of alpha-CTLA4 and alpha-PD-L1 antibodies can be used to suppress tumor (Abstract- "we have tested combination immunotherapy with alpha-CTLA-4 and alpha-PD-L1 antibody blockade in the K7M2 mouse model of metastatic osteosarcoma and show that this results in complete control of tumors in a majority of mice as well as immunity to further tumor inoculation"). Since, Lussier teaches that applying antibodies against alpha-CTLA4 and alpha-PD-L1 can result in complete control of tumors (Abstract), it would have been obvious to one of ordinary skill in the art, to have combined the teachings of Biomed with Lussier and use a bispecific antibody as disclosed by Biomed with specificity to alpha-CTLA4 and alpha-PD-L1 as taught by Lussier, because Lussier's antibodies are known to be effective in treating tumors.

As the technical feature was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I - III therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.